HEPATITIS

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Introduction

- **Viral hepatitis**: infection of the liver caused by half dozen viruses.

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D
- Hepatitis E

Hepatitis A

- A liver disease caused by the **hepatitis A virus**.
- The disease is closely associated with unsafe water, inadequate sanitation and poor personal hygiene.
  - primarily spread when an uninfected (and unvaccinated) person ingests food or water that is contaminated with the faeces of an infected person.
- Unlike hepatitis B and C, hepatitis A infection does not cause chronic liver disease and is rarely fatal
  - it can cause debilitating symptoms and fulminant hepatitis (acute liver failure), which is associated with high mortality.

- Hepatitis A occurs sporadically and in epidemics worldwide, with a tendency for cyclic recurrences.
- The hepatitis A virus is one of the most frequent causes of foodborne infection.
- Epidemics related to contaminated food or water can erupt explosively,
  - e.g. the epidemic in Shanghai in 1988 that affected about 300 000 people.

- Hepatitis A viruses persist in the environment and can withstand food-production processes routinely used to inactivate and/or control bacterial pathogens.

Geographical distribution

- **Areas with high levels of infection**
  - In developing countries with very poor sanitary conditions and hygienic practices, most children (90%) have been infected with the hepatitis A virus before the age of 10 years.
  - Those infected in childhood do not experience any noticeable symptoms.
  - Epidemics are uncommon because older children and adults are generally immune.
  - Symptomatic disease rates in these areas are low and outbreaks are rare.

- **Areas with intermediate levels of infection**
  - In developing countries, countries with transitional economies and regions where sanitary conditions are variable.
  - Children often escape infection in early childhood.
  - Ironically, these improved economic and sanitary conditions may lead to:
    - a higher susceptibility in older age groups and
    - higher disease rates, as infections occur in adolescents and adults, and
    - large outbreaks can occur.

- **Areas with low levels of infection**
  - In developed countries with good sanitary and hygienic conditions, infection rates are low.

  - Disease may occur among adolescents and adults:
    - in **high-risk groups**, such as injecting-drug users, men who have sex with men,
    - travelling to areas of high endemicity, and
    - in **isolated populations**, such as closed religious communities.

- In India, Hepatitis A virus is responsible for:
  - 10-30% of acute hepatitis and
  - 5-15% of acute liver failure cases.

Transmission

- The hepatitis A virus is transmitted primarily by the **faecal-oral route.**
- Waterborne outbreaks, though infrequent, are usually associated with sewage-contaminated or inadequately treated water.
- The virus can also be transmitted through
  - parenteral route (blood & blood products, needle stick injury) and
  - sexual route (homosexual men)

Clinical features

- The **incubation period** of hepatitis A is usually **14–28 days.**
- Range from mild to severe, and can include:
  - fever,
  - malaise,
  - loss of appetite,
  - diarrhoea,
  - nausea,
  - abdominal discomfort,
  - dark-coloured urine and
  - jaundice (a yellowing of the skin and whites of the eyes).

- Not everyone who is infected will have all of the symptoms.
- Adults have signs and symptoms of illness more often than children.
- Severity of disease and mortality increases in older age groups.
- Infected children under 6 years of age do not usually experience noticeable symptoms, and only 10% develop jaundice.
- Among older children and adults, infection usually causes more severe symptoms, with jaundice occurring in more than 70% of cases.

Who is at risk?

- Anyone who has not been vaccinated or previously infected can contract hepatitis A.
- In areas where the virus is widespread (high endemicity), most hepatitis A infections occur during early childhood.
- Risk factors include:
  - poor sanitation;
  - lack of safe water;
  - injecting drugs;
  - living in a household with an infected person;
  - being a sexual partner of someone with acute hepatitis A infection; and
  - travelling to areas of high endemicity without being immunized.

Treatment

- There is no specific treatment for hepatitis A.
- Recovery from symptoms following infection may be slow and may take several weeks or months.
- Therapy is aimed at maintaining comfort and adequate nutritional balance, including replacement of fluids that are lost from vomiting and diarrhoea.

Prevention

- **Improved sanitation, food safety and immunization** are the most effective ways to combat hepatitis A.

- The spread of hepatitis A can be reduced by:
  - Adequate supplies of safe drinking water;
  - Proper disposal of sewage within communities; and
  - Personal hygiene practices such as regular hand-washing with safe water.

- Several hepatitis A vaccines are available.
- No vaccine is licensed for children younger than 1 year of age.
- Nearly 100% of people develop protective levels of antibodies to the virus within 1 month after a single dose of the vaccine.
- Even after exposure to the virus, a single dose of the vaccine within 2 weeks of contact with the virus has protective effects.
- Still, manufacturers recommend two vaccine doses to ensure a longer-term protection of about 5 to 8 years after vaccination.

Hepatitis E

- A liver disease caused by the **hepatitis E virus**
  - a non-enveloped, positive-sense, single-stranded ribonucleic acid (RNA) virus.
- Transmitted mainly through contaminated drinking water.
- It is usually a self-limiting infection and resolves within 4-6 weeks.
- Occasionally, a fulminant form of hepatitis develops (acute liver failure), which can lead to death.

Geographical distribution

- Outbreaks and sporadic cases of hepatitis E occur around the world.
  - frequently occur in resource-limited countries with limited access to essential water, sanitation, hygiene and health services.
- In recent years, some of these outbreaks have occurred in areas of conflict and humanitarian emergencies, such as war zones, and in camps for refugees or internally displaced populations (IDP).
- An estimated 20 million infections and 3.3 million acute cases occur annually worldwide with an estimated 56 600 deaths

- In India, Hepatitis E Virus is responsible for:
  - 10-40% of acute hepatitis and
  - 15-45% of acute liver failure.

- Acute HEV has inordinately high mortality rate of 15 to 25 percent in women in the third trimester.

- Hepatitis E genotype 1 is usually seen in developing countries and causes community-level outbreaks.
- Hepatitis E genotype 3 is usually seen in the developed countries and does not cause outbreaks.

- The highest seroprevalence rates are observed in regions where low standards of sanitation increase the risk for transmission of the virus.

- East and South Asia are most affected with frequent hepatitis outbreaks
  - most commonly occurring during the rainy season when water sources become contaminated by faecal material.

Transmission

- The hepatitis E virus is transmitted mainly through the **faecal-oral route** due to faecal contamination of drinking water.

- Other transmission routes have been identified, which include:
  - foodborne transmission from ingestion of products derived from infected animals;
  - transfusion of infected blood products;
  - vertical transmission from a pregnant woman to her fetus.

Clinical features

- The **incubation period** ranges from **3 to 8 weeks**, with a mean of 40 days.
- The period of communicability is unknown.
- Symptomatic infection is most common in young adults aged 15–40 years.
- Although infection is frequent in children, the disease is mostly asymptomatic or causes a very mild illness without jaundice (anicteric) that goes undiagnosed.

- Typical signs and symptoms of hepatitis include:

  - jaundice (yellow discolouration of the skin and sclera of the eyes, dark urine and pale stools)
  - anorexia (loss of appetite)
  - an enlarged, tender liver (hepatomegaly)
  - abdominal pain and tenderness
  - nausea and vomiting
  - fever.

- In rare cases, acute hepatitis E can result in fulminant hepatitis (acute liver failure) and death.

- **Fulminant hepatitis occurs more frequently during pregnancy.**
- Pregnant women are at greater risk of obstetrical complications and mortality from hepatitis E, which can induce a mortality rate of 20% among pregnant women in their third trimester.

- Cases of chronic hepatitis E infection and Reactivation of hepatitis E infection have been reported in immunosuppressed people.

Diagnosis

- Based on the detection of specific IgM and IgG antibodies to the virus in the blood.

- Additional tests include reverse transcriptase polymerase chain reaction (RT-PCR) to detect the hepatitis E virus RNA in blood and/or stool.

Treatment

- There is no available treatment capable of altering the course of acute hepatitis.
- Prevention is the most effective approach against the disease.
- As hepatitis E is usually self-limiting, hospitalization is generally not required.
  - However, hospitalization is required for people with fulminant hepatitis and should also be considered for symptomatic pregnant women.

Prevention

- The risk of infection and transmission can be reduced by:
  - maintaining quality standards for public water supplies;
  - establishing proper disposal systems to eliminate sanitary waste.

- On an individual level, infection risk can be reduced by:
  - maintaining hygienic practices such as hand washing with safe water, particularly before handling food;
  - avoiding drinking water of unknown purity.

- In 2011, the first vaccine to prevent hepatitis E infection was registered in China.

Hepatitis B

- A potentially ***life-threatening liver infection*** caused by the **hepatitis B virus.**
- It is a ***major global health problem***.
- It can cause **chronic infection** and puts people at high risk of death from ***cirrhosis and liver cancer***.
- A vaccine against hepatitis B has been available since 1982.
  - The vaccine is ***95% effective*** in preventing infection and the development of chronic disease and liver cancer due to hepatitis B.

Geographical distribution

- Hepatitis B prevalence is ***highest in sub-Saharan Africa and East Asia,*** where between 5–10% of the adult population is chronically infected.

- High rates of chronic infections are also found in the ***Amazon and the southern parts of eastern and central Europe.***

- In the ***Middle East and the Indian subcontinent***, an estimated *2–5% of the general population is chronically infected*.
- Less than 1% of the population in Western Europe and North America is chronically infected.

- Hepatitis B is responsible for ***1.4 million deaths every year***
  - ***compared to 1.5 million deaths from HIV/AIDS and 1.2 million from each of malaria and TB.***

- ***In India***,
- Over ***40 million hepatitis B infected cases*** (second only to China)
- About 15% of the entire pool of hepatitis B in the world.
- Tribal areas have high prevalence of hepatitis B.
- Every year, nearly ***686,000 patients die from HBV infection***.
- Chronic Hepatitis B infection accounts for about *30% of liver cirrhosis and approx.45% of liver cancers.*

Transmission

- The **incubation period** of the hepatitis B virus- 75 days on average, but can vary **from 30 to 180 days.**
  - The virus may be detected within 30 to 60 days after infection and can persist and develop into chronic hepatitis B.

- The hepatitis B virus can ***survive outside the body for at least 7 days.***
  - During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine.

- **In highly endemic areas**, hepatitis B is most commonly spread:
  - from mother to child at birth (**perinatal transmission**), or
  - through horizontal transmission (**exposure to infected blood**),

- Hepatitis B is also spread by **percutaneous or mucosal exposure** to ***infected blood and various body fluids***, as well as through saliva, menstrual, vaginal, and seminal fluids.

- Transmission of the virus may also occur through:
- **Sexual route**
  - particularly in **unvaccinated** men who have sex with men and heterosexual persons with multiple sex partners or contact with sex workers.
- The **reuse of needles and syringes**
  - either in health-care settings or among persons who inject drugs.
- During medical, surgical and dental procedures, tattooing, or through the use of razors and similar objects that are **contaminated with infected blood.**

Clinical features

- Most people do not experience any symptoms during the acute infection phase.
- In some cases, there may be:
  - **acute illness** with symptoms that last several weeks, including yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting and abdominal pain.
  - **acute liver failure** which can lead to death.
  - **a chronic liver infection** that can later develop into cirrhosis of the liver or liver cancer.

- More than *90% of healthy adults who are infected with the hepatitis B virus will recover naturally from the virus within the first year.*

Who is at risk for chronic disease?

- The likelihood that infection with the virus becomes chronic **depends upon the age** at which a person becomes infected.
- **In infants and children**:
  - 80–90% of infants infected develop chronic infections;
  - 30–50% of children infected before the age of 6 years develop chronic infections.

- **In adults**:
- <5% of otherwise healthy persons who are infected as adults will develop chronic infection;
- 20–30% of adults who are chronically infected will develop cirrhosis and/or liver cancer.

Diagnosis

- Acute HBV infection: HBsAg and IgM antibody to the core antigen, HBcAg.

- During the initial phase of infection: Hepatitis B e antigen (HBeAg).
  - HBeAg is usually ***a marker of high levels of replication of the virus***.
  - *HBeAg indicates that the blood and body fluids of the infected individual are* ***highly contagious***.

- Chronic infection: Persistence of HBsAg for at least 6 months (with or without concurrent HBeAg).
  - *Persistence of HBsAg is the* ***principal marker of risk for developing chronic liver disease and liver cancer (hepatocellular carcinoma) later in life.***

Treatment

- **Oral tenofovir or entecavir**: potent drugs to suppress hepatitis B virus.
  - slow the progression of cirrhosis, reduce incidence of liver cancer and improve long term survival.
  - treatment must continue for life.

- **Interferon injections** may be considered in some people in certain high-income settings.

- **Adequate nutritional balance**, including replacement of fluids lost from vomiting and diarrhoea.

- ***Liver transplantation*** is used in people with cirrhosis, with varying success.

Prevention

- The **Hepatitis B vaccine** is the mainstay of hepatitis B prevention.
- In most cases, one of the following two options is considered appropriate:
- a 3-dose schedule of hepatitis B vaccine,
  - the first dose (monovalent) being given at birth and the second and third (monovalent or combined vaccine) given at the same time as the first and third doses of diphtheria, pertussis (whooping cough), and tetanus – (DTP) vaccine; or
- 4 doses schedule of hepatitis B vaccine,
  - a monovalent birth dose is followed by three monovalent or combined vaccine doses, usually given with other routine infant vaccines.

- The complete vaccine series induces protective antibody levels in more than 95% of infants, children and young adults.
- Protection lasts at least 20 years and is probably lifelong.
  - booster vaccination is not recommended for persons who have completed the 3 dose vaccination schedule.

- High-risk groups should be vaccinated. They include:
- People who frequently require blood or blood products, dialysis patients, recipients of solid organ transplantations;
- People interned in prisons;
- Persons who inject drugs;
- Household and sexual contacts of people with chronic HBV infection;
- People with multiple sexual partners;
- Health-care workers and others who may be exposed to blood and blood products through their work; and
- Travellers who have not completed their hepatitis B vaccination series, who should be offered the vaccine before leaving for endemic areas.

- In addition, other preventive measures include:
- Implementation of blood safety strategies, including quality-assured screening of all donated blood and blood components used for transfusion.

- Safe injection practices, eliminating unnecessary and unsafe injections.

- Safer sex practices, including minimizing the number of partners and using barrier protective measures (condoms).

Hepatitis C

- **Hepatitis C virus** (HCV) causes both acute and chronic infection.
- Acute HCV infection is *usually asymptomatic*, and is only very **rarely** associated with life-threatening disease.
- About 15-45% of infected persons ***spontaneously clear the virus within 6 months of infection without any treatment***.
- The remaining 55-85% of persons will develop ***chronic HCV infection.***
- Of those with chronic HCV infection, the risk of cirrhosis of the liver is ***15-30% within 20 years.***

Geographical distribution

- Hepatitis C is found ***worldwide.***
- The most affected regions are Africa and Central and East Asia.
- There are ***multiple strains (or genotypes***) of the HCV virus and their distribution varies by region.

- In India,
  - **Prevalence** of chronic HCV infection is around **1 %.**
  - Approximately *12 million people have chronic hepatitis C infection.*
  - Pockets of areas where ***prevalence of Hepatitis C has been observed to be relatively higher*** in **Punjab**, Haryana, Andhra Pradesh, Puducherry, Arunachal Pradesh and Mizoram.
  - Chronic HCV infection account for 12-32% of liver cancer and 10-20% cases of cirrhosis in India.

Transmission

- The hepatitis C virus is ***a bloodborne virus***. It is most commonly transmitted through:
- **injecting drug use** through the sharing of injection equipment;
- in health care settings due to the ***reuse or inadequate sterilization of medical equipment,*** especially syringes and needles;
- the ***transfusion*** of unscreened blood and blood products.

- ***Less common route***:
- HCV can also be transmitted sexually
- HCV can be passed from an infected mother to her baby.

Clinical features

- The **incubation period** for hepatitis C is **2 weeks to 6 months.**
- Following initial infection, approximately 80% of people do not exhibit any symptoms.
- Those who are acutely symptomatic may exhibit fever, fatigue, decreased appetite, nausea, vomiting, abdominal pain, dark urine, grey-coloured faeces, joint pain and jaundice (yellowing of skin and the whites of the eyes).

Diagnosis

- Due to the fact that ***acute HCV infection*** is usually ***asymptomatic***, few people are diagnosed during the acute phase.

- In those people who go on to ***develop chronic HCV infection***, the infection is ***also often undiagnosed*** because the infection remains asymptomatic until decades after infection when *symptoms develop secondary to serious liver damage.*

- **HCV infection is diagnosed in two steps**:
  - **Screening** for anti-HCV antibodies with **a serological test** identifies people who have been infected with the virus.
  - If the test is positive for anti-HCV antibodies, a nucleic acid test for HCV RNA is needed to **confirm** chronic HCV infection
    - about 15–45% of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment.
- Although no longer infected, they will still test positive for anti-HCV antibodies.

- After a person has been diagnosed with chronic hepatitis C infection:

- **An assessment of the degree of liver damage** (fibrosis and cirrhosis).
  - by liver biopsy or through a variety of non-invasive tests.

- Identify the **genotype** of the hepatitis C strain.
  - There are 6 genotypes of the HCV and they respond differently to treatment.
  - It is possible for a person to be infected with more than one genotype.

- The degree of liver damage and virus genotype are **used to guide treatment decisions and management of the disease.**

- **Screening for people who may be at increased risk of HIV infection include**:
  - people who inject drugs
  - recipients of infected blood products or invasive procedures in health-care facilities with ***inadequate infection control practices***
  - children born to mothers infected with HCV
  - people with **sexual partners who are HCV-infected**
  - people with **HIV infection**
  - prisoners or previously ***incarcerated persons***
  - people who have used **intranasal drugs**
  - people who have had ***tattoos or piercings***.

Treatment

- **Interferon and ribavirin,**
  - required *weekly injections for 48 weeks*,
  - cured approximately half of treated patients,
  - but caused frequent and sometimes life-threatening adverse reactions.

- New antiviral drugs have been developed, called **direct antiviral agents (DAA)**
  - much more effective,
  - safer and better-tolerated than the older therapies.
  - Therapy with DAAs result can cure most persons with HCV infection
  - treatment is shorter (**usually 12 weeks**).

Prevention

- No vaccine.
- Primary prevention include:
- hand hygiene: including surgical hand preparation, hand washing and use of gloves;
- safe handling and disposal of sharps and waste;
- provision of comprehensive harm-reduction services to people who inject drugs including sterile injecting equipment;
- testing of donated blood for hepatitis B and C (as well as HIV and syphilis);
- training of health personnel;
- promotion of correct and consistent use of condoms.

- **Secondary and tertiary prevention** for people infected with the hepatitis C virus:
  - education and counselling on options for care and treatment;
  - immunization with the hepatitis A and B vaccines to prevent coinfection from these hepatitis viruses to protect their liver;
  - early and appropriate medical management including antiviral therapy if appropriate; and
  - regular monitoring for early diagnosis of chronic liver disease.

The Gaps, Challenges And Priorities As Regards To Prevention, Screening, Care And Treatment Of Viral Hepatitis In India.

World Hepatitis Day: 28th July

1. Need to generate data on the magnitude of the burden of Viral Hepatitis in India
2. Identify high risk and priority population
3. Improve coverage birth dose vaccination as well as all dose coverage of HBV vaccine
4. Improve Injection safety and spread knowledge of safe injection among health care workers
5. Screening of High risk groups
6. Improving the access to treatment and availability as well as affordability of the drugs for HBV and HCV .
7. Improve sanitation and safe drinking water for prevention of HAV and HEV.
8. Vaccination HAV in the selected group.
9. Vaccination for HEV may be available soon.