

Seminar Report

# Viral Hepatitis

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## **Classification of hepatitis**

Hepatitis is an inflammation of the liver most commonly caused by viral infection, which consists of five main types: A, B, C, D and E.

Viruses can cause different patterns of onset, like acute hepatitis with rapid onset of infection with usually rapid onset of resolution and chronic viral hepatitis with an onset of 6 months or longer usually causes serious complications like: liver cirrhosis and hepatocellular carcinoma (HCC).

Hepatitis A is a Hepatovirus non-enveloped single stranded RNA from the Picornaviridae family. It consists of four polypeptides (VP1-VP4).

Hepatitis B is a double stranded DNA from the Hepadnaviridae family. It consists of outer surface protein (HBsAg), core protein (HBcAg), pre core (HBeAg) and enzyme reverse transcriptase.

Hepatitis B has 8 known genotypes (A-H).

Hepatitis C is a Hepacivirus single stranded RNA from the Flaviviridae family. It consists of structural protein (C, E1, E2) and non structural protein.

Hepatitis C has 6 major genotypes (1-6).

Hepatitis D (Delta hepatitis) is a single strand RNA virus. HDV is unable to infect a cell by itself, and require co-infection with the HBV to undergo a complete replication cycle.

Hepatitis E is a single strand RNA virus, its clinical course similar to that of HAV.

## **Global burden of disease**

### **EPIDEMIOLOGY OF VIRAL HEPATITIS**

#### **Hepatitis A**

Millions of people became infected with HAV by ingesting contaminated food and drinking water. The infection rate is strongly related to access to safe drinking water and socio-economic indicator. Generally, all high-income global regions have very low levels of HAV endemicity (< 50% of population), while low-income regions have high levels of endemicity (> 90% of population). Middle-income regions of society both have intermediate and low levels of endemicities. Globally, only 1.5 million clinical cases of HAV are reported annually while the rate of infection is much higher in highly endemic countries nearly all children get infected at an early age, with mostly asymptomatic exposure, but acquire lifelong immunity. Paradoxically, in low

endemic countries most children and adults remain susceptible to symptomatic infection and disease burden is high.

### **Hepatitis B**

Hepatitis B is globally one of the most common and severe infectious diseases that leads to significant morbidity and mortality. Approximately one-third of the World's population have been infected with HBV. Around 5% of this population are chronic carriers and a quarter of these carriers develop serious liver diseases such as chronic hepatitis, cirrhosis and hepatic carcinoma. Every year, 780000 HBV-related deaths are documented around the globe.

### **Hepatitis C**

It is estimated that 71 million people globally have chronic hepatitis C infection, who are at risk of developing liver cirrhosis and liver cancer. This accounts for 399000 deaths every year. Among various genotypes of HCV, genotype 1 is the most prevalent which accounts for 46% of all HCV infections, followed by genotype 3, which is 22% prevalent. Genotype 2 and 4 each has 13% prevalence.

## **GEOGRAPHIC DISTRIBUTION OF VIRAL HEPATITIS**

### **African continent**

Highest prevalence of HAV is observed in sub-Saharan countries where nearly all of the population develops HAV immunity. Disease burden for HBV is also high among the sub-Saharan population. About 6.1% of the African population have HBV infection and around 18 million people have chronic HCV infection.

### **Americas**

The prevalence of hepatitis A is high in the Americas, with exception of high-income North American countries. However, there has been slight reduction in Central American regions in recent years.

### **Eastern Mediterranean region**

The incidence of HAV has decreased in North African and Middle Eastern countries in the last decades and now have intermediate prevalence. It has been reported that around 3.3% of people from this region are infected with HBV and about 800000 people are HCV positive.

Eastern Mediterranean regions have low-intermediate endemicity with the exception of Somalia, Djibouti and Sudan which demonstrate a higher prevalence.

### European continent

Although prevalence of HBV is low in the European continent, it rises eastward. In Europe, approximately 1.4 million people have chronic HBV, while 9 million people have chronic HCV. The number of deaths due to HBV and HCV infections are 36000 and 86000 per year respectively.

## Local burden of disease

Recently in the 2019 statistical yearbook, the Saudi Ministry of Health (MOH) ranked viral hepatitis as the first most common viral disease, with almost 11113 new cases diagnosed in that year (63.19% HBV, 23.21% HCV, and 13.6% HAV). In the statistical yearbook Jeddah reported the highest number of HBV and HCV cases, as for HAV cases it was high in Riyadh.

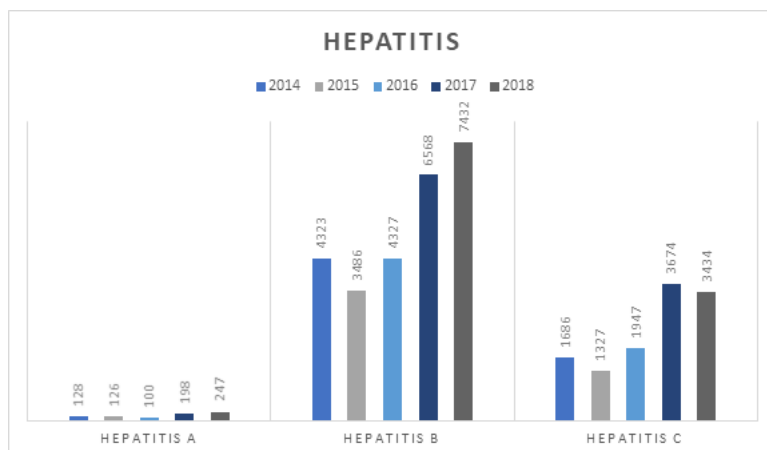


Figure 1: The prevalence of hepatitis in Saudi Arabia over the past 5 years

The country has witnessed a steady decline in prevalence of all 3 common hepatotropic viruses during the past 3 decades.

The annual incidence of seropositivity per 100,000 was highest for HBV (19.9), followed by HCV (9.94), and lowest for HAV (0.74).

**HAV:** hepatitis A virus seroprevalence in the country has reduced considerably from 13.6 to 0.74 per 100,000 from 2000 to 2019 due to the improvement in socioeconomic status and development of the Saudi community.

**HBV:** A decrease in the incident rate from 104.6 to 19.9 per 100,000 in the last two

decades from 2000 to 2019.

**HCV:** a decrease in the incident rate from 78.4 to 9.94 per 100,000 in the last two decades from 2000 to 2019.

In 2007, the Saudi Ministry of Health (MOH) ranked viral hepatitis as the second most common viral disease after chickenpox, with almost 9000 new cases diagnosed in that year (52% HBV, 32% HCV, and 16% HAV).

**HAV:** HAV prevalence is strongly affected by the community's social development, and improvement in the Saudi community so it is not surprising to see HAV declining sharply. The anti-HAV prevalence rate estimated a considerable drop from 90-100% rates reported 3 decades ago to 18.6% in 2008 (5) .

**HBV:** prevalence of HBV has witnessed a dramatic course in the last 20 years, in the first large-scale community-based epidemiological study conducted on Saudi children showed an HBsAg seroprevalence of approximately 7%, and a greater than 70% prevalence of at least one HBV marker. therefore, a catch-up vaccination program was supplemented in 1990. significant improvements have been made reflected by premarital screening data in 2008 among 74,662 individuals of whom 1.31% tested positive for HBV along with two epidemiological studies supporting this showed a marked reduction in the prevalence of HBV in KSA, averaging approximately 1.5% in general, and 2.6% within the adult population (5) .

**HCV:** Around 101,000 individuals are estimated to be viremic for chronic hepatitis C virus (HCV) in the Kingdom of Saudi Arabia (KSA) in 2014. blood donor screening data indicates prevalence rates of 0.4%–1.1%. In 2030, it is estimated that viremic prevalence will increase to 103,000 cases If no aggressive and effective strategy was projected (6) .

## **Modes of transmission**

The hepatitis A virus is found in the stool and blood of people who are infected. The hepatitis A virus is spread when someone ingests the virus (even in amounts too small) through:

### Person-to-person contact

Hepatitis A can be spread from close, personal contact with an infected person, such as through certain types of sexual contact (like oral-anal sex), caring for someone

who is ill, or using drugs with others. Hepatitis A is very contagious, and people can even spread the virus before they feel sick.

#### Eating contaminated food or drink

Contamination of food with the hepatitis A virus can happen at any point: growing, harvesting, processing, handling, and even after cooking. Contamination of food and water happens more often in countries where hepatitis A is common. Although uncommon, foodborne outbreaks have occurred in the United States from people eating contaminated fresh and frozen imported food products.

Although anyone can get hepatitis A, certain groups of people are at higher risk for getting infected and for having severe disease if they do get hepatitis A.

People at increased risk for hepatitis A

- International travelers
- Men who have Sexual contact with men
- People who use or inject drugs (all those who use illegal drugs)
- People with occupational risk for exposure
- People experiencing homelessness

Hepatitis B is spread when blood, semen, or other body fluid infected with the hepatitis B virus enters the body of someone who is not infected. People can become infected with the virus from:

- Birth (spread from an infected mother to her baby during birth)
- Sexual contact with an infected partner
- Sharing needles, syringes, or drug preparation equipment
- Sharing items such as toothbrushes, razors, or medical equipment (like a glucose monitor) with an infected person Direct contact with the blood or open sores of an infected person
- Exposure to an infected person's blood through needlesticks or other sharp instruments

Hepatitis B is not spread through food or water, sharing eating utensils, breastfeeding, hugging, kissing, hand holding, coughing, or sneezing.

Although anyone can get hepatitis B, these people are at greater risk: Infants born to infected mothers

- People who inject drugs or share needles, syringes, and other types of drug equipment

- Sexual contact with partners of people with hepatitis B
- Men who have Sexual contact with men
- People who live with someone who has hepatitis B
- Health-care and public-safety workers exposed to blood on the job
- Hemodialysis patients

The hepatitis C virus is usually spread when someone comes into contact with blood from an infected person. This can happen through:

- Sharing drug-injection equipment: today, most people become infected with hepatitis C by sharing needles, syringes, or any other equipment used to prepare and inject drugs.
- Birth. Approximately 6% of infants born to infected mothers will get hepatitis C.
- Healthcare exposures. Although uncommon, people can become infected when health-care professionals do not follow the proper steps needed to prevent the spread of bloodborne infections.
- Sex with an infected person. While uncommon, hepatitis C can spread during sex, though it has been reported more often among men who have sex with men.
- Unregulated tattoos or body piercings. Hepatitis C can spread when getting tattoos or body piercings in unlicensed facilities, informal settings, or with non-sterile instruments.
- Sharing personal items. People can get infected from sharing glucose monitors, razors, nail clippers, toothbrushes, and other items that may have come into contact with infected blood, even in amounts too small to see.
- Blood transfusions and organ transplants. Before widespread screening of the blood supply in 1992, hepatitis C was also spread through blood transfusions and organ transplants. Now, the risk of transmission to recipients of blood or blood products is extremely low.

Hepatitis C is not spread by sharing eating utensils, breastfeeding, hugging, kissing, holding hands, coughing, or sneezing. It is also not spread through food or water.

The following people are at increased risk for hepatitis C:

- People who use injection drugs or did so in the past, even those who injected only once many years ago

- People with HIV infection
- People with certain medical conditions, including those who ever received maintenance hemodialysis and those with persistently abnormal alanine aminotransferase (ALT) levels (an enzyme found within liver cells).
- Health care, emergency medical, and public safety personnel who have been exposed to the blood of someone who has hepatitis C (through needle sticks, sharps, or mucosal exposures)
- Children born to mothers who have hepatitis C

## **Risk Factors:**

### Risk factors for HAV:

Anyone who has not been vaccinated or previously infected can get infected with hepatitis A virus, most of hepatitis A infections occur during early childhood

- Poor sanitation
- Lack of safe water
- Living in a household with an infected person
- Being a sexual partner of someone with acute hepatitis A infection
- Sex between men
- Travelling to areas of high endemicity without being immunized

### Risk factors for HBV and HCV:

Certain groups are at high risk of HBV infection, includes:

- Healthcare workers; who has been exposed to infected blood, which may
- happen if an infected needle pierces your skin
- People who use IV drugs
- People with multiple sex partners
- Sex between men
- People with chronic liver disease or kidney disease
- People age >60y with diabetes
- Those traveling to countries with a high incidence of HBV infection
- People have HIV
- Received a piercing or tattoo in an unclean environment using unsterile
- equipment
- Received a blood transfusion or organ transplant before 1992



- Received hemodialysis treatments for a long period of time
- Were born to a woman with a hepatitis C infection

## **Natural history of Hepatitis:**

### A. Stages & clinical presentation:

The clinical presentation of infectious hepatitis varies with the individual, as well as with the specific causative virus. Some patients may be entirely asymptomatic or only mildly symptomatic at presentation. Others may present with rapid onset of fulminant hepatic failure (FHF).

*The classic presentation of infectious hepatitis involves four phases, as follows:*

- Phase 1 (viral replication phase) – Patients are asymptomatic; laboratory studies demonstrate serologic and enzyme markers of hepatitis
- Phase 2 (prodromal phase) – Patients experience anorexia, nausea, vomiting, alterations in taste, arthralgias, malaise, fatigue, urticaria, and pruritus. patients are often diagnosed as having gastroenteritis or a viral syndrome
- Phase 3 (icteric phase) – Patients may note dark urine, followed by pale-colored stools; in addition to the predominant gastrointestinal (GI) symptoms and malaise, patients become icteric and may develop right upper quadrant pain with hepatomegaly
- Phase 4 (convalescent phase) – Symptoms and icterus resolve, liver enzymes return to normal

### B. Incubation periods:

#### **Hepatitis A**

The incubation period of hepatitis A virus (HAV) is 2-7 weeks with common symptoms, self-limited disease.

#### **Hepatitis B**

The incubation period for hepatitis B virus (HBV) is 30-180 days. Patients then enter the prodromal, characterized by the gradual onset of anorexia, malaise, and fatigue. During this phase, as the liver becomes inflamed, the liver enzymes start to elevate, and the patient may experience right upper quadrant pain

## Hepatitis C

The incubation period for hepatitis C virus (HCV) is 15-150 days, with symptoms developing anywhere from 5-12 weeks after exposure. During acute HCV infection, symptoms may appear similar to those of HBV infection.

## Prevention and Control:

### Hepatitis A:

Prevention of HAV by:

- Vaccines:

The best way to prevent hepatitis A is through vaccination with the hepatitis A vaccine. To get the full benefit of the hepatitis A vaccine, more than one shot is needed. The number and timing of these shots depends on the type of vaccine you are given.

#### Who should get this vaccine?

Many people are recommended to receive hepatitis A vaccine, including people at increased risk for exposure to hepatitis A virus infection and people who are more likely to get seriously ill if infected with the virus.

According to CDC recommendations, people who should be vaccinated include:

- All children starting at age 1 year (12–23 months)
- All children age 2 through 18 years not previously vaccinated.
- All people infected with HIV.
- People age 6 months or older who are traveling to or working in an area with a high epidemic
- Men who have sex with men
- Users of illicit drugs, injectable or non-injectable
- People who are homeless or in temporary housing, such as a shelter.
- People who anticipate having close personal contact with an international adoptee from a country of high or intermediate levels of hepatitis A virus infection.
- People who work with HAV-infected primates or with hepatitis A virus in a research laboratory setting.
- People with any kind of chronic liver disease, including infection with hepatitis B or hepatitis C viruses, cirrhosis, fatty liver disease, alcoholic liver disease,

autoimmune hepatitis, or liver enzyme tests (ALT or AST) persistently more than twice normal levels.

How many doses of hepatitis A vaccine are recommended?

Two doses are recommended. The second dose is given no sooner than six months after the first dose.

How long does hepatitis A vaccine protect you?

Estimates for long-term protection for fully vaccinated people (i.e., full two-dose series) suggest that protection from hepatitis A virus infection could last for at least 25 years in adults and at least 14–20 years in children

Can a pregnant woman receive hepatitis A vaccine?

Yes. CDC recommends that a pregnant woman at risk of hepatitis A infection or at risk of a severe outcome of hepatitis A infection during pregnancy should be vaccinated.

What are the recommendations for the use of hepatitis A vaccine and/or IG prior to travel?

All susceptible people (individuals who have never had the infection or the vaccine) traveling to or working in countries with a high epidemicity should receive hepatitis A vaccine or IG before departure. Travelers who choose not to get the hepatitis A vaccine, who are younger than age 6 months, or who are allergic to the vaccine should be given IG only.

Can hepatitis A vaccine be given after exposure to hepatitis A virus?

Yes. People who recently have been exposed to hepatitis A and who previously have not had hepatitis A vaccine should be given a single dose of hepatitis A vaccine as soon as possible, within 2 weeks of exposure.

- Good personal hygiene and safe practices:

Practicing good hand hygiene including thoroughly washing hands after using the

bathroom, changing diapers, and before preparing or eating food plays an important role in preventing the spread of hepatitis A.

### **Hepatitis B:**

- Using vaccines:

Hepatitis B virus immunization is a critical intervention for the elimination of hepatitis B virus epidemics. Wider provision of the existing, safe and effective hepatitis B virus vaccine, including through universal childhood vaccination and by delivery of birth-dose, will drastically reduce new hepatitis B infections, reducing rates of chronic illness and death.

Who should get vaccinated against hepatitis B?

Hepatitis B vaccination is recommended for:

- All infants
- All children and adolescents younger than 19 years of age who have not been vaccinated
- People at risk for infection by sexual exposure
- People whose sex partners have hepatitis B
- Sexually active people who are not in a long-term, mutually monogamous relationship (for example, people with more than one sex partner in the past 6 months)
- People seeking evaluation or treatment for a sexually transmitted infection
- Men who have sex with men
- People at risk for infection by exposure to blood
- People who inject drugs
- People who live with someone who has hepatitis B
- People who live or work in facilities for people with developmental disabilities
- Health-care and public-safety workers at risk for exposure to blood or blood-contaminated body fluids on the job
- People who receive hemodialysis
- People with diabetes who are 19–59 years of age (people with diabetes who are age 60 or older should ask their health care professional).
- International travelers to countries where hepatitis B is common

- People with hepatitis C virus infection
- People with chronic liver disease
- People with HIV infection
- People who are in jail or prison
- All other people seeking protection from hepatitis B virus infection

Is the hepatitis B vaccine recommended before international travel?

Only people visiting countries where hepatitis B is common should get the hepatitis B vaccine before travel.

Prevention in a healthcare setting:

- hand hygiene: including surgical hand preparation, hand washing and use of gloves
- safe handling and disposal of sharps and waste
- safe cleaning of equipment
- testing of donated blood
- improved access to safe blood
- training of health personnel.

After exposure to hepatitis B virus (HBV) in occupational exposure and non-occupational exposure, appropriate and timely prophylaxis can prevent HBV infection and subsequent development of chronic infection or liver disease. The mainstay of post-exposure prophylaxis (PEP) is hepatitis B vaccine, but, in certain circumstances, hepatitis B immune globulin is recommended in addition to vaccine for added protection.

#### Prevention of mother to child transmission

If a pregnant woman has hepatitis B, is there a way to prevent her baby from getting hepatitis B?

Yes. Almost all cases of hepatitis B can be prevented in babies born to infected mothers, but these newborns must receive the necessary shots at the recommended times. The combination of hepatitis B immune globulin (known as HBIG) and hepatitis B vaccine can be given to infants born to infected mothers within 12 hours of birth to protect them from infection. To best protect your baby, follow the advice from your baby's doctor in addition. When a pregnant woman comes in for prenatal

care, she is given a series of routine blood tests, including one that checks for hepatitis B virus infection.

Prevention with blood safety strategies: including quality-assured screening of all donated blood and blood components used for transfusion.

Prevention of sexual transmission: by the promotion of correct condom use, and increasing access to medical and social services for vulnerable persons

### **Hepatitis C:**

In the absence of a vaccine for hepatitis C, prevention of HCV infection depends upon reducing the risk of exposure to the virus. Globally, most HCV infections occur in health-care settings as a result of inadequate infection control procedures, for example, the reuse of injection equipment. HCV infections in health-care settings also occur through the transfusion of blood that has not been screened for HCV antibodies

Prevention in a health care setting:

- Hand hygiene: including surgical hand preparation, hand washing and use of gloves
- Safe handling and disposal of sharps and waste
- Safe cleaning of equipment
- Testing of donated blood
- Improved access to safe blood
- Training of health personnel

Prevention among people who inject drugs: provision of comprehensive harm-reduction services, including sterile injecting equipment and effective and evidence-based treatment of dependence.

Prevention of sexual transmission: prevented the same way HBV is prevented, which is by the promotion of correct condom use, and increasing access to medical and social services for vulnerable persons

Prevention of mother-to-child transmission: there are no proven interventions to reduce this risk. Neither mode of delivery nor breastfeeding are reliably linked with transmission. The development of effective drugs against HCV that can be given safely during pregnancy might be a future option.

## How to take history if hepatitis was suspected?

Full gastrointestinal history should be taken if we suspect hepatitis infection starting with chef complain and finishing with the systematic review.

Highlighted point must be included in the history:

- IV drug use
- Sexual practice
- Needle stick exposure
- Occupation
- Blood transfusion
- Contact with a jaundiced person
- Body piercing/tattoos
- Travel to endemic area

Look at

VIRAL HEPATITIS CASE REPORT CDC.

<https://www.cdc.gov/hepatitis/PDFs/vhsp02.pdf>

## Viral Hepatitis Prevention and control in Saudi Arabia:

Ministry of Health efforts and awareness campaigns:

- MOH offers free medical care for all infected Saudi patients and free vaccinations
- Annually the MOH on the World Hepatitis Day shares awareness materials on social media that aims to educate people on the Viral Hepatitis symptoms, how to prevent it, and from where to get the proper treatment.
- most recently on April 2018, A new campaign “Give Me Your Hand” was launched specifically to educate the population on Hepatitis C

Virus-specific control & prevention methods

*Factors attributing to HAV control and prevention:*

- The Integration of Hepatitis A vaccine in the Extended Program of Immunization (EPI), which was added despite the general decline in HAV prevalence in most of the KSA regions. But, because of the mobility of the Saudi population, the continuing high rates of hepatitis A infection in some

regions like Jizan, represent a threat to other regions where an outbreak could occur.

- Improvements in hygiene and in the socioeconomic status of the population

*Factors attributing to HBV control & prevention:*

The significant decline in HBV prevalence is mainly due to the design of the HBV vaccine program and its follow-up which was part of the Preventive Strategy Program, which was designed by the Committee for Prevention of Viral Hepatitis in MOH, The following strategy was adopted:

- Integrating the HBV vaccine in the EPI program.
- Vaccinating all children who entered school between 1990 and 1996, in a catch up program
- Mandatory screening of blood donors and expatriates
- Mandatory vaccination of health personnel
- Voluntary vaccination of risk groups, starting in 1990
- Health education, especially for medical personnel

*Factors attributing to HCV control & prevention:*

- Improvement in the educational system, which according to the World Health Organization, half of the improvement in health indicators in a community can be attributed to that.
- adherence to universal infection control precautions in medical services like hemodialysis and dental clinics, sharing of needles among drug abusers, and folk medical practices like cauterization and blood letting.

HBV, HCV and HAV have shown a marked decline (more than 50%) in KSA over the last two decades. There are important causes for this decline that are common to all three viral infections. Most important in KSA are the marked socioeconomic changes.

Thanks to the Government Real Estate Bank modern houses have been built in all regions of KSA. Thus, hygiene and sanitary conditions have markedly improved. The other common factor is the decline of illiteracy in KSA, which is now about 10% compared to over 90% 40 years ago due to the comprehensive mandatory basic education system for boys and girls in KSA



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