

# **Training workshop on screening, diagnosis and treatment of hepatitis B and C**

## **Session 12**

### **Treatment of hepatitis B virus infection in special groups**

## Learning objectives

At the end of this session, participants should understand the following:

- Issues related to HBV management in special patient groups
- Recommended treatment strategies for such people
- Identifying the appropriate treatment strategy for a given patient.



At the end of this session, we shall be able to approach and manage HBV infection in a few of the special population groups that we encounter most commonly.

## What constitutes special populations?

- Those with coinfections
  - ☐ HBV coinfecting with HIV
  - ☐ HBV and HCV coinfection
  - ☐ HBV and HDV coinfection
  - ☐ HBV coinfecting with tuberculosis
- Renal impairment
- Decompensated cirrhosis
- Pregnant women
- Children and adolescents



These are the groups of HBV-infected people who need special consideration in evaluation, management and follow up.

We will be discussing a few of them that could be managed at peripheral health-care facilities.

## HBV/HIV coinfection: outcomes

HIV coinfection results in

- more rapid progression to cirrhosis
- higher risk for HCC
- higher liver-related mortality
- decreased treatment response compared to HBV mono-infection.

5–15% of HIV-infected persons are coinfecting with HBV.

HIV coinfection adversely affects the clinical course of HBV infection.

## **HBV/HIV coinfection: other considerations**

- Increased risk of liver injury
  - ART-related immune reconstitution can lead to increased hepatocyte killing >> worsening of liver injury
  - anti-HIV drugs can induce direct hepatotoxicity
- Severe liver injury may lead to fulminant hepatitis and death.

Further, a coinfecting person is also at risk of drug-induced liver injury because of antiretroviral drugs. Hence, a coinfecting person needs closer monitoring for toxicities, response and complications than a mono-infected person.

## HBV/HIV coinfection: other considerations

- Cross-resistance between HIV and HBV drugs
- Choice of ART should be based on drugs that are active against both HIV and HBV:
  - tenofovir (TDF)
  - lamivudine (3TC)
  - emtricitabine (FTC)



There is cross-resistance between HIV and HBV drugs.

HIV/HBV-coinfected persons should be simultaneously treated for both HIV and HBV infection.

Choice of ART should be based on drugs that are active against both HIV and HBV.

We prefer to use tenofovir, (TDF) lamivudine (3TC) and emtricitabine (FTC) in the ART regimen.

Entecavir is not recommended as first-line therapy because it can lead to resistance to HIV drugs.

## HBV and HCV coinfection

- 3–18% of people who are HBsAg positive are also HCV infected, and up to 25% of HCV-infected persons are HBV infected.
- Coinfection with HBV/HCV promotes rapid progression of liver disease, and increases the risk of HCC.
- Indications for treatment of HBV infection in patients with HBV/HCV coinfection are the same as in those with HBV mono-infection.
- HBV DNA monitoring may be necessary as there is a potential risk of HBV reactivation during DAA treatment.



It is not uncommon to see HBV and HCV coinfection. This situation is more common among certain high-risk population groups such as those with HIV, those who inject drugs, or those on maintenance haemodialysis.

Both HBV and HCV are hepatotropic viruses and cause liver injury. Hence, their coinfection results in relatively rapid progression of liver disease and adverse outcomes.

HBV or HCV treatment indication, drug of choice, duration, etc. are similar to those in mono-infected persons.

In most coinfecting people, HCV is actively replicating while HBV remains dormant. Successful HCV treatment may lead to reactivation of HBV, which can be detected with careful monitoring.

## HBV and HDV coinfection

- The routes of HDV transmission are the same as for HBV but vertical transmission is rare.
- 5% of HBsAg-positive persons are coinfecting with HDV globally
- Vaccination against HBV prevents HDV coinfection.
- Fulminant hepatitis is more frequently observed in HBV/HDV coinfection compared to HBV monoinfection.
- PEG-IFN is the only drug currently used for HDV treatment however relapse is high.
- TDF/ETV are not effective in HBV/HDV coinfection.



Hepatitis D virus (HDV) is an incomplete virus. HDV needs the presence of HBV surface antigen for its replication. Hence, HDV infection can occur only in an HBV-infected person. HDV infection can occur either in the form of superinfection (means HBsAg-positive person gets HDV infection) or coinfection (means HBV and HDV infect the person simultaneously).

HBV/HDV coinfection may lead to acute liver failure.

Around 5% of those with chronic HBV are also infected with HDV globally.

To date, pegylated interferon is the only drug used for HDV treatment, however relapse is high. Research for new drugs is in progress.

## HBV and tuberculosis (TB) coinfection

- Persons at increased risk of infection with HBV are also at risk of infection with TB, largely because they live in regions of the world that are endemic for both infections.
- People who inject drugs (PWID) and prisoners have a high risk of acquiring HBV and HCV, and are also at increased risk of coinfection with TB.

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HBV and HCV infections are frequently encountered in patients with tuberculosis. This is primarily because all these diseases share the same endemic regions. We need to be cautious while starting antitubercular drugs in patients with HBV or HCV infection. We need to exclude cirrhosis carefully because such patients may develop hepatotoxicity and liver failure. In the presence of cirrhosis (regardless of its cause) modification of antitubercular drugs will be needed and more frequent monitoring for drug-induced liver injury.

In the presence of HBV or HCV infection, it is difficult to interpret the antitubercular treatment (ATT)-induced hepatotoxicity because of baseline LFT derangement secondary to HBV or HCV infection.

## Management of patients with renal impairment

- All nucleos(t)ide analogues (NAs, lamivudine, tenofovir and entecavir) require dose adjustment and should be used with caution in persons with renal impairment.
- Renal function should be monitored during antiviral therapy.

All those with chronic kidney disease (CKD) are at increased risk of acquiring HBV or HCV infection. HBV treatment in the presence of CKD, especially in those on dialysis, poses the problem of fibrosis assessment because the various measures of liver fibrosis are not reliable in those on dialysis.

## Recommended dose reduction or dosing interval

Drug	Recommended dose reduction or dosing interval			
	CrCl (mL/min) <sup>c</sup>			
	≥50	30–49	10–29	<10, Haemodialysis or CAPD
<b>Tenofovir</b> <sup>a,b</sup>	One 300 mg tablet every 24 hours (7.5 scoops of powder every 24 hours)	One 300 mg tablet every 48 hours (or 160 mg [3 scoops] of powder every 24 hours)	One 300 mg tablet every 72–96 hours (or 60 mg [1.5 scoops] of powder every 24 hours)	Every 7 days or one 300 mg tablet following completion of approximately every 12 hours of dialysis (or 20 mg [0.5 scoops] of powder following completion of approximately every 12 hours of dialysis)
<b>Entecavir</b>	0.5 mg once daily <sup>d</sup>	0.25 mg once daily OR 0.5 mg every 48 hours	0.15 mg once daily OR 0.5 mg every 72 hours	0.05 mg once daily OR 0.5 mg every 7 days

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Tenofovir and entecavir, which are used for HBV treatment, need dose modification. Their doses are determined by the the glomerular filtration rate (GFR) of the patient.

## Patients with decompensated cirrhosis

- All patients with decompensated cirrhosis should be considered for urgent antiviral therapy with tenofovir or entecavir, regardless of HBV DNA level.



Decompensated liver disease is a very advanced stage of liver failure. Such patients have a very limited liver reserve. Any new, even trivial, injury may worsen the condition very fast.

Hence, all those with decompensated cirrhosis should be treated with antivirals regardless of HBV DNA level. Antiviral drugs should be continued for life. In the presence of decompensated cirrhosis, entecavir is preferred to tenofovir because of toxicities (loss of bone mineral density and reduction in GFR).

## HBV infection in pregnant women

- Mother-to-child HBV transmission must be prevented through a timely birth dose (<24 hours of birth) of HBV vaccine followed by two or three doses of the HBV vaccine.
- Indications for treatment in adults with chronic HBV infection also apply to pregnant women – for their own health. Tenofovir is the drug of choice
- Evidence is evolving globally and regionally on the use of tenofovir for prevention of mother-to-child transmission, particularly among pregnant women with a high HBV viral load, in addition to other interventions to prevent MTCT of Hep B (new WHO guidelines forthcoming)



Pregnant women with HBV infection need evaluation of their health as well as to prevent transmission of HBV to the fetus.

The most effective measure for prevention of mother-to-child transmission (PMTCT) are timely administration of the birth dose of hepatitis B vaccine followed by routine HBV vaccination.

Certain women with a high HBV DNA level may need treatment with tenofovir (new WHO global guidelines forthcoming in 2020)

## Children and adolescents

- Children with HBV infection
  - are usually asymptomatic
  - are mostly in the immune-tolerant phase.
- Treatment is not considered in this phase due to
  - low curative response rates
  - concerns about long-term safety
  - risk of drug resistance (immunotolerant – very high viral load).
- Entecavir is approved for use in children above 2 years.
- Tenofovir is approved for use in children above 12 years.



HBV infection is common among children. This high prevalence is partially contributed to by high rates of MTCT of HBV. In children, HBV infection is mostly asymptomatic and is in the immune-tolerant phase, which does not need treatment. When needed, we can use entecavir or tenofovir according to the age of the child.

## Entecavir dosing in children

Group	Drug and dose
Children 2–12 years of age and weighing ≥10 Kg	Entecavir once daily as oral solution* (mL) if available
Body weight (Kg)	Dose (mL)* once daily
10–11	3
>11–14	4
>14–17	5
>17–20	6
>20–23	7
>23–26	8
>26–30	9
>30	10

\*Solution containing 0.05 mg/mL (or 0.5 mg in 10 mL)

The dose of entecavir will need modification according to the body weight of the child.

## **Persons who inject drugs (PWID)**

- PWID who are actively injecting and sharing injecting equipment are at increased risk of infections such as HIV, hepatitis B and C.
- The priority interventions for HIV and hepatitis prevention among PWID remain harm reduction, in particular, needle and syringe programmes and opioid substitution therapy for those who are opioid-dependent.
- WHO recommends HBV vaccination of groups at highest risk of acquiring HBV infection, including PWID.



The prevalence of HBV, HCV and HIV is high among the people who inject drugs. This is primarily because of needle-sharing and use of unsafe injection equipment.

These people need active screening and linkage with care for successful treatment. To avoid spread to others and reinfection, needle exchange programmes and opioid substitution therapy should be promoted.

All such persons who are HBsAg-negative should be vaccinated against HBV.