

## Medical Guidelines

## Hepatitis B Virus (HBV) Update and Guidance 2021

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DOI: <https://doi.org/10.70302/jpsim.v2i3.2160>**Introduction**

It is rightly said and I repeat 'Once HBV infection always HBV's risk of flare up'. And it can occur even in those who were apparently cured. This summary is meant for Internists, Gastroenterologists, Hepatologists, OBGY doctors and medical students.

Pakistan has intermediate prevalence of HBV, that is > 2.0%. Hepatitis B infection is diagnosed when HBsAg is positive. Routes of HBV transmission include percutaneous, perinatal, unsafe sexual activities and may be due to close personal contacts in high endemic regions, more importantly amongst children. Most important cause of chronic infection may be due to perinatal transmission. Survival of HBV outside the body is noted to be one week at least thus contaminated articles remain infectious.<sup>1</sup> Acute exposure from HBV consists 90% risk of developing chronic infection among newborns whereas HBeAg positive mothers transmit infection to 25-30% of infants or children under 5 years and around 5% in adults.<sup>2,3,4</sup> Additionally immune-compromised individuals are more prone to develop acute infection followed by chronic HBV infection.<sup>5</sup>

Tenofovir alafenamide (TAF) has been approved for treatment of CHB and has joined the list of preferred treatment for CHB, this list now includes TAF, entecavir, tenofovir disoproxil fumarate (TDF) and Peginterferon (peg-IFN).

TDF has been elevated to preferred treatment for prevention of mother to child transmission.

TAF has similar efficacy to TDF but decreased dosage and reduced renal and bone toxicity. The approved dose of TAF is 25mg per day orally once a day with no dose adjustment required until Creatinine clearance is < 15mL/min.

**Table 1:** Following Groups in Pakistan are at high risk for HBV infection and they should be screened

- All unvaccinated persons\*
- Unvaccinated persons with diabetes
- Persons who have ever injected drugs\*

Homosexual men\*

Individuals requiring immune-suppressive drugs due to certain conditions like organ transplantation, taking chemotherapy, desire immunosuppression for gastric or rheumatologic disorders.

End stage renal disease patients of rather pre-dialysis, peritoneal dialysis, hemodialysis and home dialysis groups\*

All pregnant women\*

Infants of HBs-Ag positive mothers\*

Chronic liver disease patients i.e. HCV\*

Patients suffering from HIV\*

Needle-sharing and sexual activities with HBs-Ag positive household contacts\*

Patients seeking treatment or being evaluated for sexually transmitted diseases\*

Healthcare professionals or public safety workforce at higher risk of occupational exposure to contaminated blood, blood products and body fluids\*

\*Directs the groups must be vaccinated if sero-negative

**Screening of HBV**

Hepatitis B surface antigen and antibody must be used for initial screening or Anti-HBV may be done alternatively

In case of antigen and antibody to HBV are positive due to different current infection from previous exposure, Hepatitis B core (HBc) antibody could be used for screening.

Though, HBV vaccinated individuals do not present anti-HBc positivity

**Special Circumstance**

Screening of HBV using anti-HBc for determination of previous exposure is not recommended in routine perhaps it is a significant tool among HIV patients, who intend to undergo anticancer or HCV and other immunosuppressive drugs, donated blood (or if feasible organ transplantation) and renal dialysis.

Individuals with anti-HBc positive screening result,

even deprived of anti-HBs and negative HBV DNA should be considered potentially at risk for HBV reactivation in the setting of immune suppression or co existing HIV or HCV infection. \*The author has seen a few acute flare ups during periods of immune suppression, remaining undiagnosed for a long period and actually leading to death due to reactivation and flare up.

Most parts of Pakistan are high prevalent areas for HCV and since HBV reactivation and flare-up are possible during HCV treatment, anti-HBc testing should be done in all HCV infected individuals and HBV treatment offered if positive.

**Table 2: Persons Who Are HBsAg Positive Should:**

1. Have household and sexual contacts vaccinated
2. Use barrier protection during sexual intercourse if partner is not vaccinated or is not naturally immune
3. Not share toothbrushes or razors
4. Not share injection equipment
5. Not share glucose testing equipment
6. Cover open cuts and scratches
7. Clean blood spills with bleach solution
8. Not donate blood or organs

**Follow up:**

Patients with chronic HBV infection should be counseled regarding lifestyle modifications and prevention of transmission as well as the importance of life-long monitoring. \*I repeat Life Long monitoring for disease control, viral suppression and complications like cirrhosis and Hepatocellular Carcinoma (HCC). No specific dietary measures have been shown to have any effect on the progression of Chronic Hepatitis B (CHB) per se, but metabolic syndrome and fatty liver contribute to liver-related morbidity.<sup>(6)</sup> Ingestion of more than 7 drinks of alcohol per week for women and more than 14 drinks per week for men are associated with increased risk of cirrhosis and HCC.

All patients who are HBsAg positive, whether on treatment or those who are not on treatment MUST be followed up for life. The purpose is to make sure whether patient has adequate control of disease and if the patient has developed any complication, the most dreadful being HCC.

**On follow-up all patients must have the following tests done:**

- LFT
- HBV DNA PCR Quantitative, only Quantitative test is required.
- HBeAg

- Anti HBe Ab
- Anti HDV Ab and if positive HDV RNA PCR Quantitative
- Alfa fetoprotein
- Abdominal USG

And furthermore they should be assessed for NAFLD and NASH.

**CHB, its treatment during Pregnancy and counseling**

Vaccination for HBV is safe in pregnancy and must be vaccinated in case they are not immune or infected with HBV.

Women eligible for standard indicators of HBV treatment must be treated whilst women presenting with >200,000 IU/ml of HBV DNA during second trimester must be considered for treatment which is helpful in prevention of mother to child transmission.<sup>7</sup>

Pregnant women infected HBV and not taking antiviral therapy, stop medication or early after labor must be observed closely for sero-conversion and hepatitis flares as long as 6 months at least. Long term follow up must also be considered to see the desire of future medication.

The most probable mother to infant risk of transmission from HBV with amniocentesis must be included while comparing harms versus benefits discussion in HBs-Ag positive mothers having elevated levels of viremia.

Pregnant women infected with HBV also present with cirrhosis must be coped as high risk obstetrical practices and managed with TDF to avert de-compensation.

HBV infected sexual partners of women, identified during pregnancy must be assessed for active HBV infection and must receive HBV-vaccine if appropriate.

HBV Infected women are not prohibited to breast-feeding

**Testing to decide phase, treatment and duration of treatment for CHB.**

Following tests are needed if HBsAg is positive;

- LFT
- HBV DNA PCR Quantitative. Only Quantitative test is required.
- HBeAg
- Anti HBe Ab
- Anti HDV Ab and if positive HDV RNA PCR Quantitative
- Alfa fetoprotein
- Abdominal USG

Based on these tests the following phases can be

diagnosed

### CHB Infection or CHB Hepatitis

In patients with HBV DNA positivity, a diagnosis of HBV Infection or HBV Hepatitis is made based upon normal or raised ALT. Now these two can be further divided into HBeAg negative or HBeAg positive for the sake of treatment.

#### HBeAg positive cases

In HBV infection if HBeAg is positive and ALT is normal it will be chronic HBV infection and if ALT is raised or biopsy shows necro-inflammation than chronic HBV Hepatitis, and in such cases treatment is warranted if HBV DNA is > 20,000 IU/mL, in cases of chronic HBV hepatitis.

#### HBeAg negative cases

In HBV infection if HBeAg is negative and ALT is normal it will be chronic HBV infection and if ALT is raised or biopsy shows necro-inflammation than chronic HBV Hepatitis, and in such cases treatment is warranted if HBV DNA is > 2000 IU/mL, in cases of chronic HBV hepatitis.

#### Treatment goal

All the patients who are treated, the goal is achieving sustained HBeAg seroconversion, in patients who were HBeAg positive. And treatment goal in HBeAg negative patients is normalization of ALT and undetectable HBV DNA on quantitative estimation, highlighting again that whenever HBV DNA is tested one must ask for quantitative estimation.

In established cases of Cirrhosis diagnosed by platelets < 100, AST > ALT, Point shearwave elastography showing significant fibrosis or increased Portal vein diameter or splenomegaly or liver biopsy showing > F2 fibrosis you treat irrespective of levels of ALT and HBV DNA levels all cases, who are HBV DNA positive by PCR, indefinitely.

Out of preferred list TAF or TDF are better options followed by entecavir. The PegIFN is usually reserved for HDV RNA positive co infected cases and treatment duration is usually 48 weeks for PegIFN. Peg IFN is contraindicated in patients of Cirrhosis.

#### Treatment Duration

For HBeAg positive disease treatment can be stopped after 5 years if suppression is adequate and ALT is persistently normal. And HBeAg seroconversion has been achieved.

For HBeAg negative diseases the treatment shall be continued indefinitely. In patients who are HBsAg positive and have Cirrhosis, whether compensated or decompensated, the treatment is carried out indefinitely since it reduces decompensation in compensated cir-

rhosis and HCC in both compensated and decompensated cirrhosis is reduced significantly.

### CHB and Children

Children 2 to 18 years of age should be treated with antiviral drugs if they have elevated ALT and positive HBV DNA PCR in same way as adults using the same medication with the goal of achieving sustained HBeAg seroconversion or normalization of ALT and undetectable HBV DNA, in HBeAg negative cases.

#### References:

1. Bond WW, Favero MS, Petersen NJ, Gravelle CR, Ebert JW, Maynard JE. Survival of hepatitis B virus after drying and storage for one week. *Lancet* 1981; 1(2): 550-51.
2. Beasley RP, Hwang LY, Lin CC, Leu ML, Stevens CE, Szmuness W, Chen KP. Incidence of hepatitis B virus infections in preschool children in Taiwan. *J Infect Dis* 1982;146(1): 198-204.
3. Coursaget P, Yvonnet B, Chotard J, Vincelot P, Sarr M, Diouf C, Chiron JP, et al. Age- and sex-related study of hepatitis B virus chronic carrier state in infants from an endemic area (Senegal). *J Med Virol.* 1987; 22(1): 1-5.
4. McMahon BJ, Alward WL, Hall DB, Heyward WL, Bender TR, Francis DP, Maynard JE. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis.* 1985;151(3): 599-603.
5. Bodsworth N, Cooper D, Donovan B. The influence of human immunodeficiency virus type 1 infection on the development of the hepatitis B virus carrier state. *J Infect Dis.* 1991;163(4):1138-40.
6. Wong GL, Chan HL, Yu Z, Chan AW, Choi PC, Chim AM, Chan HY, et al. Coincidental metabolic syndrome increases the risk of liver fibrosis progression in patients with chronic hepatitis B—a prospective cohort study with paired transient elastography examinations. *Aliment Pharmacol Ther.* 2014;39(3):883-93.
7. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH; American Association for the Study of Liver Diseases. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology* 2016; 63(2): 261-83.