Pediatric Oncall Journal
DOI: https://doi.org/10.7199/ped.oncall.2026.82

TEACHING FILES (GRAND ROUNDS)

UNTREATED HEPATITIS B IN A PREGNANT LADY AND BREAST FEEDING

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ARTICLE HISTORY
Received 22 July, 2025
Accepted 13 January, 2026

KEYWORDS
HBsAg, pregnancy, high HBV viral load, transmission.

Clinical Problem

A 28-year-old married female presented with incidental finding of positive hepatitis B surface antigen (HBsAg) during her routine 4th month antenatal workup. Pregnancy was confirmed using urine pregnancy kit followed by ultrasonography (USG) of abdomen. On presentation, she had no symptoms and examination findings were normal. Hepatitis B viral (HBV) load(quantitative) at time of presentation was 19,791 IU/ml with log value of 4.30. She was not started on anti-viral therapy and advised to repeat HBV DNA levels at 28 weeks of gestation. Her husband's HBsAg was negative and was advised to take 3 doses of Hepatitis B vaccine. However, she did not follow up at 28 weeks and presented at gestational age of 38+2 weeks with HBV viral load of 65,38,475 IU/ml, log value 6.8 with normal liver function tests (LFTs) and was started on tenofovir disoproxil fumarate (TDF) 300 mg OD. She delivered a male baby with birth weight of 3.255 kgs by vaginal delivery at 39+1 weeks of gestation. He cried immediately after birth and was given hepatitis B immunoglobulin (HBIG) 100 IU and Hepatitis B vaccine immediately. Baby's HbsAg at birth was reactive and viral load was 65 IU/mL. Hepatitis B immunization was repeated at 1 month+17 days, 2 months+ 22 days and 3 months+26 days. Mother's viral load was negative at 6 months of treatment and TDF was stopped. Eight months later, she had HBV viral load of 64,925 IU/ml,log of 4.8. USG and LFT was normal. Baby was tested for HBsAg at 9 and 12 months of age which was negative and Anti HBs levels of 396.18 mIU/mL.

Question – Should the mother be restarted on antiviral therapy? Should she breast feed her baby?

Discussion

Hepatitis B is a viral infection that can transmit through bodily fluids.[1] Fetal infection with HBV often results from transplacental passage of maternal hepatitis B e antigen (HBeAg), which induces T-cell tolerance which targets the hepatitis B core antigen (HBcAg) as well as HBeAg, diminishing the ability to respond to infection.[2] Newborns are unable to produce IgM antibodies against HBcAg and hence cannot initiate an effective immune response by themselves.[2]

If the mother's viral load exceeds 200,000 IU/mL (equivalent to 5.3 $\log_{10}$ IU/mL), antiviral treatment is recommended starting at 28 weeks of gestation, for a minimum of two weeks after delivery, with some clinicians opting to extend it up to 12 weeks postpartum due to risk of hepatitis flares.[3] If the viral load is <200,000 IU/mL, treatment is not recommended unless the mother has active liver disease.[2] To prevent perinatal transmission, all infants born to hepatitis B-infected mothers must receive both the hepatitis B vaccine and HBIG,100 IU4 within the first 12 hours, preferably within first 4 hours.[3] Delay increases risk of transmission from mother to child.[2] These infants should complete the vaccination series with additional doses at 2, 4 and 6 months of age.[3] Finally, testing for HBsAg and anti-HBs should be conducted between 9 and 12 months of age, and atleast 3 months after the last vaccine dose, to assess the effectiveness of immunization.[3] In our patient, since the mother did not follow up at 28 weeks and presented straight at 38+2 weeks with a very high viral load, she was started on TDF immediately. Since her viral load took time to become negative, TDF was stopped 6 months after initiation of treatment. However, her HBV viral load increased again for which initiating antiviral therapy promptly can help manage HBV flares resulting from reactivation.6 Sometimes, patients may develop liver failure despite treatment.[6] Our patient redeveloped a high HBV viral load with a normal alanine transaminase (ALT) and no symptoms; hence antiviral treatment was not restarted. Given the high incidence of reactivation following cessation of antiviral therapy reported, ongoing biochemical monitoring is advised even after stopping prophylactic treatment.[6]

There is no documented evidence that breastfeeding leads to the transmission of HBV.[3] Breast milk has been found to contain tenofovir, rather than its bioavailable prodrug form, TDF. Studies have shown that TDF is safe for use in pediatric populations.[3] HBsAg, HBeAg and HBV DNA are excreted in breast milk of infected mothers. There is no additional risk of transmission through breastfeeding, even in the absence of immunization.[2] When the viral load is very high in the mother, breastfeeding is safe as long as the newborn receives hepatitis B vaccine and HBIG.[5] However, breastfeeding should be avoided in the presence of cracked/bleeding nipples as this causes mixing of serous exudates with breast milk and can lead to transmission.[2] Consequently, women should be given accurate information and should not be discouraged from breastfeeding.[3]

Since, our patient's baby was already 1 year old, the mother was advised to wean breastfeeding and shift

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to solid food.

Compliance with ethical standards

Funding: None

Conflict of Interest: None

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