Hepatitis B in Pregnancy

New Zealand Maternal Fetal Medicine Network

This guideline was updated in July 2015 by Dr Joana de Sousa, with input from members of the New Zealand Maternal Fetal Medicine Network and Neonatology.

Background

It is recognised that there are a group of pregnant women with chronic hepatitis B infection, who continue to have a higher chance of Hep B transmission to their baby, largely confined to time of birth, despite postnatal passive and active immunisation of the baby.

These women will normally be Hep B e antigen positive and/or have a high Hep B viral load (>log 4 copies/ml). Babies born to these mothers may have between a 5-20% chance of contracting Hepatitis B infection depending on the ethnic group, and among Chinese women, risks of transmission can up to 40-79%. It is likely to remain a chronic infection – leading to long term health issues for the child later in life.

Objective

Women with pregnancies that fit into the high transmission risk category can be identified by performing the usual first trimester booking tests, identifying those women who are Hepatitis B surface antigen positive.

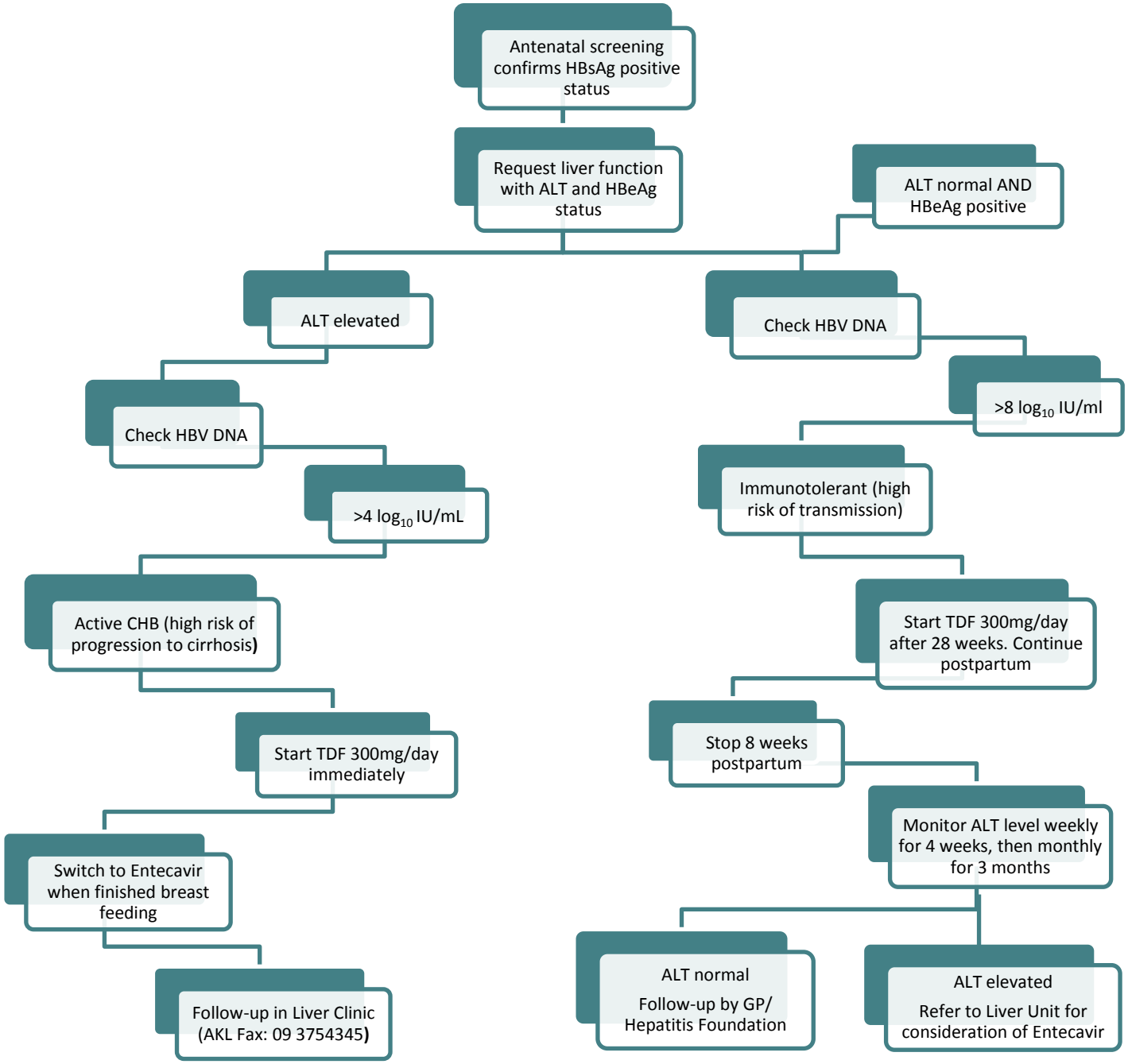
Those women who are identified with high viral load levels (>log 8 copies per ml) or have abnormal liver function tests (ALT/AST) should then be referred for specialist level review at a clinic skilled in dealing with high risk pregnancies. They can then be counselled about commencing anti-viral therapy to lower the Hepatitis B viral load prior to delivery, thereby reducing the risk of neonatal transmission of the infection.

This treatment is also likely to be effective in preventing flares of Hepatitis B activity, particularly in the postnatal period.

Case Identification

The community and hospital laboratories will provide written advice on abnormal result forms regarding what tests to perform next.
These women should then be offered a further blood test to clarify their Hep_B antigen status AND their Hepatitis B viral load AND their liver function tests (ALT/AST).
Results need to be followed up by the doctor or midwife requesting the test.
Those women with high viral load levels (>log 8 copies per ml) or abnormal levels of AST or ALT need referral for management by a service able to care for high risk pregnancies, in conjunction with an appropriate medical service (Liver service, Gastroenterology, Obstetric medicine).

Refer to flow chart 1 PAGE 2


Antenatal screening confirms HBsAg positive status
Request liver function with ALT and HBeAg status
ALT elevated
Check HBV DNA
>4 log10 IU/mL
Active CHB (high risk of progression to cirrhosis)
Start TDF 300mg/day immediately
Switch to Entecavir when finished breast feeding
Follow-up in Liver Clinic (AKL Fax: 09 3754345)
ALT normal AND HBeAg positive
Check HBV DNA
>8 log10 IU/ml
Immunotolerant (high risk of transmission)
Start TDF 300mg/day after 28 weeks. Continue postpartum
Stop 8 weeks postpartum
Monitor ALT level weekly for 4 weeks, then monthly for 3 months
ALT normal
Follow-up by GP/ Hepatitis Foundation
ALT elevated
Refer to Liver Unit for consideration of Entecavir

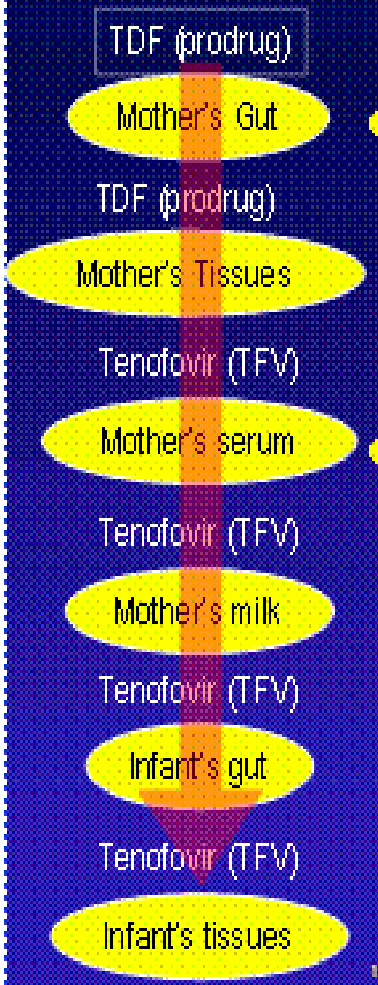
Treatment

The proposed first line therapy should be Tenofovir which has been used reasonably extensively in the pregnant population for the treatment of, and prevention of perinatal transmission in, pregnant women with HIV infection. This treatment should be commenced at the beginning of the third trimester and continued on for a total of 4 months to cover the postnatal period. To commence Tenofovir, a special authority will need to be applied for by an appropriate specialist physician (gastroenterologist, infectious diseases specialist, general physician).

There is no evidence to support the routine use of elective Caesarean Section delivery for prevention of perinatal Hepatitis B transmission. Mode of delivery should be decided on obstetric indications alone.

Women taking tenofovir is encouraged to continue breastfeed as the bioavailability in breastmilk is negligible and the overall risk to the infant is low.

Tenofovir Disprovoxil Fumerate in Lactating Women



- In humans, oral **Tenofovir Disoproxil Fumurate (TDF)** converted in tissues to **Tenofovir (TFV).** Expressed in breast milk at low concentrations (<3% serum).[1]
- **Tenofovir (TFV)** is active form but has **very low** oral bioavailability due to charged anionic, hydrophilic state.
- **If infant ingests breast milk, tissue exposure to tenofovir will be extremely low**

[1] Mirochnick M, et al. *Conference on Retroviral and Opportunistic Infections*, 2009

Investigation

For all women with positive Hepatitis B antigen

1. Hep B e antigen status
2. Liver function tests
3. If ALT raised or Hep B e antigen positive then test for level of Hep B viral load. For women who may have difficulty returning for multiple blood tests, a viral load may be arranged on the initial follow-up of the positive Hepatitis B antigen status.

For those women treated with Tenofovir

1. Monthly liver function testing throughout the pregnancy
2. After stopping Tenofovir, weekly liver function tests for one month and then monthly LFTs for three months.

All women with chronic Hepatitis B infection should be enrolled with their General Practitioner to ensure appropriate follow up through the Hepatitis Foundation of New Zealand.

On-going Management

All babies born to women with chronic Hepatitis B infection should receive both passive (Hep B immunoglobulin) and active (Hep B immunisation) within 12 hours of birth, whether or not women have received antiviral treatment during pregnancy. They should all have hepatitis serology test at 9-12 months of age with further vaccination if antiHBs < 10 and referral to paediatric gastroenteriology clinic if HBsAg remains positive.

Refer to chart 2 – Starship chart PAGE 6

Screen all women in early pregnancy for hepatitis B carriage

Woman is HBsAg positive **No** ⇨ See 'All other children' section

Yes ⇩

Discuss the care of the woman with an expert with an interest in hepatitis B or refer the pregnant woman to a high risk obstetric team.

Give the baby hepatitis B protection as follows:

At age	Action to be taken
Delivery	Give Hepatitis B specific immunoglobulin 100 IU and hepatitis B vaccine 5 µg (HBVaxPro®, MSD)
6 weeks	DTaP-IPV-HepB/Hib (INFANRIX®-*hexa*, GSK)
3 months	DTaP-IPV-HepB/Hib (INFANRIX®-*hexa*, GSK)
5 months	DTaP-IPV-HepB/Hib (INFANRIX®-*hexa*, GSK) and Take a blood test to check for hepatitis B infection (HbsAg) and for vaccine induced immunity (anti-HBs)

If HbsAg is positive refer for specialist assessment.

If HbsAg is negative and anti-HBs level is ≥ 100 IU/l at 5 months, immunity is proven.

If HbsAg is negative and anti-HBs level is ≤ 100 IU/l at 5 months, give:

6 months	Hepatitis B vaccine (HBVaxPro®, MSD)
7 months	Hepatitis B vaccine (HBVaxPro®, MSD)
8 months	Repeat HbsAg and anti-HBs serology on the baby, discuss the result with the parents and if required, refer to an appropriate specialist.

Discussion Points

Issues to discuss with the pregnant women who are identified as having a higher risk of Hepatitis B perinatal transmission, or require treatment for their own health, include….

1. The nature of Hepatitis B infection and the risks for infection for the baby.
2. The benefits of reducing the Hepatitis B viral load in preventing transmission of infection to the baby.
3. The benefit of treating the mother with antiviral agents in cases where there is increased risk of flares of Hepatitis B activity that can lead to significant liver dysfunction.
4. The potential side effects of using Tenofovir or other antiviral agents.
5. The lack of evidence for Caesarean section delivery reducing the risk of Hepatitis transmission.
6. The need for careful monitoring of liver function and pregnancy progress in the third trimester and postnatal period.
7. Breastfeeding issues while on antiviral agents.
8. The need for active and passive immunisation for the baby, with follow-up testing to ensure that the baby is Hepatitis B immune.
9. That follow-up is indicated for the patient in the postnatal period with regards to their own Hepatitis B infection.

References

- Benaboudl_2011_AAC_V55(3)P1315-1317 concentrations of TDF and FTC in breast milk of HIV infected women
- Chidziva_DART preg_CROI 2010
- Microchnick CROI 2009
- TDF HBV Pregnancy and lactation Information –US- SRO – TDF-851-17 Aug11