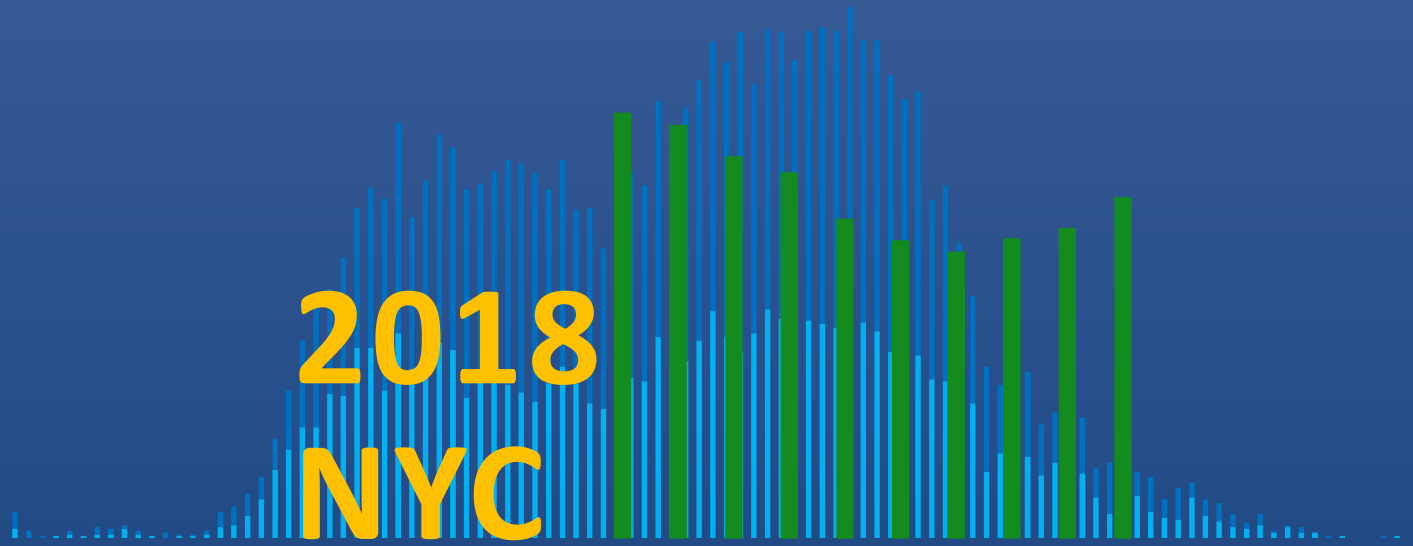

Viral Hepatitis Research Symposium

Treatment of HBV among Pregnant Individuals

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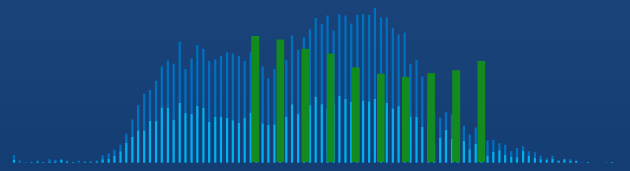


Disclosure

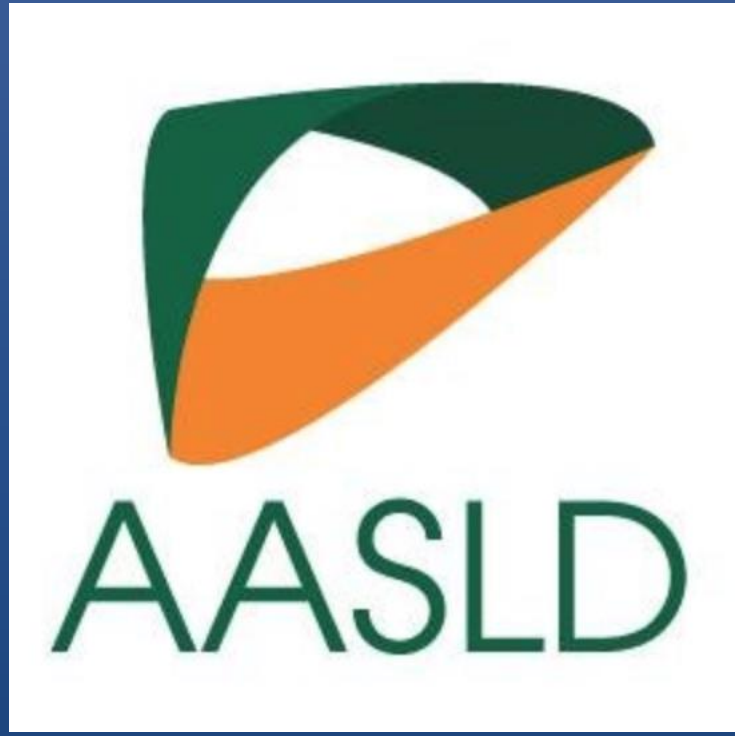
- None

Objectives

- HBV evaluation during pregnancy
- Mother-to-child transmission of HBV
- Effect of pregnancy on HBV activity
- Pregnancy care considerations

HBV evaluation during pregnancy

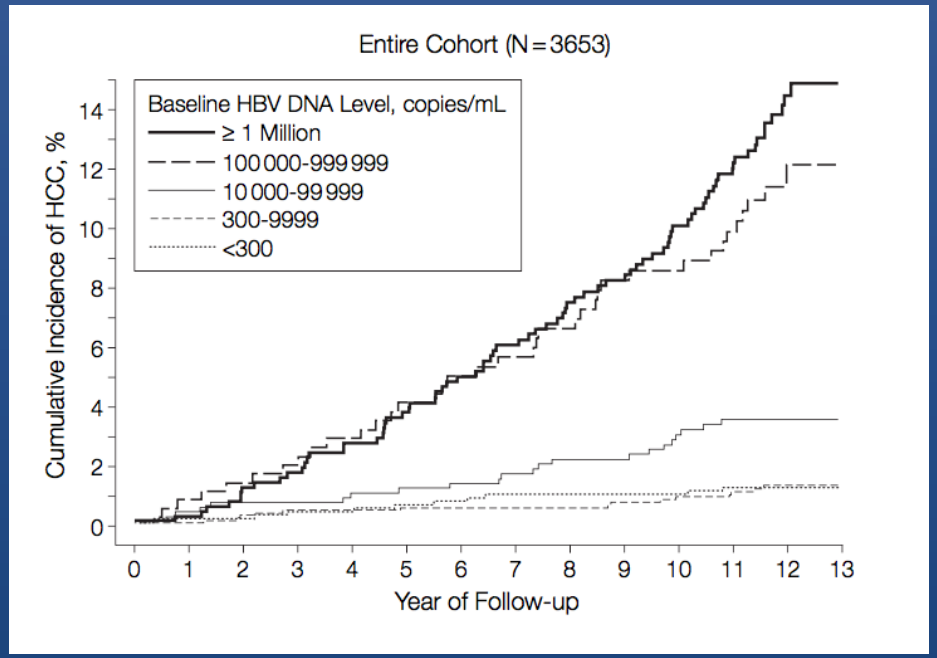
- **All pregnant women screened for HBsAg**
- **If screen negative:**
  - Provide vaccination against HBV
- **If screen positive**:
  - Sexual partners of women identified with HBV should be assessed for HBV infection
  - Chronic HBV does not affect outcome of pregnancy unless mother has cirrhosis or advanced liver disease
  - Women who meet standard indications for HBV therapy should be treated



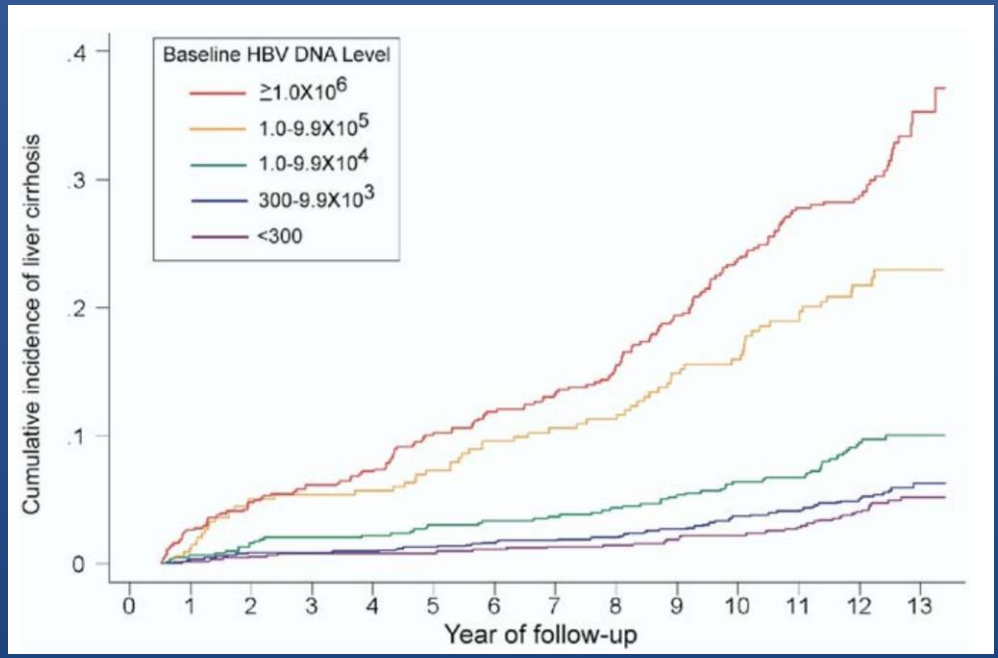
1. *Terrault et al. Hepatology 2018.*

HBV DNA predicts worse disease course

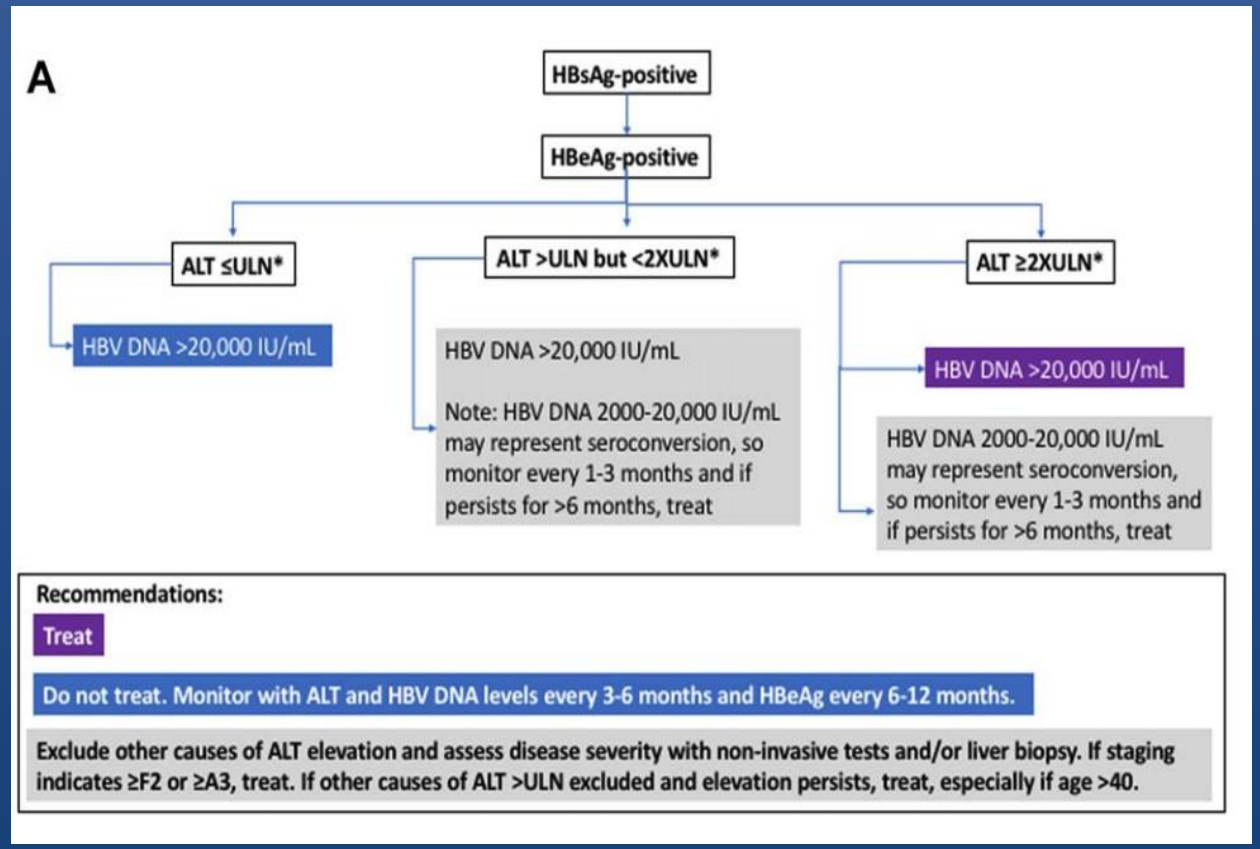
HBV Viral load and cumulative Risk of HCC

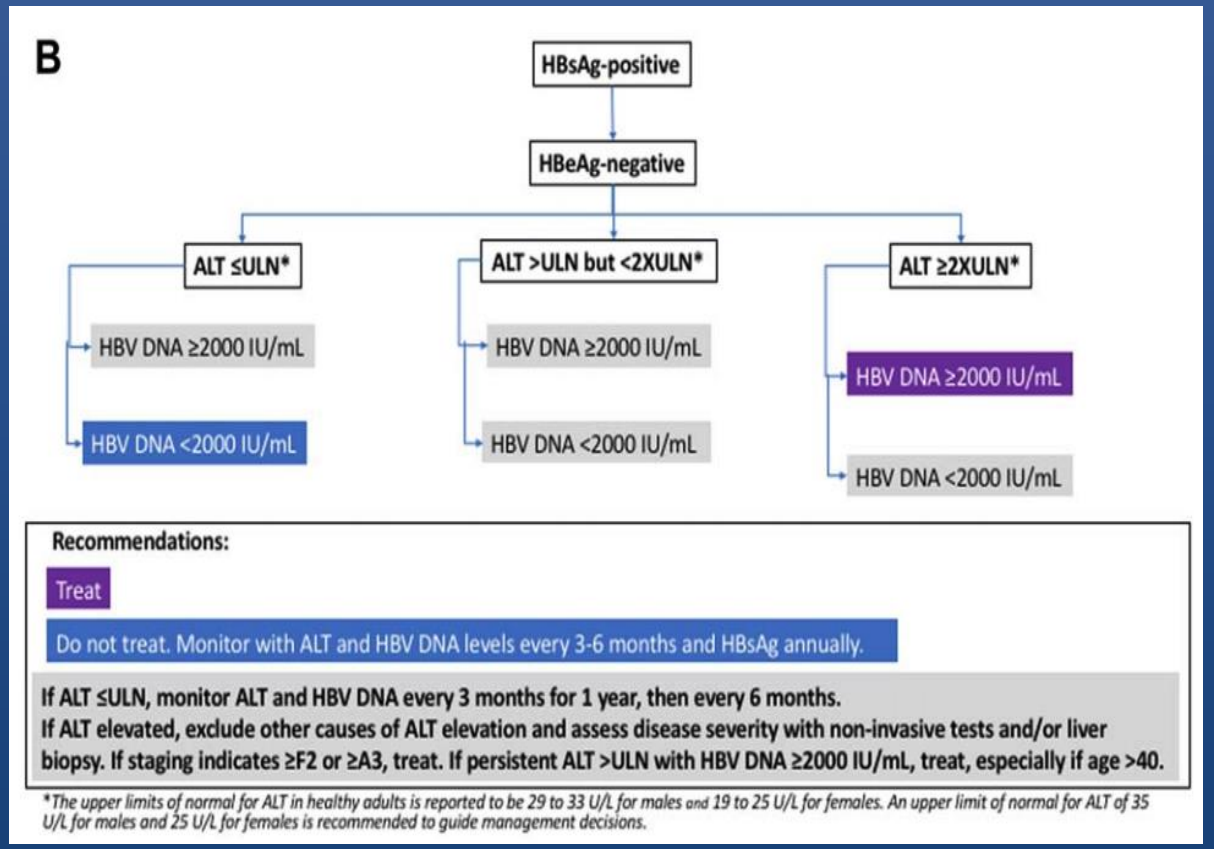


HBV Viral load and cumulative Risk of Cirrhosis



HBV Treatment indications





1. *Terrault et al. Hepatology 2018.*

Antiviral medications for HBV

	Preferred	Notes	Pregnancy
Entecavir	Yes	High potency, high genetic barrier to resistance	Category C
Tenofovir Disoproxil Fumarate	Yes	High potency, high genetic barrier to resistance	Category B
Tenofovir Alafenamide	Yes	High potency, high genetic barrier to resistance; Decreased Renal and Bone Side Effects	Insufficient human data on use during pregnancy
Peg-Interferon	Yes	Less safe in pts with cirrhosis	Contraindicated
Adefovir	No	Low genetic barrier to resistance	Category C
Lamivudine	No	Low genetic barrier to resistance	Category C
Telbivudine	No	Low genetic barrier to resistance	Category B

There is no cure for hepatitis B!

Mother-to-child-transmission of HBV

- Perinatal transmission accounts for 50% of global burden of chronic HBV
- 90% of infants with MTCT develop chronic HBV
  - 15-25% infants have premature death from liver failure or HCC
- Administration of HBV vaccine and HBIG to infant is 85-95% effective in preventing MTCT
  - 10-15% infants still develop chronic HBV infection
- Risk of MTCT increases as HBV DNA increases

Zou et al. J Viral Hep 2012.
Han et al. J Hepatol 2011.

Mother-to-child transmission (MTCT) of HBV

- Third trimester antiviral therapy reduces MTCT to 0-3% (rare transmission via placenta)

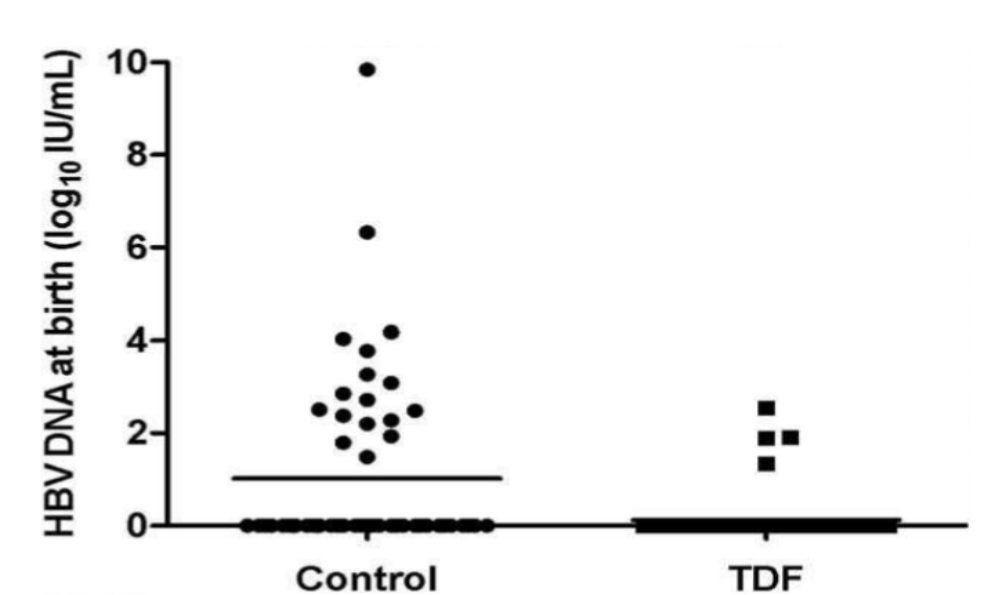
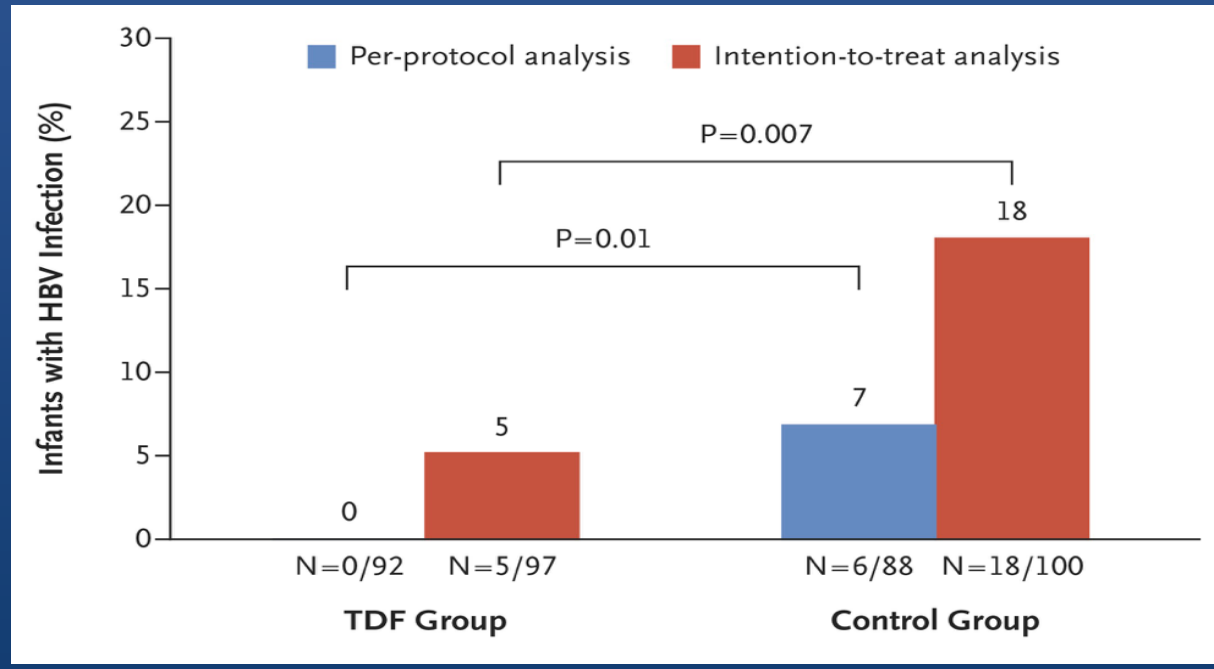


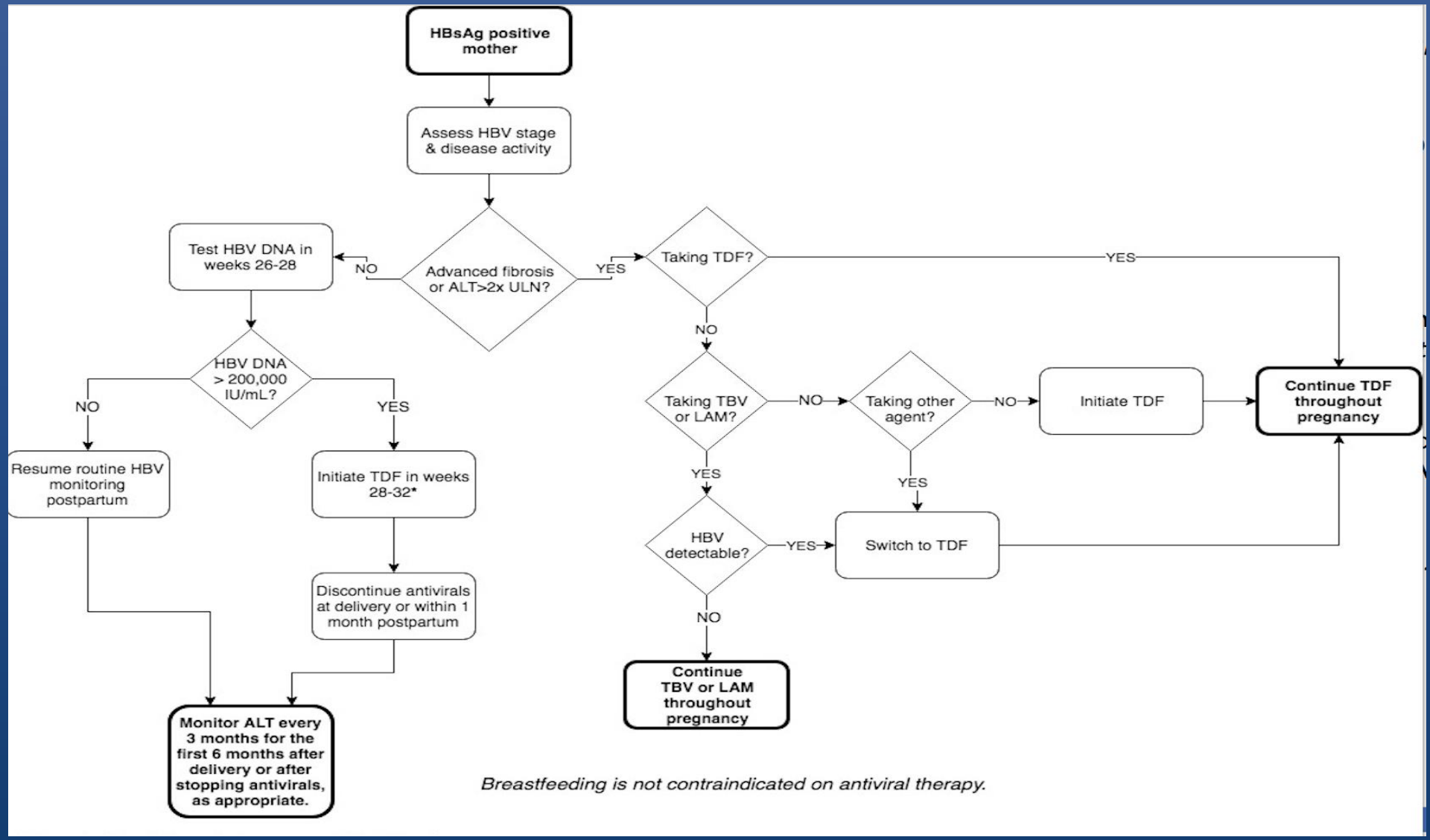
Fig. 3. Lower rates of HBV DNA positivity in the peripheral blood of infants at birth were noted in the maternal TDF treatment group in comparison to the control group (6.14% versus 31.48%, $P = 0.0003$).

Chen et al. Hepatology 2015



Pan et al. NEJM 2016

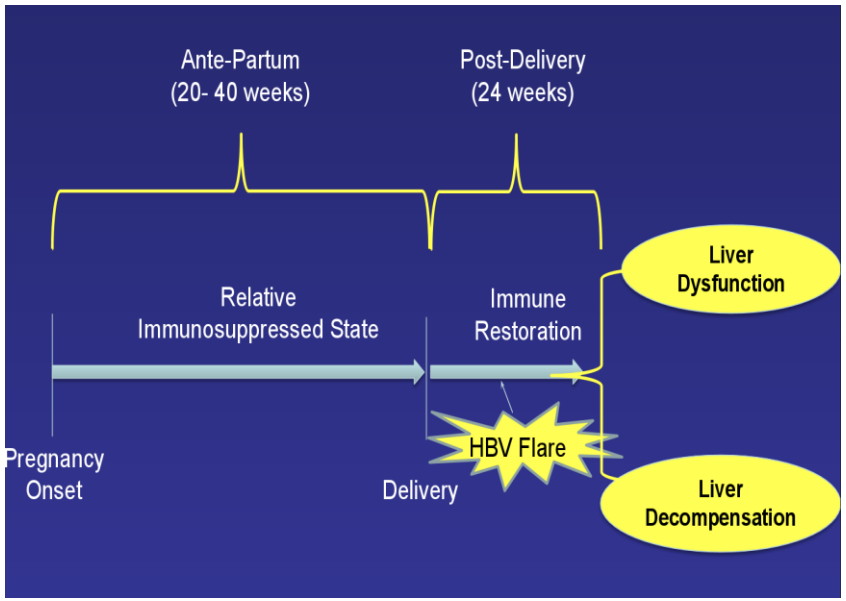
HBV treatment in Pregnant HbsAg + Women



Kushner et al. Clinical Liver Disease. Accepted for publication 2018.

HBV Disease activity in mother during pregnancy and post-partum

- Pregnancy associated hepatitis B Flares
  - Immunologic changes during pregnancy affect HBV activity
  - Decrease I IL-2 and IL-12 during pregnancy
  - Reconstitution of maternal immune system postpartum → hepatic flare
  - Fulminant liver failure reported



Liu et al. J Clin Gastroenterol 2017.

Pregnancy-associated HBV flares

Study	Country	Pregnancies (n)	ALT flare definition*	Prevalence of flare
Ter Borg et al, J Viral Hepatitis, (2008)	Netherlands	38	3x baseline	45% postpartum
Nguyen et al, Aliment Pharmacol Ther, (2014)	Australia	*101 pregnancies:* 44 early AVT cessation 43 late AVT cessation 14 untreated women	5x ULN	*Postpartum flares:* early AVT cessation: 50% late AVT cessation: 40% untreated women: 29%
Giles et al, Gut, (2015)	Australia	126	2x ULN	25% postpartum
Chang et al, Am J Gastroenterol, (2016)	US	113	5x ULN or 3x baseline	6% during pregnancy; 10% postpartum
Kushner et al, J Liver Int, (2017)	US	310	2x ULN	14% during pregnancy; 16% postpartum
Liu et al, Clin Gastro & Hepatol, (2017)	China	1097	2x ULN	11.9%- first trimester; 2.1%- at delivery; 9.8%-1 month postpartum

Monitoring women with HBV during pregnancy

- Recommendations:
  - Expectant mother should be monitored more closely during pregnancy
  - Highly viremic mothers and those with positivie HBeAg at higher risk for flare
  - Antiviral therapy can be initiated if flare does not resolve

Other Pregnancy management considerations for women with HBV

Pregnancy Management	Studies
Amniocentesis	• Alexander et al. 1999 – 21 mother-infant pairs – 0/21 infants with HBV • Yi et al. 2014 – 63 HBV+ mother-infant pairs vs. 579 controls – Higher MTCT (6.35% vs. 2.53%; p=0.226; 50% vs. 4.5 %; p=0.006 if HBV DNA> 7log10copies/ml)
Cesarean section vs. NSVD	28 studies; No RCTs – mixed data

Breastfeeding and HBV

- Does not appear to increase HBV transmission
  - No difference in rates of infection between breast-fed and formula-fed vaccinated infants

- Tenofovir safe for breastfeeding infants
  - No differences in bone development in infants at 2 years of follow-up
  - No justification for contraindicating the use of tenofovir while breastfeeding
  - Lack of long-term safety data with long-term, low-level infant exposure – discuss with mother

Hill et al. J Obstet Gynecol 2002.

Pregnancy management in patients with HBV

Summary of recommendations

	Recommendations	GRADE
1	Perform routine screening during pregnancy for HBV infection with maternal HBsAg testing.	1A Strong recommendation, high-quality evidence
2	Administer hepatitis B vaccine and HBIG within 12 hours of birth to all newborns of HBsAg-positive mothers or those with unknown or undocumented HBsAg status, regardless of whether maternal antiviral therapy has been given during the pregnancy.	1A Strong recommendation, high-quality evidence
3	In pregnant women with HBV infection, we suggest HBV viral load testing in the third trimester.	2B Weak recommendation, moderate-quality evidence
4	In pregnant women with HBV infection and viral load >6-8 log 10 copies/mL, HBV-targeted maternal antiviral therapy should be considered for the purpose of decreasing the risk of intrauterine fetal infection.	2B Weak recommendation, moderate-quality evidence
5	In pregnant women with HBV infection who are candidates for maternal antiviral therapy, we suggest tenofovir as a first-line agent.	2B Weak recommendation, moderate-quality evidence
6	We recommend that women with HBV infection be encouraged to breast-feed as long as the infant receives immunoprophylaxis at birth (HBV vaccination and hepatitis B immunoglobulin).	1C Strong recommendation, low-quality evidence
7	For HBV-infected women who have an indication for genetic testing, invasive testing (eg amniocentesis or chorionic villus sampling) may be offered. Counseling should include the fact that the risk for maternal-fetal transmission may increase with HBV viral load >7 log 10 IU/mL.	2C Weak recommendation, low-quality evidence
8	We suggest cesarean delivery not be performed for the sole indication for reduction of vertical HBV transmission.	2C Weak recommendation, low-quality evidence

HBIG, HBV immunoglobulin; *HBsAg*, hepatitis B surface antigen; *HBV*, hepatitis B virus.

Guidelines

The recommendations in this document reflect the national and international guidelines related to hepatitis B infection during pregnancy.[5,6,14,22,34,56,57]

Society for Maternal-Fetal Medicine

Dionne-Odom et al. Am J Obstet Gynecol 2016.

Conclusions

- Hepatitis B is a chronic liver disease with no cure – close follow up needed during pregnancy and after
- Treatment with antiviral therapy during pregnancy should be targeted towards women who would otherwise meet treatment guidelines
  - Tenofovir is safe and effective
- Antiviral therapy during pregnancy is indicated in highly viremic mothers with HBV DNA > 200,000 to prevent MTCT
- Close monitoring of women with HBV during pregnancy is important in order to optimize pregnancy and disease outcomes and minimize MTCT