VIRAL HEPATITIS IN PREGNANCY

Unravelling the mystery

SATURDAY, 27TH JULY 2019

(on the occasion of World Hepatitis Day 2019)

'National seminar for physicians in diagnosis and management of viral hepatitis in pregnancy'

TOPIC: Management of Newborn of HBsAg positive pregnant woman - Pediatrician *'s view point*

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Background

- Globally , an estimated 240 million people are chronically infected with HBV
- HBV has a significant contribution in deaths due to cirrhosis and liver cancer
- Perinatal transmission is the most common route of transmission specially in endemic countries

Risk of chronic carrier

Time of Infection	Risk
Perinatal	90%
Preschool children	23%
Adults	<5%

Beasley et al .J Infect Dis 1982

World Health Organization

JUNE 2016

GLOBAL HEALTH SECTOR STRATEGY ON

VIRAL HEPATITIS 2016–2021

TOWARDS ENDING VIRAL HEPATITIS

TARGET AREA	BASELINE 2015	2020 TARGETS	2030 TARGETS
Impact targets			
Incidence: New cases of chronic viral hepatitis B and C infections	Between 6 and 10 million infections are reduced to 0.9 million infections by 2030 (95% decline in hepatitis B virus infections, 80% decline in hepatitis C virus infections)	30% reduction (equivalent to 1% prevalence of HBsAg[9] among children)	90% reduction (equivalent to 0.1% prevalence of HBsAg among children)[10]
Mortality: Viral hepatitis B and C deaths	1.4 million deaths reduced to less than 500 000 by 2030 (65% for both viral hepatitis B and C)	10% reduction	65% reduction
Service coverage targets			
Hepatitis B virus vaccination: childhood vaccine coverage (third dose coverage)	82%[11] in infants	90%	90%
Prevention of hepatitis B virus mother-to-child transmission: hepatitis B virus birth-dose vaccination coverage or other approach to prevent mother-to-child transmission	38%	50%	90%
Blood safety	39 countries do not routinely test all blood donations for transfusion-transmissible infections 89% of donations screened in a quality-assured manner[12]	95% of donations screened in a quality-assured manner	100% of donations are screened in a quality-assured manner
Safe injections: percentage of injections administered with safety-engineered devices in and out of health facilities	5%	50%	90%
Harm reduction: number of sterile needles and syringes provided per person who injects drugs per year	20	200	300
Viral hepatitis B and C diagnosis	<5% of chronic hepatitis infections diagnosed	30%	90%
Viral hepatitis B and C treatment	<1% receiving treatment	5 million people will be receiving hepatitis B virus treatment	80% of eligible persons with chronic hepatitis B virus infection treated

Perinatal transmission

- Mother-to-child transmission of HBV can occur
  - ❑Intrauterine
  - ❑Intrapartum
  - ❑ Postpartum

Perinatal transmission

- Perinatal (vertical) transmission is positivity of the hepatitis B surface antigen (HBsAg) or HBV-DNA at 6–12 months in an infant born to an infected mother.

Intrauterine transmission

- IUT is defined as HBsAg positivity or detectable HBV-DNA in the neonatal blood 1–30 days after birth
- Only a minority of cases of HBV transmission.
- Can occur in placenta damage caused by contraction of the uterine muscle such as threatened abortion; invasive procedures into the uterus like amniocentesis

Intrapartum transmission

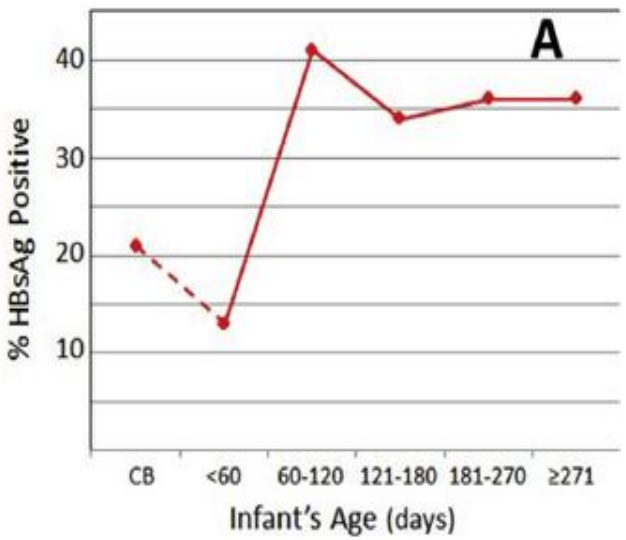
- Most common route
- Partial placental leakage occurring during delivery and instrumentation can result in mixing of fetal and maternal circulation and cause to an increase in the risk of HBV infection
- Contact with maternal blood during delivery through skin abrasions or mucous membranes or by swallowing maternal blood or infective fluid

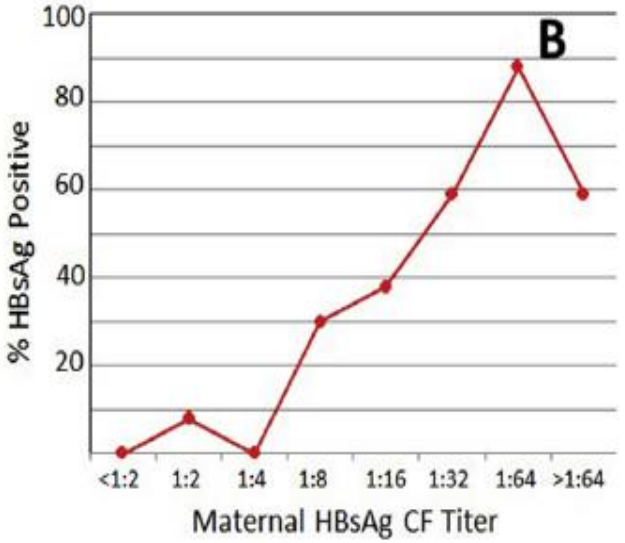
Can J Gastroenterol Hepatol. 2014;28(8):439–44.

J Pediatr 1997; 135(5): 730-5

Post partum transmission

- Defined as infection of HBV acquired through breast milk, body fluids or close contacts after delivery





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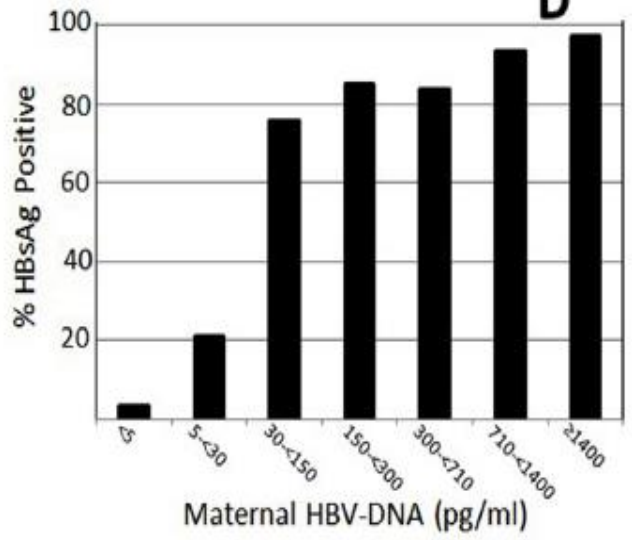
Maternal HBeAg	No. Infants	HBV Infection	Chronic HBsAg+ (%)
Positive	47	45	40 (85%)
Negative	18	3	0 (0%)



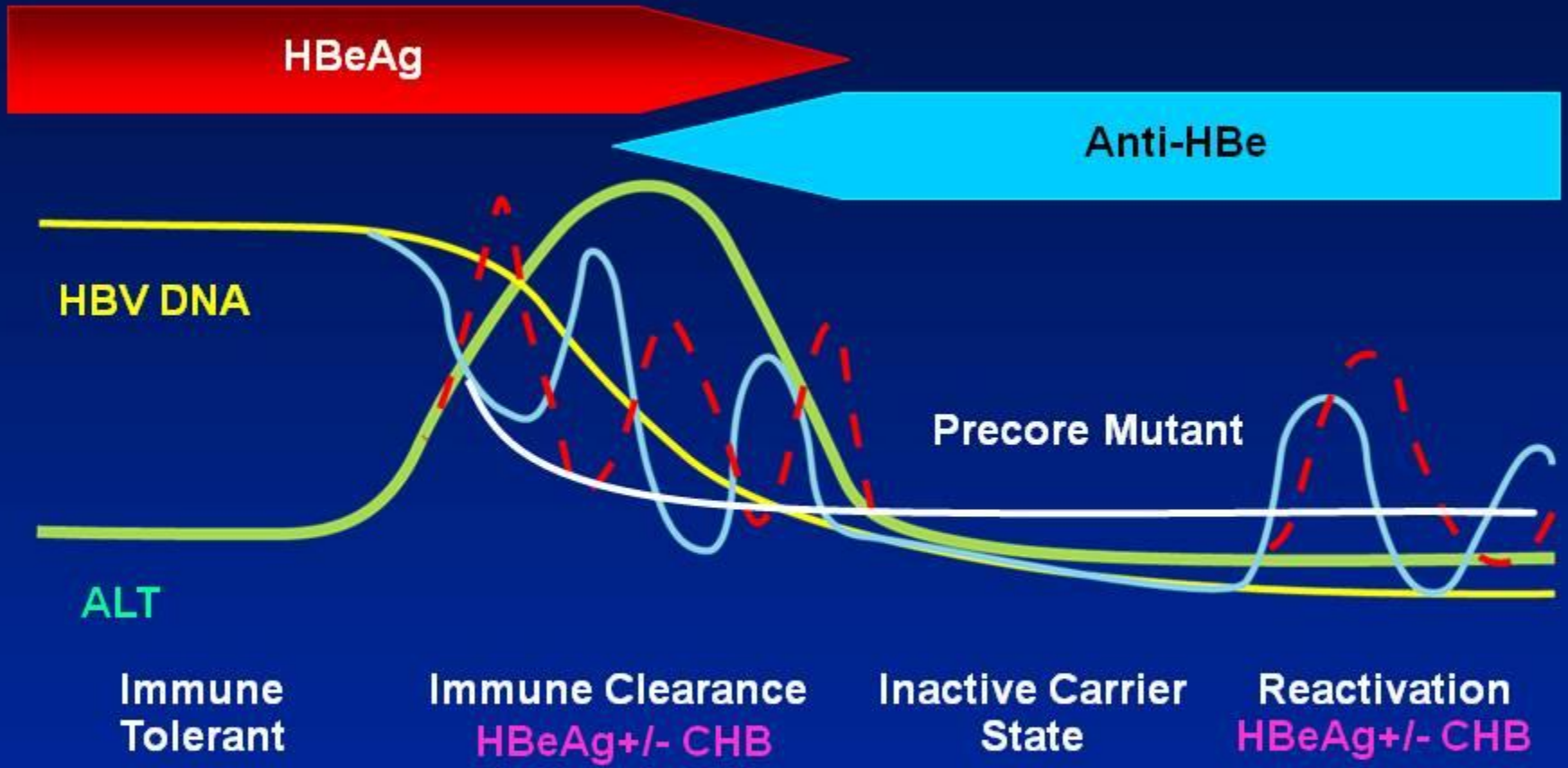
RISK FACTORS FOR PERINATAL TRANSMISSION

- High maternal HBsAg titer
- Maternal HBeAg postivity
- High viral load in maternal serum
- Infection acquired in 3rd trimester

Natural history

- Infections are usually asymptomatic and anicteric when infection is acquired vertically
- The natural history is dynamic and complex , progressing non-linearly through several phases of variable duration -

Figure 2. Typical Disease Models of Chronic Hepatitis B



Liver Histological Activity			
Mild	Moderate/Severe	None/Mild	Moderate/Severe

Strategies for Prevention

- Screening pregnant women
- Providing antiviral treatment to women with high HBV-DNA level
- Administering passive-active immunoprophylaxis to newborns of mothers who are HBsAg positive

Strategies for Prevention

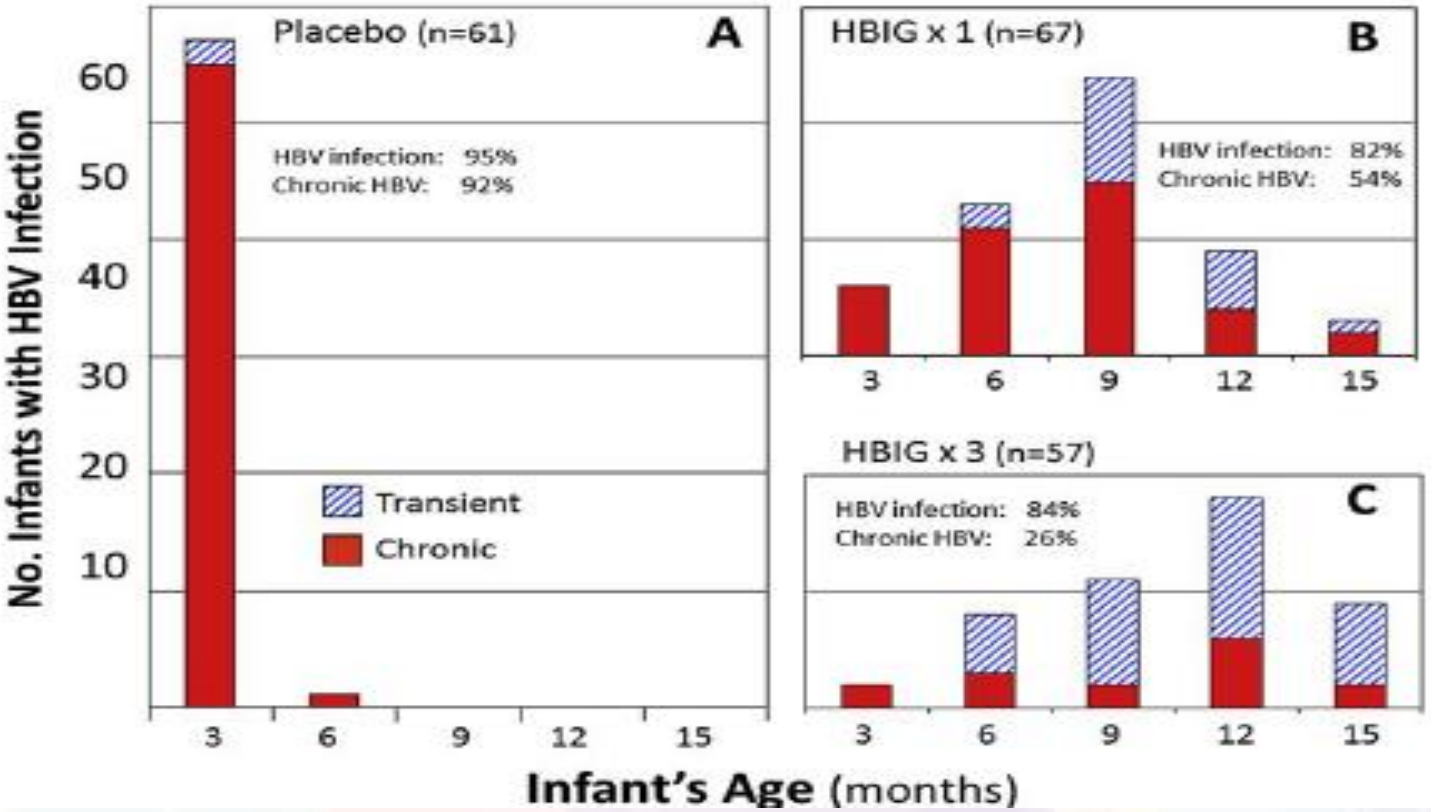
- The hepatitis B vaccine is used safely in all trimesters of pregnancy.
- Nonimmune pregnant women at risk should be vaccinated.

Immunoprophylaxis to the baby

- A combination of active and passive immune prophylaxis is the optimum strategy to prevent HBV infection in babies of HBsAg positive mothers.

- A combination initiated within 12- 24 hours of delivery - protects 85 to 95% of babies whose mothers - positive for both HBsAg and HBeAg

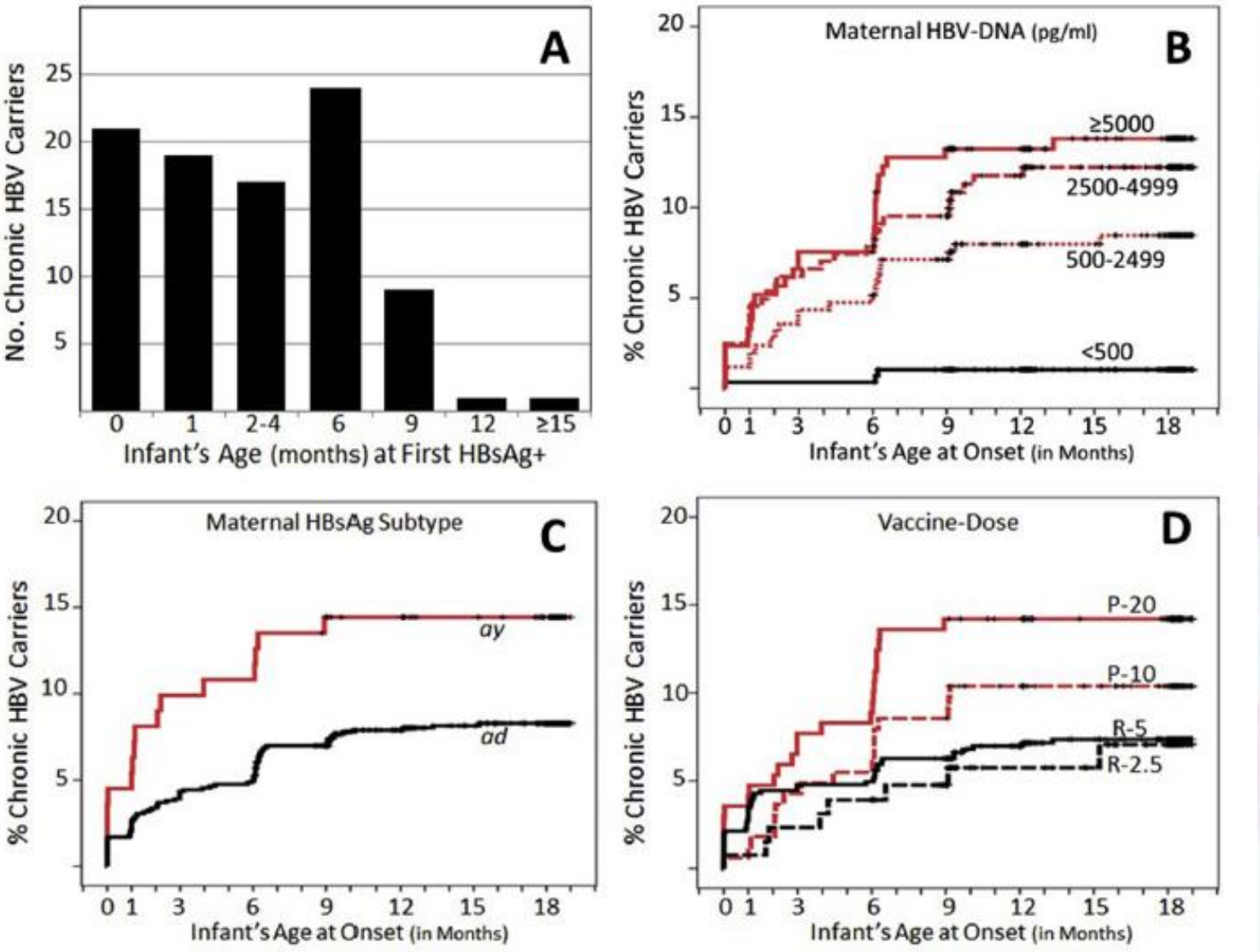
Immunoprophylaxis



C.E.Stevens et al. Biologicals 50(2017) 3-19

Passive immunization

- HBIG is used as an adjunct to the hepatitis B vaccine to prevent vertical transmission. It provides temporary protection that lasts for 3 to 6 months.
- Studies have shown that HBIG is effective when administered as late as 72 hours after birth


A
No. Chronic HBV Carriers
25
20
15
10
5
0
1
2-4
6
9
12
≥15
Infant's Age (months) at First HBsAg+
B
Maternal HBV-DNA (pg/ml)
% Chronic HBV Carriers
20
15
10
5
≥5000
2500-4999
500-2499
<500
0 1 3 6 9 12 15 18
Infant's Age at Onset (in Months)
C
Maternal HBsAg Subtype
% Chronic HBV Carriers
20
15
10
5
ay
ad
0 1 3 6 9 12 15 18
Infant's Age at Onset (in Months)
D
Vaccine-Dose
% Chronic HBV Carriers
20
15
10
5
P-20
P-10
R-5
R-2.5
0 1 3 6 9 12 15 18
Infant's Age at Onset (in Months)


BIRTH-DOSE
VACCINATION IS A
KEY INTERVENTION
FOR PREVENTION OF
HEPATITIS B VIRUS
INFECTION IN INFANTS

Hepatitis B vaccination

- Hepatitis B vaccination is carried out using the monovalent vaccine for the birth dose
- Hepatitis B vaccine soon after birth is critically important for the prevention of perinatal and early postnatal transmission of HBV infection, and is much more efficacious for this purpose than doses given after the neonatal period
- Further doses can be given as combination vaccines with other vaccines like DPT and Hib vaccines

Hepatitis B vaccination

- Combination of HBIG (0.5 ml) with HBV vaccine(0.5 ml recombinant given separate thighs) is more effective than HBV alone in prevention of transmission of hepatitis B
- Some studies have shown that when HBIG is unavailable, vaccination alone can prevent vertical transmission in 66% to 80% of cases

Vertical transmission

- In absence of any preventive interventions 70-90% for HBeAg positive mothers ; 10-40% for HBeAg negative mothers
- HB Vaccine (birth dose and two additional doses) along with HBIG dose prevent infection in 90-95% of cases
- Vertical transmission can still occur in 2-10% of HBeAg positive or mothers with high viral load

Breastfeeding

- With the introduction of immunoprophylaxis , similar risk of infection in breastfed and formula fed infants observed
- Breastfeeding is not contraindicated if babies have received immunoprophylaxis

Special situations

- In mothers with an unknown HBsAg positivity status at delivery, the birth dose of hepatitis B vaccine is administered within 24 hours of birth, and HBIG is administered as soon as possible if the mother tests positive, ideally within 72 hours of delivery
- Preterm baby: HBsAg positive mother, the birth dose is indicated even if the baby weighs < 2 kg, but should be followed by a further three doses starting at six weeks of age. This is due to the reduced immunogenicity of hepatitis B vaccine in preterms weighing <2 kg in the first month of life
- The immunogenicity - suboptimal in conditions associated with immuno-suppression, including advanced HIV infection

Follow up

- Although routine post-vaccination testing is not necessary, it is recommended for high-risk groups including babies born to mothers who are HBsAg positive, and should commence at 9 to 18 months of age, atleast 1 month after the last dose of vaccine
- HBsAg status and the anti HBs titre should be checked.
- The anti HBs levels done earlier than 9 months of age may reflect passive immunization with HBIG
- Anti HBs levels of more than 10 mIU/l indicate adequate protection, whereas babies with anti HBs levels of less than 10 mIU/l need to be revaccinated with the entire 3 dose schedule
- Babies who are HBsAg positive are infected and need to be followed up

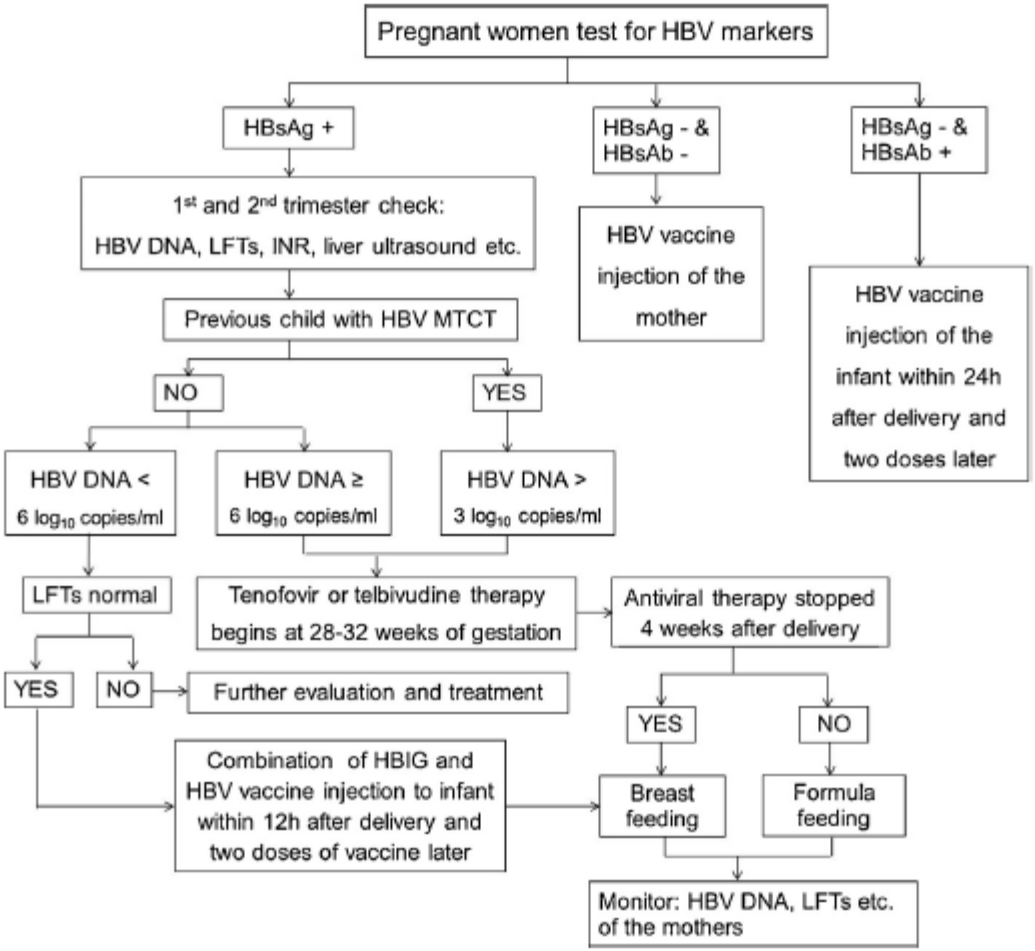


Fig. 1. Management of MTCT of HBV in pregnancy. HBsAg, Hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; ALT, alanine aminotransferase; HBV, hepatitis B virus; LFT, liver function test; INR, international normalized ratio; MTCT, mother to child transmission; HBIG, hepatitis B immunoglobulin.

Key points:

- Universal screening of all pregnant women for hepatitis B
- Use of antivirals in women with a high HBV viral load in the third trimester
- Birth dose of HBV vaccine within 24 hours of birth to all
- HBIG to all babies born to HbsAg within 12 – 24 hrs of birth
- Breastfeeding not contraindicated even in HBeAg positive mothers

Thank you!