Viral Hepatitis in Pregnancy

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Overview
- Epidemiology
- Clinical features
- Laboratory findings
- Screening
- Transmission Risks
- Perinatal Transmission
- Perinatal Prevention: Delivery, Feeding
- Infant Management
- Vaccination

Hepatitis B Virus

Chronic Hepatitis B

HBsAg Prevalence
- ≥8% - High
- 2-7% - Intermediate
- <2% - Low
Vaccine licensed HBsAg screening of pregnant women recommended Infant immunization recommended OSHA Rule enacted Adolescent immunization recommended

Hepatitis B Clinical Features

- Incubation period: Average 60-90 days Range 45-180 days
- Clinical illness (jaundice): <5 yrs, <10% ≥5 yrs, 30%-50%
- Acute case-fatality rate: 0.5%-1%
- Chronic infection: <5 yrs, 30%-90% ≥5 yrs, 2%-10%
- Premature mortality from chronic liver disease: 15%-25%

Outcome of Hepatitis B Infection by Age of Infection

- Chronic Infection
- Symptomatic Infection

Prevalence Hepatitis B in U.S.

* Provisional date
**Hepatitis B Screening in Pregnancy**

- Universal prenatal screening for HBsAg
- Only 35-65% HBsAg+ women identified when only “high-risk” screened
Hepatitis B Transmission

Concentration of Hepatitis B

<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low/Not Detectable</th>
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<tr>
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<td>urine</td>
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<tr>
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<td>feces</td>
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<td>saliva</td>
<td>sweat</td>
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<td></td>
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<td>tears</td>
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<td>breastmilk</td>
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HBV Transmission

- Sexual
- Parenteral
  - Occupational
  - Perinatal

Hepatitis B Perinatal Transmission
Perinatal Transmission of HBV

- Perinatal Transmission
  - <10% if HBeAb+
  - 15% if HBsAg+
  - 70-90% if HBsAg + and HBeAg +
    - 85-90% of infected infants → chronic HBV carriers
    - 25% of carriers die of CLD

- Timing of transmission
  - Majority of cases = intrapartum
  - Intrauterine infection: risk factors
    - HBeAg+ OR 17.1
    - Preterm labor OR 5.4
    - Invasive genetic testing???

Hepatitis B Chemoprophylaxis

- Hepatitis B insets

Lamivudine and HBIG ↓ risk of in-utero Hep B transmission

- Antepartum HBIG or Lamivudine
  - RCT: 151 HBsAg+ pregnant women, nLFTs
  - HBIG q4wks @ 28wk gestation until labor
  - Lamivudine 100mg QD @ 28wk until PPDR 30
  - Control: no antepartum intervention
  - Intrauterine infection: neonatal HBsAg and/or HBeAg @ 24hr
    - HBIG 16%, Lamivudine 16% (p<0.05 vs. controls 33%)
    - 2 log ↓ maternal HBV DNA before labor in HBIG and Lamivudine group
      - p<0.05 vs. controls

- Case series: 8 viremic pregnant ♀: Lamivudine 150mg QD x4wks
  - 12.5% transmission vs. 28% (untreated historical controls)

- Cases of vertical HBV transmission despite HBV suppression on Lamivudine
- Lamivudine + Tenofovir to prevent resistance?

Hepatitis B Mode of Delivery

- Hepatitis B insets

Be 1994; Grinstead 1994; Alexander 1998; Toews 2001

Mode of Delivery and Hepatitis B

- Observational study; n=301
- All mothers HBsAg +
- 144 NSVD, 40 forceps/vacuum, 117 C-S
- All neonates received HBlg and HBV vax
- No difference in neonatal HBsAg by delivery mode
  - NSVD: 8.1%
  - Forceps/vacuum: 7.7%
  - Cesarean delivery: 9.7%

Wang Chin Med J 2002

Hepatitis B Breastfeeding

Breastfeeding and Hepatitis B

- Hepatitis B surface Ag found in breastmilk
  - Much lower levels than serum
- No apparent transmission to infants
  - Even before HBV vaccine available for exposed infants
- Observational study: n=369
  - 101 breastfed; 268 formula fed
  - No differences in maternal HBeAg or LFT abnl
  - Neonatal infection by 9-15 months of age (HBsAg +)
    - 0% breastfed vs. 3% formula fed

www.cdc.gov (accessed 1/06); JR Ob-Gyn 2002

Hepatitis B Management of Exposed Infant
Management of HBV Exposed Infant

- HBIG to infant @ birth, 1-2 mos, and 6 mos
- HBV vax @ birth, 1-2 mos, and 6 mos
  - 65-96% efficacy
- HBIG + vax effectiveness
  - 85-95% at preventing chronic HBV

USPSTF 1996; Mele JD 2001

Hepatitis B Vaccination

HBV Vaccination in Pregnancy

- Considered safe in pregnancy
- Efficacy
  - 49% after 2 of 3 doses (HIV-neg pregnant women)
    - vs. 59-70% in non-pregnant
- Factors assoc with failure to seroconvert (pregnancy)
  - Smoking OR 7.5 (2.0-27.7)
  - BMI ≥ 34 OR 16.2 (1.7-154.7)
  - Age ≥ 25 yo OR 3.9 (1.1-14.4)
- Pre-test vaccination (anti-HBc Ab)
  - Cost-effective if prevalence > 20%
- Post-vaccination testing for certain groups
- Double dose in immunocompromised


Hepatitis C Virus
Prevalence of Acute HCV
U.S. 1960-1999

WHO 1999

HCV Has Broad Global Prevalence

Decline in injection drug users
Decline in transfusion recipients

Incubation period
Average 6-7 wks
Range 2-26 wks

Acute illness (jaundice)
Mild (≤20%)

Case fatality rate
Low

Chronic infection
75%-85%

Chronic hepatitis
70% (most asx)

Cirrhosis
10%-20%

Mortality from CLD
1%-5%

Features of HCV Infection

Hepatitis C
Clinical Features
Risk Factors for Chronic HCV

- Increased alcohol intake
- Age > 40 years at time of infection
- HIV co-infection
- Genotype 1a
- Other possible risk factors
  - Male gender
  - Other co-infections (e.g., HBV)

Serologic Pattern of Acute HCV Infection with Recovery

Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection

Hepatitis C Screening in Pregnancy
**Perinatal HCV Screening**

- **Indications**
  - Current or past IDU
  - Transfusion or organ transplant prior to July 1992
  - Long-term hemodialysis (patients and staff)
  - ↑ LFTs
  - Known exposure to HCV
  - HIV or HBV infection
  - History of piercing or tattoos
  - IVF participants with anonymous donors
  - Sexual partners of people with HIV, HBV, HCV
- **Universal screening:** $1.1 million/QALY
  - High risk screening will miss 50% of HCV + women

**Clinical Course of HCV in Pregnancy**

- **Conflicting data**
- **Overall, likely no significant change in clinical course**
  - Improvement of transaminase levels
  - Possible linear increase in viremia
- **Post-partum**
  - Mild ↑ ALT but not HCV-RNA
  - Histopathological exacerbation of HCV

**Hepatitis C Medical Management**

- LFTs, (AFP), HCV RNA*, genotype*
- HAV and HBV serology → VAX if non-immune
- Avoid EtOH, hepatotoxic medication/herbs
- RUQ sono if ↑ LFTs
- Liver bx typically deferred until after pregnancy
- Standard HCV treatment in adults = contraindicated in pregnancy
  - Ribavirin + Interferon
  - Interferon
  - Potentially neurotoxic
  - Ribavirin: teratogenic and embroyolethal in nearly all species
  - Found in semen of treated men

**Standard HCV treatment in adults**

- HAV and HBV serology → VAX if non-immune
- Avoid EtOH, hepatotoxic medication/herbs
- RUQ sono if ↑ LFTs
- Liver bx typically deferred until after pregnancy
- Standard HCV treatment in adults = contraindicated in pregnancy
  - Ribavirin + Interferon
  - Interferon
  - Potentially neurotoxic
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  - Found in semen of treated men
**Hepatitis C Transmission**

- Prevalence: 1-2% among health care workers
- 2% among health care workers

**Transmission of HCV**

- **Percutaneous**
  - Injection drug use
  - Clotting factors before viral inactivation
  - Transfusion, transplant from infected donor
  - Therapeutic (contaminated equipment, unsafe injection practices)
  - Occupational
- **Permucosal**
  - Perinatal
  - Sexual

**Occupational Transmission of HCV**

- Inefficiently transmitted
- Average incidence 1.8% following needle stick from HCV-positive source
  - Associated with hollow-bore needles
- Case reports of transmission from blood splash to eye
  - No reports of transmission from skin exposures to blood
- Prevalence 1-2% among health care workers
  - Lower than adults in the general population
  - 10 times lower than for HBV infection

**Hepatitis C Perinatal Transmission**
Potentially cost-effective for HIV-HCV

Not adjusting for HCV viral load, not distinguishing elective C/S

Cost-effective if HCV transmission by 77%

Cost-effectiveness if HCV: OR 2.0 (1.0-3.7)

HCV transmission by 77%

Hepatitis C

Mode of Delivery

Perinatal HCV Transmission

- Timing of transmission
  - Mostly intrapartum, however...
  - n=54 HCV infants: 31% HCV DNA+ w/in 3 days of life
- Transmission risk:
  - RNA neg 1-3% vs. RNA pos 4-6%
  - HIV-negative 5% (10% if HCV-viremic)
  - HIV-positive 17% (28% if HCV viremic)
- Meta-analysis of HCV risk factors
  - HCV viremia
  - HIV co-infection: OR 2.8 (1.8-4.4)
  - HCV viremic: HIV+ vs. HIV-: OR 2.0 (1.0-3.7)
- Honolulu cohort: 244 exposed infants
  - ROM > 6 hours: OR 9.3 (1.5-179.7)
  - Internal fetal monitoring: OR 6.7 (1.1-35.9)

Delivery Route and HCV Transmission

- Prospective cohort 441 mother-child pairs
  - Elective c-section (n=31): 0%
  - Emergency c-section (n=54): 5.9%
  - NSVD (n=339): 7.7%
  - Elective C/S vs. NSVD/emergent C/S: OR 0 (0.0-0.87), no adjustment for HCV viremia (p=0.04)
  - Only in HIV+HCV co-infected women (p=0.06)
- European Pediatric HCV Network
  - 1474 HCV+ (503 of whom HIV+)
  - C-section (elective/non-elective) vs. NSVD OR 0.7 (0.4-1.2)
- Cost-effective if HCV transmission by 77%
- Potentially cost-effective for HIV-HCV
  - Not adjusting for HCV viral load, not distinguishing elective C/S

Hepatitis C

Breastfeeding
Breastfeeding and HCV

- HCV RNA found in breastmilk, but no apparent transmission
- Gibb cohort (n=441 mother-child pairs)
  - Bottlefed 6.7% vs. breastfed 7.7%; OR 1.5 (0.35-5.12)
- European Pediatric Hepatitis C Virus Network
  - N=HCV+ women
  - 35% (n=503) co-infected with HIV
  - Breastfed vs. Non-breastfed OR = 1.07, P = 0.83
- Honolulu cohort: n=244; 63 HCV+ breastfeeding
  - HCV transmission: Breastfed OR 0.8 (0.2-3.9)
  - 51% HCV RNA + milk → no transmissions
- ACOG, AAP, CDC support breastfeeding among HCV+ mothers
- Recommend pump/dump if cracked/bleeding nipples

Gibb 2000; Mast JID 2005; MMWR 1998

Management of Infant Exposed to HCV

- Infant follow-up
  - HCV RNA PCR on 2 occasions 3-4 months apart after 2 months of age
  - Anti-HCV Antibody after 15-18 months
  - Don’t test umbilical blood for HCV Ab

Management of Exposed Infant

- Management of Infant Exposed to HCV

Hepatitis C
Management of Exposed Infant

- Hepatitis C
- Management of Exposed Infant

- Honolulu cohort: n=244; 63 HCV+ breastfeeding
  - HCV transmission: Breastfed OR 0.8 (0.2-3.9)
  - 51% HCV RNA + milk → no transmissions
- ACOG, AAP, CDC support breastfeeding among HCV+ mothers
- Recommend pump/dump if cracked/bleeding nipples

Summary: Management of HBV in Pregnancy

- Universal HBsAg screening
- If HBsAg positive:
  - Consult with GI
  - LFTs, HBeAg, HBV DNA
  - Others: HBsAb, HBeAb, HBCAb, Hep D Ab, Hep E Ab
  - HAV and HCV panel → HAV VAX if non-immune
  - Lamivudine (+/- Tenofovir) if viremic
  - HBIG + HBV vaccination to infant
  - Trial of labor (avoid FSE??)
  - Breastfeeding NOT contraindicated

NIH Assisi 2006
Summary: Management of HCV in Pregnancy

- Screening for HCV among high-risk women
- If HCV Ab positive:
  - Consult with GI
  - LFTs, HCV RNA, HCV genotype (and HIV, of course)
  - Rpt HCV RNA at 6 months if RNA negative
  - HAV and HBV panel → VAX if non-immune
  - Trial of labor (consider c/section if HIV-coinfected)
  - Shorten duration of ROM, Avoid FSE
  - Breastfeeding NOT contraindicated

Resources

- UCSF Reproductive Infectious Disease Service
  - 24/7 pager: 415-719-8726
- Centers for Disease Control and Prevention
  - www.cdc.gov
  - www.hivandhepatitis.com
- Advisory Committee on Immunization Practice
  - http://www.cdc.gov/niP/ACIP/default.htm

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