Infectious Diseases in Pregnancy: A Management Perspective

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NSW RDN Obstetrics Procedural Conference
Marriott Hotel, Sydney
Sunday 29th May 2008

Some significant infections in pregnancy

- CMV
- Rubella
- Varicella Zoster / Chickenpox
- Parvovirus B19
- CMV
- Toxoplasmosis
- Hepatitis C
- HIV
- Listeria
- Hepatitis B
- Herpes Simplex Virus
- CMV

CMV

A woman presents to your colleague in a rural practice asking to be tested for CMV. She has no history suggestive, but she has been reading about CMV and it seems to be pretty worrying so she would like reassurance. She works in a day care centre.

- Your colleague tests for CMV
- The results show IgM and IgG positivity in the first trimester
- Does she have active CMV and what do you do now?

CMV

- Need to differentiate between primary & recurrent CMV. Why?
- Primary CMV: 40-60% of babies are congenitally infected
  (LEADING CAUSE OF CONGENITAL INFECTION)
- Recurrent CMV: 1.5% of babies are congenitally infected
- Risk mainly in first trimester: termination of pregnancy should be considered
**CMV**

- How do we tell between primary and recurrent CMV?
  - IgM seroconversion
  - IgG avidity testing
  - Isolation of virus from blood
  - Amniocentesis
- Low IgG avidity is linked to primary infection, whereas high avidity is linked to recurrent disease
- Consider referral to a tertiary fetal medicine centre – why?

- Amniocentesis +/- ultrasound
- If amniocentesis culture is performed more than 6 weeks after infection or >23 weeks gestation (when virus excreted in fetal urine), sensitivity is 96%
- PCR commonly used for diagnosis
- qPCR can determine viral load

**CMV**

- If confirmed primary maternal CMV, 50% risk of transmission to fetus
  - Microcephaly
  - Hydrops
  - Intracranial or Extracranial calcifications
- 90% of neonates have asymptomatic CMV without sequelae
- Of those with features on US, 90% have sequelae
- Test infants with head US, hearing and fundoscopy

**Varicella Zoster / Chickenpox**

- Effects in first trimester:
  - Neurotropic, denervates fetal structures
  - 3-5% of infected fetuses in first trimester will have features:
    - Focal cutaneous ulcerations with scarring
    - Reduction deformities of limbs
    - Microphthalmia & cataracts
    - Microcephaly
    - Other CNS defects
- Usually seen 3-12 weeks post exposure
- No specific fetal therapy available
Varicella Zoster / Chickenpox
(Advice where history of contact with a person with chickenpox)

- Take history for previous documented infection: highly reassuring but test serology anyway
- IgM & IgG can detect acute or previous
- URGENT serology if history uncertain
- IgM seen in acute and about 70% of patients with herpes zoster
- If IgG seropositive, reassurance alone
- If seronegative or serology not available with no history or uncertain history, assess the time of exposure:
  - <96 hours, give passive immunisation with ZIG
  - >96 hours, only give oral acyclovir if at risk i.e. Second half of pregnancy, underlying lung disease, immunocompromised or smoker
- Seek medical attention if chickenpox develops
- (BUT AVOID ANTENATAL CLINIC)

Varicella Zoster / Chickenpox
(Development of chickenpox less than 7 days before delivery)

- Varicella infection of the newborn (previously congenital varicella)
- = VZV infection in early neonatal life resulting from maternal infection near the time of delivery or immediate postpartum
- Up to 50% of babies infected if maternal infection 1-4 weeks before delivery and ~25% of these develop clinical varicella (despite high titres of maternal antibody)
- Worst if born within 7 days of maternal rash as cord antibody levels low
- Neonate should be given ZIG
- Infant should be monitored for signs of infection for 14-16 days
- If neonatal infection occurs, treat with acyclovir
- VZIG is of no benefit once neonatal chickenpox has developed
- ...
- ...

Toxoplasmosis

- A parasitic infection
- Infection rates for exposed fetuses may be as high as 30-40% throughout pregnancy
- >75% of exposed fetuses unaffected
- 10% have severe disease
  - T1 infection risk low (15%) but if infected >60% damage
  - T2 intermediate risk of infection and damage
  - T3 high risk of infection but <10% damage
**Toxoplasmosis**

- **early pregnancy transmission**
  - 12% mortality
    - Chorioretinitis
    - Microcephaly
    - Hydrocephaly
    - Intracranial calcifications
    - Thrombocytopenia
    - Anaemia
    - Hydrops
  - 80% of infants with severe infection show ocular and CNS abnormalities
  - Apparently asymptomatic infants at risk for later development of mental retardation, deafness and ocular problems

**Toxoplasmosis**

- **diagnosis of fetal infection**
  - Toxoplasmosis PCR is available as is amniotic fluid culture
  - Ultrasound:
    - Random brain calcifications
    - Cataracts and microcephaly
    - Polyhydramnios
    - Placentomegaly
    - Hepatosplenomegaly
  - TOP if ultrasound abnormal
  - In the absence of sonographic anomalies, aggressive maternal treatment with pyrimethamine and sulfadiazine may reduce the fetal risk

**Parvovirus**

- A 24 year old woman is referred to you because her 3 year old son has just been confirmed to be suffering from slapped cheek syndrome (parvovirus B19 infection). She is currently 12 weeks pregnant. Outline your advice on management......

**Parvovirus**

- Infected individuals may be asymptomatic
- Or may have a rubella-like generalised rash with low-grade fever and flu-like symptoms
- 50-75% of adult women are immune
- But, fetal infection may result in anemia with hydrops leading to stillbirth or neonatal death – fetal bone marrow suppression +/- myocarditis

**Parvovirus**

- Risk of congenital infection 20-30%
- Highest and first and second trimesters
  - Benign infection in half
  - Risk of fetal death due to hydrops from severe anaemia approximately 10%
    - 17% <20 weeks if fetus infected
    - 6% > 20 weeks if fetus infected
- Risk of fetal damage overall 2-5% of mothers with Parvovirus B19
**Parvovirus (plan of surveillance)**

- Viral serology
- B19 IgM, IgG +/- B19 DNA
- IgM appear Day 3, disappear after 30-60 days
- IgG appear Day 7 after onset of illness, lifelong persistence
- Prior exposure => reassure
- Current infection => fetal surveillance
- No evidence current infection => repeat 4/52

**Parvovirus (plan if evidence of maternal B19)**

- No maternal therapy available
- Refer for fetal medicine review
- Hydrops develops 3-13 weeks after infection
- Most cases 16-32 weeks gestation
- Fetal sonography for anaemia for about 10 weeks after infection
  - Signs of hydrops
  - Hepatosplenomegaly
  - Anaemia as measured by MCA

**Parvovirus (fetal treatment for parvovirus hydrops)**

- Fetal blood transfusion for fetal hydrops & anaemia
- High haematocrit O negative irradiated blood in neonatal packs
- Spontaneous resolution will occur
- Weekly sonography after transfusion
- May not need to repeat
- Ascites may take weeks to clear

**HIV**

- A 32 year old African healthcare worker comes to see you to discuss her plans for pregnancy. She is known to be HIV positive and wants to know what the medical management plan will be during the gestation

**HIV Reduction in Vertical Transmission**

- Risk of mother to child HIV transmission:
  - No intervention 15-20% Europe, 25-35% Africa
  - Intrapartum 15-30%
  - Postpartum (breast feeding) 10-20%
  - Optimum management may result in <1%
- Maternal plasma HIV RNA level = strongest risk factor for transmission
  - >10,000 copies / ml 41%
  - 1,000-10,000 17%
  - <1000 <0%
  - BUT no absolute level below which risk is zero
HIV

Major measures that may reduce vertical transmission

- Antiretroviral Therapy (ART)
  - mother antenatal and intrapartum, infant for first 6 weeks of life
  - IV Zidovudine 4 hours prior to surgery until cord clamping
- HAART
- Elective Caesarean Section
- Avoidance of invasive obstetric procedures
- Alternatives for breast feeding
- Treat other STDs
- Limit duration of rupture of the membranes

One RCT 2000:
- Median follow up 24 months
- Breast fed 36.7% infected
- Bottle fed 20.5% infected
- HAART suppresses cell-free HIV-1 RNA but not cell associated DNA in breast milk and latter probably important in transmission
- No RCTs of transmission in women breast feeding on HAART

HIV

The Neonate

- Bathe infant as soon as possible after birth and before invasive procedures
- Cleanse skin thoroughly before Vit K, BSL and newborn screening
- Neonatal Zidovudine 8-12 hours after birth and oral for 6 weeks +/- single dose of Nevirapine
- Check for neonatal HIV RNA by PCR in first week
- (100% show transplacental maternal IgG)

Hepatitis C

- A 26 year old books under your care for confinement in a rural district hospital. She is fit and healthy, but gives a history of Hepatitis C, related to a past history of intravenous drug use.
- She would like some information about the management of pregnancy, labour and delivery and the puerperium

- Parenteral transmission, approximately 75% of those who are positive have contracted from intravenous drug use
- Blood or blood products, rarely (<5%) sexually transmitted
- 60% may get chronic infection
- 20% of these develop slow progressive cirrhosis over decades
**Hepatitis C management**

- Joint care with Infectious Disease specialists or hepatologists
- Take a history to find when infection occurred, also current i.v. Drugs or alcohol.
- Test for associated infections such as HIV, Hep B and STDs.
- Baseline LFTs may be helpful
- Outside pregnancy, interferon-alpha and tribavirin may be used, not used in pregnancy.

**Antibody and Viral Assays:**
- If HCV Antibody positive, then test for HCV viral load assay
- Those with a positive HCV viral load have a 10% risk of vertical transmission to the fetus
- Those who have a negative HCV viral load have a negligible risk of vertical transmission
- HCV is not associated with fetal anomalies or adverse pregnancy outcome, but there may be an increased risk of obstetric cholestasis.

**Hepatitis C obstetric management**

- No influence on mode of delivery
- Avoid fetal scalp sampling and scalp electrodes
- Double gloving and protective clothing (all deliveries and invasive procedures)
- Breastfeeding not contraindicated as transmission is uncommon
- No vaccines for the neonate and immune globulin not recommended
- Infectious Disease team follow up for puerperium

**Rubella**

- Rare and mostly avoidable
- Vaccination
- 14-21 days incubation => fever, malaise, upper respiratory inflammation.
- Fine pink maculopapular rash

**Congenital Rubella Syndrome**

- Chance of CRS:
  - <8 weeks 90%
  - 8-12 weeks 50%
  - 12-20 weeks 20%
  - >20 weeks ~0%
- Ultrasound for anomalies, Amnio for PCR
  - Microcephaly, Cataracts, Congenital deafness
  - Anaemia, thrombocytopenia
  - Cardiac defects
  - IUGR
  - Encephalitis
  -
Listeriosis

- RARE: 1:30,000 births
- Biphasic febrile illness in T3
  - Non-specific flu-like symptoms
  - Second attack within 10-15 days of premature delivery, likely reinfected contaminated placenta
- Culture to diagnosis
- May be associated with early (<34wks) meconium stained liquor

Infection in T2 – T3 associated with up to 50% fetal mortality
- Neonatal mortality >20%, higher if premature
- If infection during pregnancy, babies ill at birth or within hours:
  – RDS, cyanosis
  – Hepatosplenomegaly, jaundice
  – Purulent conjunctivitis
- Miliary necrosis of tissues, white nodules on placenta or abscesses on maternal side

Treatment:
- Ampicillin / amoxycillin plus Gentamicin
- Treat for 1 week after fever falls
- Avoid:
  – Unpasteurised foods
  – Chilled pre-prepared foods
  – N.B. THE MAJORITY OF SOFT CHEESES ARE PASTEURISED

Hepatitis B

- HBsAg is screening test, may indicated chronic or acute state if present
- Further screening: HBeAg, anti-HBeAb
- Highest risk are HBeAg
- Most common with i.v. Drug abuse, prostitution
- Check LFTs
Hepatitis B

- Risk of transmission
  - T1 and T2 10%
  - T3 75%
- Supportive management
- No data for mode of delivery
- Give neonate:
  - HBIg and vaccine at birth
  - Vaccine at 2, 4 and 12 months
- Breast feeding OK

Herpes Simplex Virus

- Main risk is primary infection during pregnancy
- <1% risk of transmission from overt lesions at time of vaginal delivery
- May be up to 3% if “shedding” but this is mostly cervical
- HSV-2 more recurrent than HSV-1
- Most recurrences are asymptomatic
- Serial cultures are not predictive of shedding in labour

Herpes Simplex Virus - avoidance

- Main concern is delivery around a primary attack or if a primary attack has occurred during the pregnancy
- Acyclovir in the last 4 weeks in pregnancy may prevent genital herpes
- Avoid invasive procedures during labour
- There is now no clear evidence for Caesarean Section for recurrent HSV
  - RCOG recommendations
  - Extensive experience in Netherlands (no cases in 20 years from vaginal delivery)