The baby at risk of HIV

Dr. J. P. Dadhich
New Delhi
Outline of the Presentation

- Overview
- Review of evidence on risk factors
## HIV Transmission Efficiency Rates

<table>
<thead>
<tr>
<th>Type of Exposure</th>
<th>Efficiency of single exposure</th>
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<tbody>
<tr>
<td>Blood Transfusion</td>
<td>&gt; 95%</td>
</tr>
<tr>
<td>Vertical Transmission</td>
<td>30% (12-40)</td>
</tr>
<tr>
<td>Breast Milk</td>
<td>14-20%</td>
</tr>
</tbody>
</table>
Timing of Mother-to-Child Transmission

Early Antenatal (<36 wks)

Late Antenatal (36 wks to labor)

Late Postpartum (6-24 months)

Early Postpartum (0-6 months)

Pregnancy

Labor and Delivery

Breastfeeding

Antenatal (36 wks to labor)

5-10%

10-20%

10-20%

<48hrs

7-90 days

Adapted from N Shaffer, CDC
MTCT in 100 HIV+ Mothers by Timing of Transmission

- **Uninfected:** 63
- **Breastfeeding:** 15
- **Delivery:** 15
- **Pregnancy:** 7
Risk Factors for HIV Transmission
Maternal Risk Factors For Transmission of HIV

- Immune/health status
- Plasma viral load
- Placental factors
- Breast milk virus
- Breast inflammation (mastitis, abscess, bleeding nipples)
- New HIV infection
- Viral Characteristics
Placental Risk Factors for transmission of HIV

- Transmission may occur through an intact placenta by transcytosis
- Risk increases if placental is damaged i.e. chorioamnionitis, smoking
- Usually in last trimester due to materno - fetal transfusion
Risk factors for Intrapartum Transmission

- First born twin
- Vaginal Delivery
- PROM > 4 hrs
- Difficult labor, Instrumentation
- Genital Infection
- Fetal Scalp Electrodes
Infant Risk Factors For Transmission of HIV

- Non-exclusive BF
- Age (first months)
- Lesions in mouth, intestine
- Infant immune response
Maternal viral load

- Indirect evidence of advanced maternal disease
- Important predictor of \textit{intra-partum} MTCT (Leroy et al, 2001; Semba et al, 1999)
- Risk factor during \textit{breastfeeding}
- The threshold below which there is no risk has not been identified

Kenya (Richardson et al, 2003), Tanzania (Fawzi et al, 2002), West Africa (Leroy et al, 2003)
# Maternal Virus Load and Perinatal Transmission

<table>
<thead>
<tr>
<th>Viral Load</th>
<th>Transmission Rate (%)</th>
</tr>
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<tbody>
<tr>
<td>&lt; 1000 copies/ml</td>
<td>0</td>
</tr>
<tr>
<td>1000–10000</td>
<td>16.6</td>
</tr>
<tr>
<td>10,001–50,000–</td>
<td>21.3</td>
</tr>
<tr>
<td>50,001–100,000–</td>
<td>30.9</td>
</tr>
<tr>
<td>&gt; 100,000</td>
<td>40.6</td>
</tr>
</tbody>
</table>

Garcia BM. NEJM, 1999
Maternal Viral Load

Risk of HIV transmission per day of BF (%)

Low Viral Load

High Viral Load

Richardson et al, 2003
Maternal viral load

Adjusted HR for Postnatal Transmission in West Africa Combined Analysis

Adjusted Hazard Ratio

ZDV 1.15
Plasma log10 viral load 2.65
CD4 < 500 3.14

Leroy et al 2003
Maternal immune status

HIV transmission from 6 w - 24 mo in West Africa by maternal baseline CD4

Leroy et al 2003
Maternal immune status

Hazard ratio for postnatal HIV transmission

BHITS meta-analysis, Read et al (CROI 2003)
Neonatal Period

- higher prevalence of mastitis, breastfeeding problems
- infant gut more immature, permeable
- greater exposure (higher concentration of cells)

(Nduati et al, 2000; John et al, 2001)
Neonatal Period

Estimated postnatal transmission during the first month of life

- Kenya: 4.5%
- Durban: 1.9%
- SAINT Study: 2.9%
- PETRA: 1.8%
Multiple gestation

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>Twin A</th>
<th>Twin B</th>
</tr>
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<tbody>
<tr>
<td>Vaginal</td>
<td>50%</td>
<td>19%</td>
</tr>
<tr>
<td>Caesarian</td>
<td>38%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Breastfeeding and HIV
How does HIV transmission during breastfeeding occur?

- Exact mechanisms unknown
- HIV virus in blood passes to breast milk
  - cell-associated, cell-free virus observed
  - virus appears intermittently (undetectable ~ 25-35%)
- Virus may also come directly from infected cells in mammary gland
  - produced locally in mammary macrophages, lymphocytes, epithelial cells (Becquart et al, 2002)
How does HIV transmission during breastfeeding occur?

- **Infant consumes HIV**
  - HIV enters/infects infant through permeable mucosal surfaces, lymphoid tissues, and/or lesions in mouth, intestines
  - Although BF infant may consume >500,000 virons, >25,000 infected cells per day, majority do NOT become HIV infected (Lewis et al, 2001)

- **Immune factors** in BM, saliva play a role (Miller et al, 2002; Sabbaj et al, 2002; Farquhar et al, 2002; Van der Perre et al, 1999; 1993; 1988)
Risk factors for postnatal transmission: Breast Pathology

- Breast inflammation & mastitis → increased risk of postnatal transmission (Embree et al; John et al; Semba et al)

- Nipple lesions, breast abscesses → increased transmission (Fawzi et al, 2002; Embree et al, 2000; Ekpini et al, 1997)


Estimated fraction of MTCT due to breast infection

<table>
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<tr>
<th>Country</th>
<th>Fraction</th>
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<tbody>
<tr>
<td>Malawi</td>
<td>18%</td>
</tr>
<tr>
<td>Kenya</td>
<td>20%</td>
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</table>
Association between breast inflammation and breast milk virus

Hoffman et al, 2003
Breast Pathology

Prevalence of breast pathologies in HIV+ women in Africa

**Mastitis (clinical or sub-clinical):**
- Clinical exam: 7-11% (Embree, 2000; John et al, 2001)
- Na+/K > 1.0: 11-12% at 6, 14 wk (Willumsen et al, 2000)
- Na+ > 12 mmol/L: 16.4% at 6 wk (Semba et al, 1999)

**Nipple lesions:**
- Clinical exam: 11-13% (Embree, 2000; John et al, 2001)
- Clinical exam: 10% (Ekpini et al, 1997)
- Hospitalized infants: 11% (Kambarami et al, 1997)

**Breast abscesses:**
- Clinical exam: 12% (John et al, 2001)
- Clinical exam: 3% (Ekpini et al, 1997)
Early Mixed breastfeeding

Cumulative HIV transmission Durban, SA

Birth 3 mo 6 mo 15 mo

% EBF to 3 mo Partial BF

Coutsoudis et al, 1999; 2001
Zidovudine Prophylaxis to mother and Rate of Perinatal transmission

<table>
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<tr>
<th>TEST Group</th>
<th>Placebo Group</th>
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<tbody>
<tr>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>7.6</td>
<td>22.6</td>
</tr>
<tr>
<td>(95% CI 4.3-12.3)</td>
<td>(95% CI 17-29)</td>
</tr>
</tbody>
</table>

Pediatric AIDS clinical trial group protocol 076. NEJM 1994
Maternal Malaria and MTCT

Among women dually infected with malaria and HIV, high-density placental malaria (>10,000 parasites/mL) was associated with increased risk for perinatal MTCT (ARR 2.0)

Conclusions

- Perinatal Transmission of HIV is preventable
- Antenatal counseling and testing
- Prophylaxis
- Avoidance of various risk factors

In USA, rate of vertical transmission is less than 2%
Thanks !!!!