Incident HIV Infection in Pregnancy/Breastfeeding – Prevention, Management.

Daya Moodley (PhD)
Womens Health and HIV Research Unit, Nelson R Mandela School of Medicine, University of KwaZulu Natal, South Africa
Definitions

• Incident HIV Infection: recently acquired

• Acute HIV Infection: Viraemia (10-20\textsuperscript{th} day)

• Early HIV Infection: Seroconversion (30\textsuperscript{th} - 90\textsuperscript{th} day)
UNAIDS Global AIDS Response

Target 3

- **Eliminate** mother-to-child transmission of HIV by 2015 and substantially reduce AIDS related maternal deaths
MOTHER-TO-CHILD TRANSMISSION RATES

De Cock KM, Fowler MG, Mercier E et al. JAMA 2000; 283: 1175-82
Prevention of MTCT in the US

% Transmission

1993: WITS
1994: PACTG 076
1997: PACTG 185
1999: WITS
2001: PACTG 247
2002: PACTG 316

24.5%
7.6%
5.0%
3.3%
2.0%
1.5%
Efficacy and safety of an extended nevirapine regimen in infant children of breastfeeding mothers with HIV-1 infection for prevention of postnatal HIV-1 transmission (HPTN 046): a randomised, double-blind, placebo-controlled trial

Hoosen M Coovadia, Elizabeth R Brown, Mary Glenn Fowler, Tsungai Chipato, Dhayendre Moodley, Karim Manji, Philippa Musoke, Lynda Stranix-Chibanda, Vani Chetty, Wafaie Fawzi, Clemensia Nakabiito, Lindwe Msweli, Roderick Kisesge, Laura Guay, Anthony Mwatha, Diana J Lynn, Susan H Eshleman, Paul Richardson, Kathleen George, Philip Andrew, Lynne M Mofenson, Sheryl Zwerski, Yvonne Maldonado, for the HPTN 046 protocol team

Figure 3: Kaplan-Meier analysis of cumulative rates of HIV-1 infection, by study group
Several Other Studies

- SWEN-Uganda, Ethiopia, India – 6.9%
- PEPI-Malawi – 5.2%
- MITRA-Tanzania – 1.2%
- KIBS-Kenya – 2.6%
- And others……
Estimated number of children (<15 years) newly infected with HIV  |  2011

Total: 330,000 [280,000 – 380,000]
Distribution of ART regimens for PMTCT 22 Priority Countries (2004-2010)

- Limited access to HCT
- Limited access to optimal PMTCT interventions
- Limited access to ARV treatment

Source: Aggregated data from HIV estimates files, UNAIDS 2011
What are we missing?

• Misdiagnosis – POC tests with poor sensitivity
• Window Period – seroconversion
• HIV acquisition subsequent to HCT
<table>
<thead>
<tr>
<th>Location</th>
<th>Reference</th>
<th>Pregnancy Rate</th>
<th>Post Delivery Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uganda</td>
<td>Gray R, Lancet 2005</td>
<td>2.3/100wy</td>
<td>1.3/100wy</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>Dube S, AIDS 2008</td>
<td>4.8/100wy</td>
<td></td>
</tr>
<tr>
<td>Tanzania</td>
<td>Urassa W, Scand J Pub Hlth, 2006</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>Nielsen K, Retrovirol, 2008</td>
<td>0.2/100wy</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>Birkhead, Int Confr AIDS, 2006</td>
<td>5.3/1000wy</td>
<td></td>
</tr>
<tr>
<td>Botswana</td>
<td>Lu L, 3rd HIV Ped Workshop, 2011</td>
<td>1.3%</td>
<td>3.8%</td>
</tr>
<tr>
<td>S Africa</td>
<td>Moodley D, AIDS, 2009</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>KZN, S Africa</td>
<td>Moodley D, JID, 2011</td>
<td>3.4% (2.5/100wy)</td>
<td></td>
</tr>
<tr>
<td>KZN, S Africa</td>
<td>Chetty, Moodley, JCV, 2012</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>Munjoma MW, BMC Pub Hlth, 2010</td>
<td>5.7/100wy</td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td>Kinuthia J, Curr HIV Res 2010</td>
<td>2.6% (68/100wy)</td>
<td></td>
</tr>
<tr>
<td>Malawi</td>
<td>Keating, MA, Plos One, 2012</td>
<td>1% (4/100py)</td>
<td></td>
</tr>
</tbody>
</table>
Continued Exposure to HIV During Pregnancy and Postdelivery

• Pregnancy is not protective against sexual transmission of HIV—irrespective of being married or being monogamous.
  – Sexual Activity
  – Condom Use
Sexual Activity among Women during Pregnancy and Postpartum– South Africa (n=2835)

<table>
<thead>
<tr>
<th></th>
<th>A: &gt; ONCE PER WEEK</th>
<th>B: ONCE/TWICE PER MONTH</th>
<th>C: ONCE IN 6 MONTHS</th>
<th>D: CURRENTLY ABSTAINING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>37%</td>
<td>43%</td>
<td>2%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Sexual Activity during early pregnancy, late pregnancy, postpartum, and non-pregnant study groups – Malawi (n=1087)

High sexual risk behavior among postpartum women in urban South Africa: implications for HIV prevention: The SAHAPS Study (South Africa)

Stankard, Maman, Moodley et al. High sexual risk behavior among postpartum women in urban South Africa: implications for HIV prevention. IAS 2012
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>N Infected</th>
<th>% MTCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuttall, et al</td>
<td></td>
<td>5</td>
<td></td>
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<tr>
<td>Rudin et al</td>
<td>Switzerland</td>
<td>2/4</td>
<td>50 %</td>
</tr>
<tr>
<td>Hague et al</td>
<td>UK</td>
<td>5/9</td>
<td>56 %</td>
</tr>
<tr>
<td>Nielsen-Saines et al</td>
<td>Brazil</td>
<td>3/9</td>
<td>33 %</td>
</tr>
<tr>
<td>Moodley D et al</td>
<td>South Africa</td>
<td>8/39</td>
<td>20.5% (vs 9%)</td>
</tr>
<tr>
<td>Lu, LS, 3rd HIV Ped Workshop, 2011</td>
<td>Botswana</td>
<td>275/377</td>
<td>73%</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>N Infected</td>
<td>% MTCT</td>
</tr>
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</tr>
<tr>
<td>Colebunders</td>
<td>DRC</td>
<td>1/3</td>
<td>33 %</td>
</tr>
<tr>
<td>Palasanthiran</td>
<td>Australia</td>
<td>3/11</td>
<td>27 %</td>
</tr>
<tr>
<td>Hira</td>
<td>Zambia</td>
<td>3/19</td>
<td>16 %</td>
</tr>
<tr>
<td>Van der Perre</td>
<td>Rwanda</td>
<td>8/15</td>
<td>53 %</td>
</tr>
<tr>
<td>Embree</td>
<td>Kenya</td>
<td>5/12</td>
<td>42 %</td>
</tr>
<tr>
<td>Liang</td>
<td>China</td>
<td>38/106</td>
<td>36 %</td>
</tr>
<tr>
<td>Lu L, 3rd HIV Ped Workshop, 2011)</td>
<td>Botswana</td>
<td>397/1103</td>
<td>36 %</td>
</tr>
<tr>
<td>Humphrey</td>
<td>Zimbabwe</td>
<td>/334</td>
<td>24 %</td>
</tr>
</tbody>
</table>
Primary Infection
Possible acute HIV syndrome
Wide dissemination of virus
Seeding of lymphoid organs

Clinical latency

Opportunistic diseases

Constitutional symptoms

Death

CD4 T Cells/mm³

Plasma Viraemia Titre

Weeks

Years
HIV IN PREGNANCY – VIRAL LOAD
WOMEN AND INFANTS TRANSMISSION STUDY (WITS): GARCIA ET AL., 1999

HIV Viral Load (copies/ml)

MTCT (%)
### HIV During Labour and Delivery – Viral Load

**Shaffer et al., JID (1999)**

<table>
<thead>
<tr>
<th>Maternal HIV RNA at Delivery (copies/ml)</th>
<th>MTCT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6,573</td>
<td>0%</td>
</tr>
<tr>
<td>6,573-13,177</td>
<td>10%</td>
</tr>
<tr>
<td>13,178-33,759</td>
<td>20%</td>
</tr>
<tr>
<td>33,760-93,126</td>
<td>30%</td>
</tr>
<tr>
<td>&gt;93,126</td>
<td>50%</td>
</tr>
</tbody>
</table>
HIV IN BREASTMILK – VIRAL LOAD

Rousseau et al, JID 2003; 187.
HIV Seroconversion and Breastfeeding Transmission

Women positive at baseline and at risk of breastfeeding associated transmission
- All postnatal seroconverters
- Postnatal seroconverters with seroconversion interval ≤90 days

Cumulative probability of infection

Days of HIV exposure

Log viral load

Plasma
Breast milk supernatant

Estimated time since maternal infection (days)

Humphrey J H et al. BMJ 2010;341:bmj.c6580
Maintaining high plasma HIV-1 RNA load after acute infection

- The proportion of extended high viremics was 34% [95% confidence interval (CI) 23–44%] during the period 100–300 days p/s
- The median (IQR) duration of HIV-1 RNA load at least 100,000 copies/ml among extended high viremics was 271 (188–340) days p/s
- Estimated that Early HIV index cases are responsible for 19%-52% of HIV transmissions in Lilongwe. Results suggest that the initial period of elevated transmissibility may be fairly long (~5 months), and that transmissibility during EHI is 30 times as great as during Chronic HIV.


Early Diagnosis of HIV Infection in Women
Repeat Antibody Testing

- Strategies to detect seroconversion during pregnancy are well established and cost-effective. A second anti-HIV during the third trimester along with rapid testing in labor to untested late presenters is an approach to detect late seroconversion (after the 2nd test):


“Repeat screening in the third trimester is recommended in certain jurisdictions with elevated rates of HIV infection among pregnant women.”
POC Tests for Early Diagnosis

• Sensitivities for early HIV infection
  – 3rd generation 55–57%
  – 4th generation 76–88%

Detecting Acute HIV Infections
Pooled NAAT Testing

Pooling is an established strategy for a timely diagnosis of HIV acute infection in seronegative/serodiscordant patients.

*Pilcher, 2002; Pilcher, 2005; Fiscus, 2007*

<table>
<thead>
<tr>
<th>Citation</th>
<th>Antenatal HIV Prevalence</th>
<th>N (NAAT+) / HIV - tested</th>
<th>Incidence of Acute HIV</th>
<th>Median Viral Load copies/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>30.2%</td>
<td>5/2321</td>
<td>0.21%</td>
<td>1,324,766</td>
</tr>
<tr>
<td>Gay et al, 2010 <em>Diagn Microbiol Infect Dis</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>37.3%</td>
<td>4/467</td>
<td>0.9%</td>
<td>386260 (64,200 -1,228,130)</td>
</tr>
</tbody>
</table>
Cost Implications for Pooled NAAT Testing

• **South Africa** (Kharsany, HIV Med 2010):
  – 4 of 467 tested RNA positive.
  – Cost of identifying a single case of AHI was $1313.

• **US** (Pilcher, JAMA 2002):
  – 5 of 8155 tested RNA positive.
  – the cost of identifying a single case of AHI was $4109.
The UN Four-Pronged Strategy for PMTCT

<table>
<thead>
<tr>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevention of HIV in young people</strong>&lt;br&gt;<strong>Prevention of HIV infection in women of childbearing age (including their partners)</strong></td>
<td><strong>Prevention of unintended pregnancies in HIV-positive women</strong></td>
<td><strong>Prevention of HIV transmission, from an HIV-positive woman to her infant</strong></td>
<td><strong>Care &amp; support for the mother and her family</strong></td>
</tr>
</tbody>
</table>
Preventing and Managing Incident HIV Infections During Pregnancy and Breastfeeding

**ART-PrEP If HIV Uninfected & At Risk**

**HCT & Risk Reduction Counselling**

**Repeat HIV Test & Risk Reduction Counselling**

**Early ART Treatment If HIV Infected**

**Early ART Treatment If HIV Infected**

**CC Female Condom Use**

**MICROBICIDE (CAP004)**

**ART-PrEP If HIV Uninfected & At Risk**

**Treatment Of STIs**

**ART-PrEP If HIV Uninfected & At Risk**

**Male Condom Use**
UNAIDS Global AIDS Response

• Target 3: Eliminate mother-to-child transmission of HIV by 2015 and substantially reduce AIDS-related maternal deaths
  – Percentage of HIV-positive pregnant women who receive antiretrovirals to reduce the risk of mother-to-child transmission
  – Percentage of infants born to HIV-positive women receiving a virological test for HIV within 2 months of birth
  – Mother-to-child transmission of HIV (modelled)
  – Percentage of women who are retested for HIV during pregnancy and breastfeeding
  – Percentage of women who seroconvert during pregnancy and breastfeeding
THANK YOU!