Neonatal HIV Case Series: Challenges in Diagnosis and Management

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Outline

• Background
• Mowbray Maternity Hospital High Risk HIV Transmission Protocol
• Aim and objectives
• Methods
• Results
• Conclusion & recommendations
Background: Transmission Risk

- Mother-To-Child-Transmission (MTCT) risk is increased with:
  - Unsuppressed maternal viral load
  - Incident maternal HIV infection
  - Inadequate maternal ARV prophylaxis

- SAPMTCTE study 2010:
  - MTCT rate at 4 – 8 weeks of age = 3.5% (95% CI 2.9 – 4.1%)

- Further gains may be possible by:
  - Identifying high risk transmission scenarios
  - Use of multi-ARV infant prophylaxis
  - Early neonatal HIV diagnosis and ART initiation
Background: Early Neonatal HIV Diagnosis

- **6 week HIV PCR testing:**
  - Current standard-of-care in SA PMTCT programme
  - Aims to detect *in utero* & *intrapartum* HIV transmissions

- **Birth HIV PCR testing:**
  - Detects *in utero* transmissions only
  - May facilitate very early ART initiation in HIV+ neonates

- **CHER study (2008):**
  - “Early HIV diagnosis and early antiretroviral therapy reduced early infant mortality by 76% and HIV progression by 75%.”
Background: Multi-ARV Infant Prophylaxis

- Nevirapine (NVP) for 6 weeks is current standard-of-care
- Transmission risk peaks during brief intrapartum period
  - Amenable to post-exposure prophylaxis
- “In neonates whose mothers did not receive ART during pregnancy, prophylaxis with a two- or three-drug ART regimen is superior to zidovudine alone for the prevention of intrapartum HIV transmission.”
  (Nielsen-Saines NEJM 2012)
Mowbray Maternity Hospital (MMH), Cape Town

- October 2013: Protocol implemented on recognition and management of mother/newborn pairs at increased risk of HIV transmission

- Protocol defines increased risk of infection and makes provision for:
  - Infant HIV PCR testing at birth or within 48 hours of delivery
  - Infant prophylaxis with NVP + AZT
  - Guidance on safe feeding practices
MMH High Risk HIV Transmission Protocol

- **Maternal factors:**
  - Maternal antiretroviral therapy < 8 weeks
  - Maternal viral load > 1000 copies/ml
  - Maternal viral rebound
  - Maternal comorbidity
  - Maternal substance abuse
  - Incident/recent infection (initial HIV test negative, subsequent tests positive)
  - Adolescent pregnancy (possible perinatally acquired HIV infection, more likely to have problems with follow up)
  - Likely resistance to non nucleoside reverse transcriptase inhibitors (NNRTI)

- **Infant factors:**
  - Symptomatic
  - Preterm delivery regardless of cause and/or LBW infants
  - Abandoned infants (if Alere Determine test or HIV ELISA test positive)
Study: Aim & Objectives

• **Aim:**
  - To evaluate the performance of the MMH High Risk HIV Transmission Protocol

• **Objectives:**
  1. To determine the number and proportion of confirmed positive and negative HIV PCR tests in relation to the number of HIV exposed neonates:
     - Within 48 hours of birth (in utero transmission rate)
     - 6 weeks of age (intrapartum / early postpartum transmission rate)
  2. To describe the management of neonates diagnosed HIV-positive within 48 hours of birth
Study Method

- Retrospective descriptive folder review
- All neonates who underwent HIV PCR testing within 48 hours of birth at MMH
- Study period: 1 Nov 2013 – 31 April 2014 (6 months)
- Patients were identified from the MMH HIV register (UCT HREC REF No.: R040/2014)
Results: Early HIV PCR Tests

600 HIV-exposed neonates during study period

117 had HIV PCR test within 48 hours of birth (19.5%)

9 confirmed positive (7.7%)

108 negative (92.3%)

In utero HIV transmission rate = 7.7%
Results: Indications for early HIV PCR testing among HIV-infected neonates

- 9 neonates HIV PCR + within 48 hours of birth
  - 5 mothers on ART
    - 3 for < 8 weeks
      - Failing 1st line ART
        - VL: 2290 copies/ml; $\log_{10} 3.36$
    - 2 for > 8 weeks
      - On 2nd line ART
        - VL 49823 copies/ml; $\log_{10} 4.7$
  - 3 mothers not on ART
    - Unbooked, newly diagnosed
## Characteristics: HIV – Infected Neonates

<table>
<thead>
<tr>
<th>Case</th>
<th>GA (wks)</th>
<th>Birth weight (g)</th>
<th>Co-morbidities</th>
<th>Baseline CD4 cells/mm³ / (%)</th>
<th>Baseline VL copies/ml (log₁₀)</th>
<th>Age (days) at ART initiation</th>
<th>ARV regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>1740</td>
<td>Congenital syphilis</td>
<td>1026 (22.4%)</td>
<td>16801 (4.23)</td>
<td>25</td>
<td>AZT, 3TC, KLT</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>2310</td>
<td>Congenital CMV</td>
<td>807 (21.41%)</td>
<td>636456 (5.8)</td>
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<tr>
<td>3</td>
<td>36</td>
<td>1920</td>
<td>None</td>
<td>440 (43%)</td>
<td>9292 (3.92)</td>
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<td>AZT, 3TC, KLT</td>
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<tr>
<td>4</td>
<td>32</td>
<td>1380</td>
<td>None</td>
<td>1933 (50%)</td>
<td>6701098 (6.07)</td>
<td>13</td>
<td>AZT, 3TC, NVP</td>
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<tr>
<td>5</td>
<td>32</td>
<td>1260</td>
<td>None</td>
<td>1933 (50%)</td>
<td>2962535 (6.47)</td>
<td>13</td>
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<tr>
<td>6</td>
<td>38</td>
<td>3520</td>
<td>None</td>
<td>3776 (51.88%)</td>
<td>314312 (5.5)</td>
<td>35</td>
<td>ABC, 3TC, KLT</td>
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<tr>
<td>7</td>
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<td>3260</td>
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<td>1744 (49.06%)</td>
<td>385653 (5.49)</td>
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<tr>
<td>8</td>
<td>38</td>
<td>3280</td>
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<td>942 (39.11%)</td>
<td>343 (2.54)</td>
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<td>-</td>
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<tr>
<td>9</td>
<td>29</td>
<td>1245</td>
<td>✗ None ✗</td>
<td>3880 (52.65%)</td>
<td>1146 (3.06)</td>
<td>None</td>
<td>-</td>
</tr>
<tr>
<td>Median</td>
<td>36</td>
<td>1920</td>
<td></td>
<td>1774 (49.06%)</td>
<td>314312 (5.5)</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

GA = gestational age
Results: Deaths among HIV – Infected Neonates

• Three neonates died:
  • Two before initiating ART
    • Lethal congenital cardiac anomaly (day 39)
    • Very low birth weight neonate with fulminant staphylococcal / pseudomonas septicaemia (day 13)
  • One on ART:
    • ART initiated on day 30
    • Recurrent ICU admissions
    • Fungal pneumonia and disseminated cytomegalovirus
Results: Infants on ART

- Six infants remain alive:
  - Three have features of evolving spastic cerebral palsy
  - Two remain well on ART
  - One is currently lost to follow-up
Results: 6-week HIV PCR Tests in Infants with Negative Early HIV PCR Test

Birth PCR negative: 108

6 week PCR: 75 results found (69%)
- 2 positive (2.7%)
- 73 negative (97.3%)

6 week PCR: 33 results not found (31%)

Intrapartum / early postpartum transmission rate: 2.7% (2/75)
Limitations of study

• Study design
  • Retrospective, preliminary, single-site, pilot study
  • No control group to assess HIV transmission in low-risk mother-infant pairs
  • Limited duration of follow-up (6 weeks)

• Missing 6-week HIV PCR test data
Conclusion & recommendations

• A risk-based HIV transmission protocol incorporating HIV PCR testing within 48 hours of birth and provision of dual ARV infant prophylaxis may be a useful strategy to further reduce mother to child transmission rates and improve outcomes for HIV-infected neonates.

• In this study, neonates with intrauterine transmission of HIV infection experienced significant morbidity and mortality.

• Further research and evaluation of this strategy is warranted.
Acknowledgments

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