Retention and long-term virologic outcomes in children and adolescents receiving HIV/ART care at a public sector tertiary level hospital in Zimbabwe

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Parirenyatwa Hospital Family Care Centre
Background

- Provision of HIV care in the public sector in low and middle income countries remains a challenge
- Successful outcomes on ART requires
  - life-long retention in care
  - adherence to ART
Methods

- Assessing long-term retention in care
  - Retrospective review of medical records
    - HIV positive children and adolescents (0-19 yrs) enrolled at Parirenyatwa HIV clinic between Jan 2004 – Dec 2011

- Determining clinical and virological outcomes
  - Cross sectional evaluation
    - Children and adolescents in care and on ART for at least 12 months
    - Clinical evaluation, CD4 count and viral load testing
    - Genotypic analyses of isolates from sub-set of children with evidence of virologic failure

- Tracing outcomes
  - Prospective evaluation of those enrolled in Cross-sectional study
    - evaluating follow up efforts
Parirenyatwa Hospital OI Clinic
Study Setting

- Parirenyatwa Hospital Family Care Center
  - Established in 2004
  - Affiliated with a public academic teaching institution
  - Children require 2 caregivers for ART initiation
  - Pre-ART and continuous counseling offered
  - HIV related medications and CD4 T-cell monitoring available at no cost to patient
  - No viral load monitoring at the time of study
2293 children and adolescents (ages 0-19 years) enrolled in care from 2004 to Dec 2011

Data extracted with double verification, and entered into an electronic database
Demographic Characteristics

- Median age at enrollment is 71 months
  - 26% of children enrolled in infancy
  - No change in infant enrollment overtime

- Equal gender distribution, though slight increase in female representation in adolescence.

- Mother primary care giver in 52.6%
  - Decreasing role of mother as primary caregiver in adolescence

- Over 50% of children present in WHO Stage 3 and 4 disease
Clinical Outcomes in children in care

- Engagement in care
- Retention in Care
- Successful outcomes in care

<table>
<thead>
<tr>
<th>Unaware of HIV infection</th>
<th>Aware of HIV infection (not in care)</th>
<th>Receiving some medical care but not HIV care</th>
<th>Entered HIV care but lost to follow-up</th>
<th>Cyclical or intermittent user of HIV care</th>
<th>Fully engaged in HIV care</th>
</tr>
</thead>
</table>

Not in HIV Care    Engaged in HIV Care

Gardner CID 2011; 52(6):793
High Rates of Early Program Attrition

- Excluded PMTCT children who subsequently tested negative – 50 children

- 752 children (33.2%) were linked but not engaged in care

- 1511 children (66.8%) were engaged for at least 3 months
Factors associated with being Linked and Not Retained in Care

- Age at enrollment. Infants are most vulnerable to being linked and not engaged
  - Infants (<2 years) HR 1
  - Young Children HR 0.49 (95%CI 0.27-0.74, p=0.002)
  - Older Children HR 0.56 (95%CI 0.37-0.85; p=0.01)
  - Adolescents HR 0.58 (95%CI 0.38-0.87; p=0.01)
- History of Pulmonary TB (HR 1.72, 95%CI 1.2-2.49, p=0.004),
- WHO stage III/IV disease (HR 2.34, 95%CI (1.64-3.34, p<0.001),
- Malnutrition with weight for age z-score <-2 (HR 1.56, 95%CI 1.08-2.29, p=0.02) were all associated with increased risk of LNE
- ART initiation reduced the likelihood of being LNE (HR 0.15 (95%CI 0.1-0.21, p<0.001)
Factors associated with Retention at 12 months

Factors associated with increased risk of not being retained in care at 12 months

- Severe immunosuppression (HR 0.86; 95% CI 0.77-0.96, p<0.01)
- Pulmonary TB (HR 0.76; 95% CI 0.65-0.90, p=0.001)
- WHO stage III/IV (HR 0.85; 95% CI 0.76-0.95, p=0.01)
- Malnutrition with weight for age z-score <-2 (HR 0.82; 95% CI 0.70-0.95)
- Not initiating ART (HR 0.52, 95% CI 0.45-0.60, p<0.001)
Long term retention in care

Retention Rate (%) over Months:
- On ART:
  - 6 months: 97%
  - 12 months: 90%
  - 18 months: 85%
  - 24 months: 81%
  - 36 months: 74%
  - 48 months: 69%
  - 60 months: 67%
- No ART:
  - 6 months: 79%
  - 12 months: 55%
  - 18 months: 44%
  - 24 months: 36%
  - 36 months: 24%
  - 48 months: 19%
  - 60 months: 16%
Clinical Outcomes in children in care

- Engagement in care
- Retention in Care
- Successful outcomes in care

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<tr>
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<th>Engaged in HIV Care</th>
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Gardner CID 2011; 52(6):793
# Results – Cross sectional analysis demographics & baseline clinical data

<table>
<thead>
<tr>
<th></th>
<th>Total n=702</th>
<th>&lt; 5 yrs n=103</th>
<th>5 to &lt; 10 yrs n=181</th>
<th>10 to &lt; 15 yrs n=210</th>
<th>15-19 yrs n=208</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Age (median, IQR)</strong></td>
<td>11.4 (7.1,16.0)</td>
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<td></td>
</tr>
<tr>
<td><strong>Mother as primary caregiver (n / %)</strong></td>
<td>337 / 48.1%</td>
<td>74 / 71.8%</td>
<td>120 / 66.3%</td>
<td>84 / 40.0%</td>
<td>59 / 28.6%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Caregiver employed (n/%)</strong></td>
<td>279 / 42.3%</td>
<td>38 / 38.4%</td>
<td>76 / 44.7%</td>
<td>85 / 42.1%</td>
<td>80 / 42.6%</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Severe immunosuppression</strong></td>
<td>286 / 44.3%</td>
<td>42 / 43.8%</td>
<td>55 / 31.4%</td>
<td>91 / 47.2%</td>
<td>98 / 53.9%</td>
<td>0.0002</td>
</tr>
<tr>
<td><strong>History of TB</strong></td>
<td>257 / 37.8%</td>
<td>24 / 24.0%</td>
<td>55 / 31.4%</td>
<td>86 / 41.8%</td>
<td>92 / 46.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>HAZ score &lt; -2</strong></td>
<td>30 / 39.5%</td>
<td>6 / 6.8%</td>
<td>46 / 25.6%</td>
<td>174 / 82.9%</td>
<td>203 / 98.1%</td>
<td></td>
</tr>
<tr>
<td><strong>WAZ score &lt; -2</strong></td>
<td>15 / 15.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HIV status disclosed</strong></td>
<td>430 / 61.4%</td>
<td>7 / 6.8%</td>
<td>46 / 25.6%</td>
<td>174 / 82.9%</td>
<td>203 / 98.1%</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
# Results cross sectional analysis

## Clinical & Immunological outcomes

<table>
<thead>
<tr>
<th></th>
<th>Total n=700</th>
<th>&lt; 5 yrs n=103</th>
<th>5 to &lt; 10 yrs n=181</th>
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<th>15-19 yrs n=207</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at ART initiation (median, IQR)</td>
<td>8.0 (3.0, 12.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time on ART (years)</td>
<td>3.0 (1.7, 4.5)</td>
<td>1.6 (1.0, 2.5)</td>
<td>3.2 (1.7, 4.5)</td>
<td>3.4 (1.8, 4.8)</td>
<td>3.5 (2.5, 4.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CD4 percent</td>
<td>584 / 24.5%</td>
<td>102 / 29.3%</td>
<td>143 / 33.8%</td>
<td>164 / 26.1%</td>
<td>175 / 11.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Severe immunosuppression</td>
<td>64 / 9.2%</td>
<td>8 / 7.8%</td>
<td>4 / 2.2%</td>
<td>11 / 5.3%</td>
<td>41 / 19.9%</td>
<td>0.0002</td>
</tr>
<tr>
<td>HAZ score &lt; -2</td>
<td>217 / 42.4%</td>
<td>30 / 39.5%</td>
<td>34 / 22.8%</td>
<td>90 / 55.2%</td>
<td>63 / 50.8%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

## ART Regimen

<table>
<thead>
<tr>
<th>ART Regimen</th>
<th>Total n=700</th>
<th>&lt; 5 yrs n=103</th>
<th>5 to &lt; 10 yrs n=181</th>
<th>10 to &lt; 15 yrs n=209</th>
<th>15-19 yrs n=207</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D4T based regimens</td>
<td>430 / 67.9%</td>
<td>39 / 38.6%</td>
<td>101 / 63.9%</td>
<td>129 / 72.1%</td>
<td>159 / 17.6%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NVP based regimens</td>
<td>510 / 80.5%</td>
<td>78 / 77.2%</td>
<td>132 / 83.5%</td>
<td>149 / 83.3%</td>
<td>149 / 76.8%</td>
<td></td>
</tr>
<tr>
<td>PI based regimen</td>
<td>55 / 8.7%</td>
<td>20 / 19.8%</td>
<td>10 / 6.3%</td>
<td>6 / 3.4%</td>
<td>19 / 9.8%</td>
<td></td>
</tr>
</tbody>
</table>
Results – Cross sectional analysis

Virologic outcomes

Overall 31.1% of study participants had evidence of virologic failure

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Virologic Failure</th>
<th>Without Virologic Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants &amp; Younger children (&lt;5 years, n=103)</td>
<td>27.2%</td>
<td>72.8%</td>
</tr>
<tr>
<td>Older children (5 to &lt;10 years, n=181)</td>
<td>26.0%</td>
<td>74.0%</td>
</tr>
<tr>
<td>Younger adolescents (10 to &lt;15 years, n=209)</td>
<td>28.6%</td>
<td>71.4%</td>
</tr>
<tr>
<td>Older adolescents (15 to 19 years, n=207)</td>
<td>39.9%</td>
<td>60.1%</td>
</tr>
</tbody>
</table>
Results – genotypic analysis

- 36 (28.8%) patients no mutation
- 77 (71.2%) patients with mutation
  - 62.3% with M 184 V mutation
  - 32.5% with K 103 N mutation
  - 40.3% with Y 181 C mutation

<table>
<thead>
<tr>
<th>Drug Resistance Mutation</th>
<th>Confers resistance to...</th>
<th>Frequency</th>
<th>% of Isolates (N=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M184VI</td>
<td>3TC/FTC</td>
<td>48</td>
<td>62.3%</td>
</tr>
<tr>
<td>TAM1 (M41L, L210W, T215Y)</td>
<td>D4T/AZT</td>
<td>11</td>
<td>14.3%</td>
</tr>
<tr>
<td>TAM2 (D67N, K70R, 219Q)</td>
<td>D4T/AZT</td>
<td>16</td>
<td>20.8%</td>
</tr>
<tr>
<td>K65R</td>
<td>TDF</td>
<td>2</td>
<td>2.6%</td>
</tr>
<tr>
<td>L74IV</td>
<td>ABC/DDI</td>
<td>4</td>
<td>5.2%</td>
</tr>
<tr>
<td>Q151M</td>
<td>ZDV/D4T, all NRTIs except TDF</td>
<td>1</td>
<td>1.3%</td>
</tr>
<tr>
<td>NNRTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K103N</td>
<td>EFV</td>
<td>25</td>
<td>32.5%</td>
</tr>
<tr>
<td>Y181C</td>
<td>NEV</td>
<td>31</td>
<td>40.3%</td>
</tr>
<tr>
<td>PROTEASE INHIBITORS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L10F/I/R/V, V32I, M46I/L,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I54V/M/L, V82A/F/T/S,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I84V/A/C, L90M</td>
<td></td>
<td>5</td>
<td>6.5%</td>
</tr>
</tbody>
</table>
Conclusions

Success of public ART program for children and adolescents is threatened by:

- Early program attrition
- Poor long-term retention rates
- High virologic failure rates
  - Clinically significant resistance mutations
“Africa’s under-five population will swell by 51% by 2050, and its under-18s will increase by two thirds to almost 1 billion. The number of adolescents will grow by 83% to almost half a billion. By 2100, Africa will be home to almost half the world’s children under 18”
Acknowledgements

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- Nurses
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- Peer Counselors
- Laboratory Staff
- Medical Records Team

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- Sr. Mujaji
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  - Dr. Bwakura
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