Growth evolution and stunting among HIV-infected adolescents in the multiregional IeDEA cohort consortium

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Conflicts of interest

• Nothing to disclose
Growth and nutrition during adolescence

- 10-19 years = 2\textsuperscript{nd} period of growth during life, highest energetic needs
- High burden of stunting (>50% in some developing countries)
- “Adolescents are a neglected group in terms of Nutrition” (Save the children)
- Among HIV-infected adolescents, few estimates available, no specific nutritional recommendations

- Delayed pubertal development associated with stunting (Height-for-age Z-score (HAZ) <-2)

Pubertal staging, Tanner scale

One unit lower pre-ART HAZ delayed age on reaching each stage

\textit{Szubert et al., AIDS 2013}
Objective and choice of study population

• To assess the prevalence of stunting among HIV-infected adolescents and explore growth trajectories

• Need to assess growth separately by mode of transmission
  – Delayed puberty and growth retardation due to chronic disease may occur for perinatally-infected ++ compared to behaviourally-infected adolescents
  – Lack of documentation on mode of transmission - difficult to distinguish

=> Objective restricted to perinatally-infected adolescents as a first step
How to define HIV-transmission mode among adolescents?

• If transmission mode not documented, threshold of age often used as a proxy
  – Previous analyses (e.g. CIPHER global cohort) have assumed perinatal infection if children enter care <10 years of age.

• However, in our data, when mode of transmission was recorded
  – most adolescents entering care between 10-15 years old were documented as perinatally infected.

• Definition selected in our study (if transmission mode not documented):
  – Perinatal infection = children entered in care before 15 years of age
  – Behavioural infection = children entered in care after 15 years of age
Methods

• Study design and population
  – HIV-infected adolescents from the IeDEA consortium: multiregional collaboration including cohorts of patients routinely followed-up in clinical care centres worldwide

• Inclusion criteria
  – Enrolment at < 15 years of age from 2003 to 2016, considered as perinatally-infected
  – With height measurement available while aged 10-19 years old

• Stunting
  – Height-for-Age Z-score (HAZ) < -2 SD (WHO child growth standards)

• Curves
  – Stratified by gender
  – By age at ART initiation, immunodeficiency and stunting at ART initiation/ at 10 years
Total N=28,884
28 countries, 267 centers

Between 10 and 19y old:
Median follow-up time = 4.1y (IQR 2.0-6.5)
Median number of visits = 9 (IQR 3-19)
Descriptive results

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (N=28,884)</th>
<th>West Africa (N=2666)</th>
<th>Central Africa (N=1753)</th>
<th>Southern Africa (N=19,777)</th>
<th>Asia-Pacific (N=3521)</th>
<th>CCASAnet (N=1167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatally infected* on the overall population, %</td>
<td>76</td>
<td>96</td>
<td>83</td>
<td>71</td>
<td>98</td>
<td>78</td>
</tr>
<tr>
<td>Girls, %</td>
<td>52</td>
<td>49</td>
<td>53</td>
<td>52</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>On ART, %</td>
<td>98</td>
<td>95</td>
<td>88</td>
<td>100</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td>Severe immunodeficiency for age† at 10y old, %</td>
<td>13</td>
<td>11</td>
<td>15</td>
<td>12</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Severe immunodeficiency for age at 15y old, %</td>
<td>17</td>
<td>22</td>
<td>18</td>
<td>17</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>Stunting ‡ at 10y old, %</td>
<td>38</td>
<td>26</td>
<td>31</td>
<td>40</td>
<td>42</td>
<td>21</td>
</tr>
<tr>
<td>Stunting at 15y old, %</td>
<td>45</td>
<td>37</td>
<td>36</td>
<td>50</td>
<td>36</td>
<td>27</td>
</tr>
</tbody>
</table>

* Documented as perinatally-infected or if not, entered in care before 15 years of age
† Severe: CD4 count<250/ml, ‡ Stunting: Height-for-age Z-score < -2 SD
Evolution of growth for girls and boys

**Girls**

- **Height-for-age Z-score**
- **Height gains, cm/year**

**Boys**

- **Height-for-age Z-score**
- **Height gains, cm/year**

In black: Median height velocity according to 2000 CDC growth charts
Evolution of growth by age at ART initiation

Girls

Boys

HAZ

Age (years)

0-5 years old

5-10 years old

>10 years old
By stunting at ART initiation (top) / 10 years old (bottom)

- **No stunting** (HAZ>-2 SD)
- **Moderate stunting** (HAZ=[-3;-2] SD)
- **Severe stunting** (HAZ<-3 SD)

**Girls**

**Boys**

By CD4 count at ART initiation (top) / 10 y old (bottom)
Conclusions, synthesis of the results

• High prevalence of stunting among perinatally-infected adolescents (20 to 50%)

• Growth was greater for
  – those initiated early on ART,
  – those not stunted at ART initiation/10y
  – those not severely immunodeficient at 10y

• Growth trajectories differ between boys and girls
  – Could be explained by differences in pubertal delay and growth spurt
  – By age 19y, better Height-for-age Z-score for girls because growth spurt happened earlier than for boys
Conclusions, limits and perspectives

• Survival bias
  – Sicker, perinatally-infected children may have died before the age of 10
  – Healthier children, with a higher probability to survive until adulthood, could have better height gains

• Indication bias
  – Children could have entered care between 10 and 15 years because they are sick

• Next steps: modelling of growth during adolescence
  – Separately for perinatally and behaviourally mode of transmission
  – Separately for boys and girls, taking into account the inflection point observed on the growth trajectories
  – Identifying the start of growth spurt could help for further nutritional interventions targeting HIV-infected adolescents
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