Followed in clinics involved in the IeDEA consortium in sub-Saharan Perinatal CCASAnet. HAZ increasing at late adolescence. Logistic regressions to estimate factors associated with difference in puberty development between ≥ 1 height measurement during adolescence, CCASAnet Health Sciences, Uppsala, Sweden; 2/ Faculty of Health Sciences, Wits Reproductive Health and HIV Research Institute, University of the Witwatersrand, Johannesburg, South Africa; 10/ Centre for Whistleblower Disease Research in Zambia, Luaka, Zambia; 11/ Department of Child Health and Paediatrics, School of Medicine, College of Health Sciences, Nko University, Edin, Kenya; 12/ Ryan White Center for Pediatric Infectious Disease and Global Health, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, Indiana, USA, 14/ Vanderbilt University School of Medicine, Nashville, TN, USA. 14/ Division of Epidemiology, The Ohio State University, College of Public Health, Columbus, OH, USA.

Methods

Study population: - HIV-infected adolescents 10-19 years, - ≥ 1 height measurement during adolescence, - Followed in clinics involved in the IeDEA consortium in sub-Saharan Africa, Asia-Pacific, and Caribbean, Central and South America regions, between 2003 and 2016.

Main outcome: Stunting Height for Age Z (HAZ) < -2 SD, (WHO Child Growth Standards)

Explanatory variables and definitions: - Perinatal/behavioral infection (if not documented) = having entered care before or after 15 years of age - Immunodeficiency by age: no=550, moderate=350-500, severe=350 CD4 cells/mL - Age at ART initiation and first ART regimen, sex - Entering care = initial enrollment in cohort - Leaving care = death, transfer out, drop out, lost to follow-up

Statistical analyses: (using SAS software) - Logistic regressions to estimate factors associated with stunting at age 10-15 and 18 years - Description of growth HAZ curves, stratified by sex, with prevalence of stunting and sex ratio while entering or leaving care between 10-15 and 15-19 years.

Results: Flow-chart

One visit between 10-19 years old: N=68 461
One height measurement available (all visits): N=54 414, 79%
One height measurement available between 10-19 years: N=50 461, 93%
One HAZ available between 10-19 years: N=50 434, *100%

Among the increasing cohort of HIV-infected adolescents worldwide, little is known about their growth.

In the International AIDS Database to Evaluate AIDS (IeDEA) consortium of programmatic cohorts, where data come from routine HIV care, our aim was:
- To estimate the prevalence of stunting and associated factors
- To describe growth curves of HIV-infected adolescents

Variables

- Total
- West Africa
- Central Africa
- East Africa
- Southern Africa
- Asia-Pacific
- CCASAnet

Perinatally infected, % 70 96 84 60 71 98 78
Girls, % 60 53 66 66 51 58
On ART, % 95 96 85 83 100 96 94
Age at ART initiation, median [IQR] 11.6 [7.9-16.2] 9.3 11.2 11.7 12.5 7.0 8.5
Stunting at ART initiation, % 38 41 27 30 34 50 26
Severe immunodeficiency at 10 years of age, % 12 16 15 10 15 16

Prevalence of stunting and associated factors

At 10y of age N= 19 078 36%
At 15y of age N= 14 292 45%
At 18y of age N= 11 332 27%

Multivariate analysis (adjusted by regions)

<table>
<thead>
<tr>
<th>Variable</th>
<th>At 10y of age</th>
<th>At 15y of age</th>
<th>At 18y of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (girls vs boys)</td>
<td>1.21 [1.14-1.28] &lt;0.001</td>
<td>0.91 [0.80-0.93] &lt;0.001</td>
<td>0.23 [0.21-0.26] &lt;0.001</td>
</tr>
<tr>
<td>Age at ART initiation (vs 0-5y)</td>
<td>&lt;0.001</td>
<td>1.25 [0.87-1.82]</td>
<td>1.27 [1.22-2.61]</td>
</tr>
<tr>
<td>5-10 years</td>
<td>1.78 [1.65-1.93]</td>
<td>1.64 [1.39-1.95]</td>
<td>1.51 [1.26-1.84]</td>
</tr>
<tr>
<td>10-15 years</td>
<td>1.26 [1.19-1.32]</td>
<td>2.05 [2.11-2.97]</td>
<td>1.35 [1.23-1.48]</td>
</tr>
<tr>
<td>15-19 years</td>
<td>-</td>
<td>-</td>
<td>1.26 [1.22-2.77]</td>
</tr>
<tr>
<td>Not on ART</td>
<td>1.52 [1.18-1.93]</td>
<td>1.35 [1.10-1.73]</td>
<td>0.82 [0.53-1.29]</td>
</tr>
<tr>
<td>First ART regimen (vs NNRTI-based)</td>
<td>0.003</td>
<td>0.005</td>
<td>0.029</td>
</tr>
<tr>
<td>PI-based</td>
<td>0.89 [0.83-0.95]</td>
<td>0.88 [0.81-0.96]</td>
<td>0.94 [0.84-1.06]</td>
</tr>
<tr>
<td>NNRTI or unknown</td>
<td>0.81 [0.71-0.93]</td>
<td>1.07 [0.92-1.25]</td>
<td>1.27 [1.04-1.55]</td>
</tr>
<tr>
<td>Immunodeficiency by age (vs no)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.005</td>
</tr>
<tr>
<td>Severe</td>
<td>1.12 [1.00-1.26]</td>
<td>0.86 [0.76-0.99]</td>
<td>0.77 [0.63-0.92]</td>
</tr>
<tr>
<td>Moderate</td>
<td>1.93 [1.74-2.13]</td>
<td>1.30 [1.16-1.45]</td>
<td>1.01 [0.87-1.18]</td>
</tr>
<tr>
<td>Missing</td>
<td>1.20 [1.11-1.29]</td>
<td>1.14 [1.04-1.25]</td>
<td>1.03 [0.91-1.18]</td>
</tr>
<tr>
<td>Mode of transmission (perinatally vs behaviourally)</td>
<td>-</td>
<td>-</td>
<td>1.25 [1.04-1.51] 0.017</td>
</tr>
</tbody>
</table>

Conclusions and Discussions

Stunting = major concern among HIV-infected adolescents worldwide.
- Late age at ART initiation strongly associated with stunting all along adolescence
- Severe immunodeficiency and NNRTI-based regimen possibly associated with stunting at 10-15 years.
- Perinatally infected children were slightly more stunted than behaviourally infected children, likely due to their long-life infection.

Growth evolution during adolescence differed between 10-15 and 15-19 years and between girls and boys.
- Mixed population: perinatally and behaviourally infected adolescents, with patients entering or leaving care during adolescence, all with different advancement on the HIV disease.
- Difference in puberty development between girls and boys could explain why boys are more stunted than girls during this period

The heterogeneity of the HIV-infected adolescent population followed in HIV programs should be taken into account, especially for the development of future nutritional programs.

Acknowledgments

All adolescents enrolled in the IeDEA consortium in the ecologic studies and investigators from the IeDEA regions.

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