Virological characterization of new HIV diagnoses in adolescents in Spain

OR-15

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Importance: Why adolescents?

**Definition:** period in human growth and development that occurs after childhood and before adulthood, **from ages 10 to 19** (WHO and UNAIDS)

Key phase of human development:
- biological and psychological transitions
- learn behaviors and establish identity
- risky behaviors related with acquiring HIV

Slogrove. Curr Opin HIV AIDS. 2018
Global concern HIV in Adolescents

Adolescents living with HIV by 2018
- Total=1.7E+006
- 88.82% All ages
- 11.18% Adolescents (10-19)

Newly infected with HIV
- 1.6 million
  - [1.1 million-2.3 million]

Dying of AIDS-related causes
- 190.000
  - [59.000-380.000]
- 33.000
  - [22.000-47.000]

Adolescent living (10-19) with HIV
- 1.6 million
  - [1.1 million-2.3 million]

Chi square for trend: p<0.00001

HIV is now the number 2 cause of death among adolescents. WHO 2016.

UNAIDS 2019 estimates
Global concern HIV in Adolescents

HIV adolescents: population at greater risk of being **lost to follow-up** and dying than younger children and adults living with HIV

Poor adherence to treatment, treatment failure and high rate of HIV transmission due to sexual behaviors

**HIV Drug resistance**

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**Global Action Plan on HIV drug resistance (HIVDR) and its five Strategic Objectives**

1. **PREVENTION AND RESPONSE**
   - Implement high impact interventions to prevent and respond to HIVDR.

2. **MONITORING AND SURVEILLANCE**
   - Obtain quality data on HIVDR and HIV service delivery from periodic surveys, while expanding routine viral load and HIVDR testing.

3. **RESEARCH AND INNOVATION**
   - Encourage relevant and innovative research which will have the greatest public health impact in minimizing HIVDR.

4. **LABORATORY CAPACITY**
   - Support and expand use of viral load testing and build capacity to monitor HIVDR.

5. **GOVERNANCE AND ENABLING MECHANISMS**
   - Ensure country ownership, coordinated action, awareness/advocacy and sustainable funding are in place to support action on HIVDR.
New HIV diagnoses in adolescents in Spain: Clinical and Virological characterization

Collaborative study of

12 - < 20 year-old

CoRIS pe

From 2008, patients in follow-up since 1995 in pediatric HIV units in Spain.

From 2004, naïve patients in follow-up in more than 40 adult HIV units since 1981

357 adolescents diagnosed with 12 - < 20 year-old (1981-2017)

Epalza Cristina. Reunión docente de la RIS 2019
New HIV diagnoses in adolescents in Spain

Prevention, monitoring and timely response to population levels of HIV drug resistance (HIVDR)

Critical to achieving the WHO/UNAIDS 95–95–95 targets for 2030

HIV drug resistance report 2019. WHO/CDS/HIV/19.21

Scarse data published in adolescents population

**OBJETIVE:** to analyze virological outcomes (HIVDR, HIV variants) among adolescents diagnosed between the ages of 12 to <20 years under-follow up in pediatric and adult sites in Spain until 2017.
Methods

New HIV diagnoses in adolescents in Spain (1981-end 2017)

≥12 - < 20 year-old

HIV-1 pol (PR and RT) sequences amplified by NESTED-PCR or recorded from clinical routine until 2017

Most sequences are previously published in the pediatric population studies.

2011

2012

2018
357 adolescents diagnosed with ≥12 - < 20 year-old (1981-2017)

112 (31%) adolescents with available HIV-1 pol (PR and RT) sequences closest to diagnosis from 2003 to 2017

- Resistance mutations (HIVDR) were analysed according to the International AIDS Society 2019 list and interpreted using the Stanford algorithm 8.9.
- HIV-1 variants were characterized by phylogenetic analysis (ML+GTR).
### Results: Differences between total and virological cohort?

<table>
<thead>
<tr>
<th>Demographical features</th>
<th>Total Cohort (N=357)</th>
<th>Virological Cohort (N=112)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR)</td>
<td>18.7 (17.8-19.5) years</td>
<td>19.0 (18.1-19.59) years</td>
<td>ns</td>
</tr>
<tr>
<td>Male sex No (%)</td>
<td>269 (75.4%)</td>
<td>92 (82.14%)</td>
<td>ns</td>
</tr>
<tr>
<td>Mode of infection No (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertical</td>
<td>10 (3%)</td>
<td>1 (0.8%)</td>
<td>ns</td>
</tr>
<tr>
<td>Transfusion</td>
<td>6 (2%)</td>
<td>3 (2.7%)</td>
<td>ns</td>
</tr>
<tr>
<td>Behaviourally MSM</td>
<td>330 (92.2%)</td>
<td>103 (91.9%)</td>
<td>ns</td>
</tr>
<tr>
<td>Behaviourally Htsex</td>
<td>84 (24%)</td>
<td>26 (23.2%)</td>
<td>ns</td>
</tr>
<tr>
<td>Behaviourally PWID</td>
<td>54 (15%)</td>
<td>9 (8%)</td>
<td>ns</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (3%)</td>
<td>3 (2.7%)</td>
<td>ns</td>
</tr>
<tr>
<td>Country of birth No (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>225 (62%)</td>
<td>73 (65.2%)</td>
<td>ns</td>
</tr>
<tr>
<td>Other</td>
<td>131 (38%)</td>
<td>39 (34.8%)</td>
<td>ns</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.3)</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Latin America</td>
<td>93 (69%)</td>
<td>31 (79.5%)</td>
<td>ns</td>
</tr>
<tr>
<td>Other countries</td>
<td>38 (31%)</td>
<td>8 (20.5%)</td>
<td>Ns</td>
</tr>
<tr>
<td>Late presenters</td>
<td>123 (34.5%)</td>
<td>33 (29.5%)</td>
<td>ns</td>
</tr>
</tbody>
</table>

MSM: men who have sex with men  
Htsex: Heterosexual contact  
PWID: patients who infect drugs

No significant differentes among cohorts.  
The Virological cohort could represent the virological status of total cohort.
Results: Demografical features in the Virological cohort

By age at HIV diagnosis

- 12 to <18: early and middle adolescence
- 18 to <20: late adolescence

Error Bars: CI95%

Sex
- Male: 65% (p=0.0174), 35%
- Female: 87%, 13%

Origin
- Spain: 61%, 68%
- Foreign: 39%, 34%

Mode of Infection
- Blood: 0%, 8%
- PWID: 13%, 9%
- HTsex: 22%, 24%
- MSM: 52%, 66%
- Unknown: 4%, 2%

↑ Female adolescents (p=0.0174)
↑ blood recipient (p=0.0006)
with available genotype diagnosed in early-middle adolescence vs. those in late adolescence
Results: **Late presenters** adolescents in the virological cohort *(CD4<350/µl)*

Antinori et al. HIV Medicine 2011

Late diagnosis (CD4<350 cells/µl)

By age at HIV diagnosis

- **Total cohort**: 33/112
- [12-<18]: 7/23
- [18-<20]: 28/89
- Blood: 3/3
- Unknown: 2/3
- PWID: 3/9
- **Htsex**: 10/26
- MSM: 15/71
- Spanish: 18/73
- Foreign: 15/39

By risk group

- Blood group vs MSM (p=0.0018)
- Htsex (p=0.04)
- PWID (p=0.04)

By Origin

- **Total cohort** (adults and adolescents)
  - Spanish: 33/112
  - Foreign: 7/23
  - PWID: 28/89

Vigilancia epidemiológica del VIH y el SIDA en España. Actualización 30 de junio de 2019

Results: Prevalence of HIV drug resistance in adolescents

Naïve: Transmitted Drug Resistance (TDR)

- WHO 2009
- Dotted line: 8.3% TDR prevalence in Europe
- 12% TDR prevalence in adults from Spain

Pretreated: Acquired Drug Resistance (ADR)

- All NRTI-experienced
  8/12 (67%) had PI-experience
- Dotted line: 29% of global ADR in adults
  HIV drug resistance report 2019,WHO

↑ TDR rate to any drug class ↑ NNRTI TDR in naive adolescents
↑ ADR (33%) → one in three adolescents have ADR to any ARV
  → one in four adolescents have ADR to IP after 2.6 years of treatment
Results: **TDR prevalence** in newly diagnosed adolescents by group

- **no statistical differences** in TDR prevalence within groups
  - LP: late presenter, NLP: no late presenter
43% prevalence of TDR E138A
6/14 adolescents

Results: Punctual TDR in newly diagnosed adolescents

E138A is a polymorphic mutation that ranges in prevalence from about 1% to 5% depending on subtype
The presence of E138A prior to therapy may reduce the antiviral activity of *Rilpivirina*.
Prevalence of non-B HIV variants in the newly diagnosed adolescents is 19%, 10% carried recombinants, 7% pure non-B variants and 1% URF variants.

In the Spanish adult population the prevalence of non-B variants is 17%

Conclusions

- Our data suggest a relative high TDR prevalence (14%) among adolescents HIV diagnosed between 12 to <20 years of age, specifically among diagnosed in early and middle adolescence (12-<18 years old), born in foreign countries and late presenters.

- These findings could have implications during the choosing of initial regimens for ART-naïve adolescents, specially in NNRTI-based first-line regimens.

- One in four adolescents under ART presented HIVDR major to PI, this suggests a periodic surveillance within this group of patients.
Acknowledgements

África Holguín
Miguel Gutiérrez
Marina Rubio
Ana Valadés

Cristina Epalza
Eloísa Cervantes

Marisa Navarro
Santiago Jiménez de Ory
**HIV drug resistance: Impact**

**Spain**: baseline genotypic resistance testing to reverse transcriptase (RT) and protease (PR) in plasma is recommended. DR test must be known before starting ART only when NNRTI is considered in the initial therapy.

**Table 1**: Projected impact of HIV drug resistance on AIDS deaths, new infections and ART costs in sub-Saharan Africa (pretreatment HIVDR > 10% in Fast-Track countries) during 2016–2020 and 2016–2030, assuming the use of NNRTI-based regimen in first-line ART.

<table>
<thead>
<tr>
<th></th>
<th>AIDS deaths</th>
<th>New HIV infections</th>
<th>ART costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount attributable to HIVDR</td>
<td>135 000</td>
<td>890 000</td>
<td>105 000</td>
</tr>
<tr>
<td>Percentage attributable to HIVDR</td>
<td>5.7%</td>
<td>16%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>


WHO's 10% threshold for changing first-line non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART to integrase inhibitor-based ART.
New HIV diagnoses in adolescents in Spain

357 adolescents diagnosed with ≥12 - < 20 year-old (1981-2017)

Epalza Cristina. PO-12. GeSIDA. Toledo. 2019

Change in trend = 2005 (95% CI 2000-2009)
P-trend=0.025

Before vs. after 2005

↑ Men (p 0.012)

↑ ↑ Sexual (p<0.001)

↑ ↑ MSM

↑ Heterosexual

↑ Foreigners (p<0.001)