Molecular Epidemiology and HIV-1 Drug Resistance in Infected African Migrants Followed-up in Portugal

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on behalf of the Portuguese HIV-1 Drug Resistance Study Group

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In 2015, 37% of new HIV diagnosis in the EU were among migrants.
HIV Infection in Migrants in Europe

Higher proportions of people from Sub-Saharan Africa and South and South-East Asia (both 56%) had CD4 counts of below 350 cells per mm3 at diagnosis than non-migrants (47%) and other migrant groups (Figure 1.8).
HIV Infection in Migrants in Europe

- Some studies indicate that many of the migrants, even those originating from regions of high HIV prevalence, acquire HIV after arriving in the EU.

- This indicates that prevention strategies need to be developed specifically for this vulnerable population.
In Portugal, in 2015, 24.8% of the new HIV cases were diagnosed among migrants, 18.6% of which in migrants from Sub-Saharan Africa.
OBJECTIVES

- To analyze the molecular epidemiology of HIV-1 infection in migrants originating from Portuguese speaking African countries, followed up in Portugal.

- To analyze the prevalence and characteristics of Transmitted Drug Resistance (TDR) in migrants originating from Portuguese speaking African countries.

- To analyze the prevalence and characteristics of Acquired Drug Resistance (ADR) in migrants originating from Portuguese speaking African countries.
METHODS

- Observational retrospective study with convenience sampling.

- Patients selected from the Portuguese HIV Drug Resistance, which includes clinical, demographic and genomic (Sanger sequencing for drug resistance testing) information from patients followed up in several Portuguese hospitals, ranging from North to South of the country.

- Patients included originated from Portuguese speaking African countries: Angola, Mozambique, Guinea-Bissau and Cape Verde.

- Data was collected between July 2001 and December 2014.

- 855 patients were included:
  - 537 (63%) before starting antiretroviral (ARV) treatment;
  - 303 (35%) after starting ARV treatment.
Gender distribution

- Male, 51%
- Female, 47%
- Unk, 1%

Distribution by country of origin

- Angola, 32%
- Cape Verde, 29%
- Guinea-Bissau, 29%
- Mozambique, 10%
**Distribution of HIV-1 Subtypes in Migrants**

**Most prevalent subtypes:**
- CRF02_AG (26.4%)
- Unique Recombinant Forms (20.2%)

**Subtype distribution in migrants**

![Subtype distribution in migrants](image_url)

**Subtype distribution in the population of Portuguese HIV-1 infected patients**

![Subtype distribution in the population](image_url)
DISTRIBUTION OF HIV-1 SUBTYPES IN MIGRANTS
DISTRIBUTION OF HIV-1 SUBTYPES IN MIGRANTS

Subtypes stratified according to country of origin

Moçambique  Guiné-Bissau  Cape Verde  Angola
Molecular epidemiology of HIV-1 infection in African migrants followed up in Portugal: Conclusions

- There is a gradual increase of CRF02_AG in migrants followed up in Portugal.
- The prevalence of HIV-1 subtypes in migrants largely varies and is consistent with the subtype distribution at the patients’ country of origin.
- This compartmentalization of HIV-1 subtypes according to the country of origin may indicate:
  - The migrants are infected predominantly in Portugal, but inside communities of migrants from the same country and/or;
  - The migrants are infected in their country of origin and arrive to Portugal already infected with HIV-1.

We’re trying to answer these questions through two other projects: BEST-HOPE and MIGRANT-HIV.
HIV-1 Drug Resistance in African Migrants Followed up in Portugal

**TDR in DN patients:**

- Single class TDR 5.8% (31) [95% CI, 4.1-8.1]
- Double class TDR 1.9% (10) [95% CI, 1.0-3.4]
- Triple class TDR n=1

**ADR in treated patients:**

- Single class ADR 18.2% (55) [95% CI, 4.1-8.1]
- Double class ADR 39.6% (120) [95% CI, 34.3-45.4]
- Triple class ADR 5.6% (17) [95% CI, 1.0-3.3]
### HIV-1 TDR in African Migrants Followed up in Portugal

<table>
<thead>
<tr>
<th>TDR</th>
<th>Angola % (n)</th>
<th>Cape Verde % (n)</th>
<th>Guinea-Bissau % (n)</th>
<th>Mozambique % (n)</th>
<th>Overall % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDR any class</td>
<td>6.3 (10)</td>
<td>6.8 (10)</td>
<td><strong>10.6</strong> (18)</td>
<td>6.6 (4)</td>
<td><strong>7.8</strong> (42)</td>
</tr>
<tr>
<td>NRTIs TDR</td>
<td>3.1 (5)</td>
<td>3.4 (5)</td>
<td><strong>5.9</strong> (10)</td>
<td>3.3 (2)</td>
<td><strong>4.1</strong> (22)</td>
</tr>
<tr>
<td>NNRTIs TDR</td>
<td>6.3 (10)</td>
<td>3.4 (5)</td>
<td>5.3 (9)</td>
<td><strong>6.6</strong> (4)</td>
<td><strong>5.2</strong> (28)</td>
</tr>
<tr>
<td>PIs TDR</td>
<td>0.0</td>
<td><strong>1.4</strong> (2)</td>
<td>1.2 (2)</td>
<td>0.0</td>
<td><strong>0.7</strong> (4)*</td>
</tr>
</tbody>
</table>

* Indicates value significantly different from the corresponding value calculated in the HIV-1 Portuguese population.
**HIV-1 ADR in African Migrants Followed up in Portugal**

<table>
<thead>
<tr>
<th>ADR</th>
<th>Angola % (n)</th>
<th>Cape Verde % (n)</th>
<th>Guinea-Bissau % (n)</th>
<th>Mozambique % (n)</th>
<th>Overall % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR any class</td>
<td>68.5 (74)</td>
<td><strong>71.7 (71)</strong></td>
<td>45.9 (34)</td>
<td>59.1 (13)</td>
<td>63.4 (192)*</td>
</tr>
<tr>
<td>NRTIs ADR</td>
<td>59.3 (64)</td>
<td>56.6 (56)</td>
<td>39.2 (29)</td>
<td>45.5 (10)</td>
<td>52.5 (159)*</td>
</tr>
<tr>
<td>NNRTIs ADR</td>
<td>47.2 (51)</td>
<td><strong>56.6 (56)</strong>*</td>
<td>31.1 (23)</td>
<td>36.4 (8)</td>
<td>45.5 (138)</td>
</tr>
<tr>
<td>PIs ADR</td>
<td>16.7 (18)</td>
<td>16.2 (16)</td>
<td>14.9 (11)</td>
<td><strong>18.2 (4)</strong></td>
<td>16.2 (49)*</td>
</tr>
</tbody>
</table>

* Indicates value significantly different from the corresponding value calculated in the HIV-1 Portuguese population.
**E V O L U T I O N  O F  T D R  A C R O S S  T I M E  I N  M I G R A N T S**

### Rates of TDR per year 2007-2014

**Before 2007 -> No TDR detected in migrants**
Evolution of ADR across time in migrants

Rates of ADR per year 2007-2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Any class</th>
<th>NRTI</th>
<th>NNRTI</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>63.9%</td>
<td>63.9%</td>
<td>63.9%</td>
<td>63.9%</td>
</tr>
<tr>
<td>2008</td>
<td>38.7%</td>
<td>38.7%</td>
<td>38.7%</td>
<td>38.7%</td>
</tr>
<tr>
<td>2009</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>2010</td>
<td>63.0%</td>
<td>63.0%</td>
<td>63.0%</td>
<td>63.0%</td>
</tr>
<tr>
<td>2011</td>
<td>36.8%</td>
<td>36.8%</td>
<td>36.8%</td>
<td>36.8%</td>
</tr>
<tr>
<td>2012</td>
<td>53.3%</td>
<td>53.3%</td>
<td>53.3%</td>
<td>53.3%</td>
</tr>
<tr>
<td>2013</td>
<td>63.6%</td>
<td>63.6%</td>
<td>63.6%</td>
<td>63.6%</td>
</tr>
<tr>
<td>2014</td>
<td>71.4%</td>
<td>71.4%</td>
<td>71.4%</td>
<td>71.4%</td>
</tr>
</tbody>
</table>

Any class = green, NRTI = red, NNRTI = yellow, PI = blue
HIV-1 DRUG RESISTANCE IN AFRICAN MIGRANTS FOLLOWED UP IN PORTUGAL: CONCLUSIONS

7.8% TDR in migrants
- Not significantly different from the portuguese HIV-1 population of the Drug Resistance database, except for PIs where rates of TDR were significantly lower in migrants

- Increasing rates of TDR to NRTIs in the last years.

- Other studies:
  - 8.4% TDR in a similar study with African immigrants in Spain (1996-2010) and 13% between 2007-2010
  - In an ongoing prospective study (BESTHOPE), we found 9.3% TDR in the population of migrants (n=54) included (2015-2017)
HIV-1 Drug Resistance in African Migrants Followed up in Portugal: Conclusions

63.4% ADR in migrants
- Significantly lower than the rates of ADR for the portuguese HIV-1 population of the Drug Resistance database, except for NNRTIs however

- Increasing rates of ADR to all classes since 2011

- Migrants from Guinea-Bissau presented the lower rates of ADR 45.9% (despite higher rates of TDR – 10.6%)

- Migrants from Cape Verde presented the higher rates of ADR (71.7%), with significantly higher rates of NNRTIs ADR than portuguese patients.
• Prospectives studies ongoing: Best-Hope e Migrant-HIV (newly diagnosed patients)

• To compare the results of migrants with the population of patients originated and living in each one of these 4 countries: Angola, Mozambique, Guinea-Bissau and Cape Verde

• To use transmission chain reconstruction to further analyse these results.
BEST HOPE AND MIGRANT HIV

Objectives:

• To analyse and characterize TDR in newly diagnosed patients in Portugal;

• To determine clinical and socio-behavioral risk factors for acquiring HIV infection, whether or not associated with TDR;

• To analyse risk factors for transmission of HIV, with or without TDR, in specific vulnerable populations (MSMs and migrants) – through socio-behavioral questionnaires, specifically designed for each population, combined with phylogenetic reconstruction of transmission chains and drug resistance data;
FUNDING

- “Genomics, socio-behavioral and clinical data to prevent HIV transmission in migrants: an innovative approach” (FCT PTDC/DTP-EPI/7066/2014)

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TEAM

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