HIV-1 transmitted drug resistance mutations and subtypes in ARV-naïve pregnant women in north central Nigeria

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Int. Workshop on HIV Transmission
Introduction

- Rapid scale-up of ART in resource-limited countries requires periodic surveillance for transmitted drug resistance.
- This will help in determining the usefulness and preservation of the limited options of ARV drugs used for treatment and interventions such as PMTCT and Prep.
- WHO has recommended a simple and cost-effective way of determining the prevalence of TDR.
HIV and ART in Nigeria

- Current national HIV prevalence: 3.6%
- People living with HIV: 3.3 million
- Approximately 220,000 people died from AIDS in Nigeria in 2009.
- Through national ART scale-up since 2001 and with support from PEPFAR since 2004, 400,000 of 1.5 million eligible patients are now on ART

Figure: ART scale-up in Nigeria, 2001-2012
Estimation of prevalence of transmitted drug resistance mutations

• Not estimated precisely but rather classified for each drug or drug class as <5%, 5-15%, and >15%
  – If <5% to all relevant drugs = Repeat survey after 2 years
  – If higher categories = Do more surveys or resource-intensive surveillance and take additional public health action
Figure 1. HIV Transmitted Resistance in Six African Countries –(Hamers et al. Lancet Infectious diseases 2011;11:750-59)

Figure 2: Prevalence of HIV-1 primary drug-resistance in antiretroviral-naive individuals in the PASER-M cohort by region and drug class
People with at least one drug-resistance mutation shown as proportion of all people by region and drug class. Regions are clustered by country and sorted by descending calendar year of roll-out of antiretroviral therapy. NRTI=nucleoside reverse transcriptase inhibitor. TAM=thymidine analogue mutation. NNRTI=non-NRTI. PI=protease inhibitor. *Multiclass is resistance to at least two drug classes.
Aims and Objectives

To determine the prevalence and pattern of HIV transmitted drug resistance and subtypes among HIV positive ARV naïve pregnant women detected during antenatal enrollment.
Materials and Methods

• Duration of Study: of May 2010 to March 2012
• Subjects: 34 ARV-naive pregnant women newly detected as HIV-infected at antenatal enrolment
• Study sites: three hospitals in Jos (JUTH, OLA and SOLAT) were recruited under the Harvard School of Public Health PEPFAR/APIN Nigeria-sponsored program.
Materials and methods

• Subjects: Selection Criteria
  – Pregnant women newly detected as HIV-infected at antenatal enrolment
  – ARV Naive
  – First pregnancy,
  – Age 25 years (WHO) and modified to 25 years and above for this study (30 subjects = 30 years and less, 4 subjects = Confirmed recent HIV infection with BED assay, CD4 and Viral load.

Laboratory tests

- CD4- Partec Cyflow
- Viral load Assay: Roche Amplicor version 1.5
- HIV-1 Genotyping for Drug Resistance: Abbott Viroseq and Stanford Algorithm
- Genetic Analyser 3130,
- Subtyping: Clustalx2 and NJPlot software
Figure 2. Pregnant women in antenatal clinic, JUTH, Jos
Figure 3. Project sites: JUTH, OLA, SOLAT at Jos, Nigeria

Jos University Teaching Hospital

Our Lady of Apostles Hospital

SOLAT Women’s Hospital
Figure 3. Laboratory Testing Sites: APIN, JUTH Jos, Nigeria and HSPH, Boston, USA
<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.1 ± 4.2</td>
<td>25.5</td>
<td>20-38</td>
</tr>
<tr>
<td>CD4 Count/µl</td>
<td>325 ± 182</td>
<td>286</td>
<td>101-917</td>
</tr>
<tr>
<td>Viral Load Log/ml</td>
<td>4.4 ± 0.8</td>
<td>4.2</td>
<td>3.2-6.1</td>
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</tbody>
</table>
### Table 2. Mutations and Subtypes

<table>
<thead>
<tr>
<th>Lab ID No</th>
<th>Age</th>
<th>CD4 Count</th>
<th>VL log</th>
<th>PI DR Mut</th>
<th>NRTI DR Mut</th>
<th>NNRTI DR Mut</th>
<th>Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>J024</td>
<td>22</td>
<td>229</td>
<td>3.8</td>
<td></td>
<td></td>
<td>A98G</td>
<td>G prime+</td>
</tr>
<tr>
<td>J045</td>
<td>28</td>
<td>374</td>
<td>3.2</td>
<td>V11I</td>
<td>A98G</td>
<td>G</td>
<td></td>
</tr>
<tr>
<td>J008</td>
<td>24</td>
<td>217</td>
<td>4.5</td>
<td>L10I</td>
<td>G prime+</td>
<td>CRF02_AG</td>
<td></td>
</tr>
<tr>
<td>J035</td>
<td>26</td>
<td>561</td>
<td>4.7</td>
<td>L10V</td>
<td>CRF02_AG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J102</td>
<td>27</td>
<td>512</td>
<td>3.4</td>
<td>A71T</td>
<td></td>
<td>CRF02_AG</td>
<td></td>
</tr>
<tr>
<td>J106</td>
<td>27</td>
<td>112</td>
<td>3.6</td>
<td>M41L* G190A*</td>
<td></td>
<td></td>
<td>G prime+</td>
</tr>
</tbody>
</table>

- **Four PI mutations noted but none on the WHO SDRM list = <5%**
- **One NRTI SDRM Mutation (M41L) detected = < 5%**
- **Three NNRTIs mutations detected with only one (G190A) listed as SDRM. = < 5%**
Figure 4. Phylogenetic Tree for the 34 HIV-1 Subtypes

- CRF02_AG: 15 (44.12%)
- Gprime*: 12 (35.3%)
- G: 6 (17.6%)
- CRF06_cpx: 1 (2.94%)

Conclusions

• Knowledge of HIV DRMs and subtypes is useful in ART choice for PMTCT and treatment

• The rate of TDR mutations in 34 evaluated patients is low
  – <5%:0/34 for PI
  – 1/34 for NRTIs and NNRTIs

• WHO mutations detected were specific for NRTIs (M41L) and NNRTIs (G190A)
Conclusions

• Increased use of ARVs in Jos since 2004 does not appear to have promoted emergence of TDR

• Subtypes detected are similar to previous reports.

• The impact that DRMs not on the WHO SDRM list have on MTCT and treatment interventions deserve further elucidation.
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