Socio-Demographic Factors associated with Success of Antiretroviral Treatment among HIV Patients in Tanzania

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Outline

• General Introduction

• Methods

• Research Studies
  – Gender differences in HIV disease progression and treatment outcomes among HIV patients
  – Factors influencing adherence to ART by HIV patients in an urban and rural setting
  – Clinical and virological response to ARV drugs among HIV patients on first line treatment
  – Prevalence of genotypic resistance to ARV drugs in treatment naïve youths

• Conclusion
HIV in Tanzania

• The estimated HIV prevalence is 5%
• ART is currently being scaled up
• CTC are being established to support HIV patients
HIV Disease Progression

- Immunological markers
- Virological markers
- Clinical markers

Treatment of HIV
ARV Drugs in Tanzania

• ARV for first line treatment in Tanzania:
  – 2NRTI+1NNRTI
  – 3NRTIs

• ARV for the second line treatment in Tanzania:
  – PI (Boosted LPV/r or ATV/r) + 2NRTI
  – PI (Boosted LPV/r or ATV/r) + 1NRTI
Objectives

The purpose of our study was to:

– Collect epidemiological data with regard to ART and treatment response in Tanzania

– Provide evidence that can be used to set up affordable measures to improve treatment response in Tanzania

– Investigate socio-demographic factors with a special focus on gender and adherence

– Assess the impact of current treatment practices on drug resistance development and transmission of drug resistance
Methods

• Prospective cohort and cross-sectional study designs
• Structured questionnaire and patients’ record review
  – Socio-demographic
  – Clinical and treatment information
• We collected blood for CD4 testing, viral load testing and virus genetic analysis
• We performed epidemiological analyses using
  – Standard phylogenetic tests
  – Standard statistical tests
Gender Differences in HIV Disease Progression and Treatment Outcomes Among HIV Patients One Year After Starting ART in Dar es Salaam, Tanzania

To study the difference in clinical, immunological and virological HIV disease progression between men and women on ART

www.pathfinder.org

Mosha et al. BMC Public Health, 2013
Differences on Baseline Characteristics Between Women and Men

- **Women**
  - Larger proportion tested for HIV before developing AIDS (P=0.04)
  - Started ARVs with higher mean BMI (P<0.01)
  - Started ARVs with lower Viral loads (P=0.05)

- **Men**
  - More educated (P<0.01)
  - Higher monthly income (P<0.01)
  - More knowledgeable on ARVs (P<0.01)
  - Started ARVs at Stage IV (P=0.04)
Outcomes After One Year of ART

• Death 35 (15%)
  – Women 21 (13%): Men 14 (20%); P=0.2

• Loss to follow up 63 (27%)
  – Women 42 (26%): Men 21 (30%); P=0.5

• More women than men
  – Had undetectable Viral load (P<0.01)
  – Higher mean BMI (P=0.02)

• More men than women
  – Mean CD4 increase (P=0.05)
Kaplan-Meier Survival Curves on Time to Death, for 234 patients

Relative hazard for death for males 1.94; P=0.08
Main Findings

- Males were reporting for care with a more advanced disease than females
- Patients accessed care after developing AIDS
- Males had a better economic status and knowledge
- After one year on ART, females lost their immunological advantage
- Significant number missed their monthly appointments
- Mortality is likely to be underestimated due to the high number of Lost to follow-up
Factors Influencing Adherence to ART by HIV Patients in an Urban and Rural setting, Tanzania

To investigate factors affecting adherence to ARV drugs in an urban and rural setting in Tanzania

Mosha et al. Accepted BMC 2014
Comparison of Adherence to ARV Drugs Between Urban and Rural Settings

- Adherence based on consistency of keeping appointments
  - Urban 318 (77%); Rural 293 (55%); P<0.01
- Adherence based on consistency of taking ARV (VAS)
  - Urban 234 (56%); Rural 428 (81%); P<0.01
- Adherence based on 4 days recall
  - Urban 362 (87%); Rural 423 (80%); P<0.01
Predictors of Adherence

• Positive predictors with statistical significance
  – Being on ART > 1 year (Both)
  – Satisfaction with Health Services (Both)
  – Early presentation to CTC (Both)
  – Attending CTC > 1 year (Both)
  – Having treatment support (Both)
  – Knowledge on ARV use (Both)

• Negative predictors with statistical significance
  – Paying transport cost to CTC (> Rural)
  – Use of traditional Medicine (> Rural)
  – Taking alcohol (> Rural)
  – Employment (> Urban)
Main Findings

• Adherence in this study was lower compared to previous studies

• Differential attention in rural compared to urban settings are needed to influence ARV adherence

• Patients in the rural settings will benefit more from:
  – A better transport system
  – Easy access to CTC
  – Seeking in traditional medical practitioners allies

• Patients in the urban areas may benefit more from access to CTC outside working hours
Clinical and Virological Response to ARV Treatment in Dar-es-Salaam, Tanzania

- To investigate factors predicting ART clinical response and associate them with virological response in patients taking ARV drugs in Tanzania

Mosha et al. JIDC, 2014
Characteristics of ART Clinical non-responders and responders

• Clinical responders (71) than non-responders (79) were more likely to have:
  – Better immunological response (P=0.03)
  – Better percentage weight gain (P<0.01)
• 25 viraemic 10 [(14%) responders; 15 (19%) non responders: P=0.3]
• Any ARV resistance mutation 20 (83%) (P=0.13)
• Dual NRTI and NNRTI resistance mutations 16 (67%) (P=0.7)
• NRTI resistance mutations 17 (71%) (P=0.5)
• NNRTI resistance mutations 19 (79%) (P=0.4)
Percentage of observed Subtypes and Recombinants

![Pie chart showing the percentage of observed subtypes and recombinants. The chart is labeled with different colors and categories: A, CRF02_AG, D, CRF10_CD, URF_CA, and C. Each category is represented by a different color segment of the pie chart.]
Observed ARV Resistance Mutations

- **M184V**: 12 Non-responders, 6 Responders
- **K70R**: 6 Non-responders, 1 Responders
- **K219Q**: 5 Non-responders, 6 Responders
- **D67N**: 2 Non-responders, 6 Responders
- **T215I**: 4 Non-responders, 0 Responders
- **M41L**: 2 Non-responders, 0 Responders
- **L210W**: 0 Non-responders, 1 Responders
- **L74I**: 1 Non-responders, 1 Responders
- **T69D**: 2 Non-responders, 2 Responders
- **A62V**: 1 Non-responders, 1 Responders
- **G190A**: 7 Non-responders, 2 Responders
Main Findings

- Initiation of therapy at advanced disease stage was associated with clinical and not virological treatment failure.
- The criteria for defining clinical failure to ART are not reflecting the actual virological failure.
  - There were many patients defined to have clinical failure that were actually not virologically failing.
- The prevalence of ARV drug resistance was high among virologically failing patients.
Prevalence of Genotypic Resistance to Antiretroviral Drugs in Treatment Naive Youths infected with Diverse HIV-1 Subtypes and Recombinant Forms in Dar es Salaam, Tanzania

• To establish the prevalence of ARV drug resistance in drug naïve population

Mosha et al. AIDS Res Hum Retroviruses 2011
## Subtype and Recombinant forms

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Env Region</th>
<th>Gag Region</th>
<th>Pol Region</th>
<th>Full genome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtype A</td>
<td>16 (46%)</td>
<td>12 (25%)</td>
<td>16 (36%)</td>
<td>7 (27%)</td>
</tr>
<tr>
<td>Subtype C</td>
<td>6 (17%)</td>
<td>13 (27%)</td>
<td>16 (36%)</td>
<td>6 (23%)</td>
</tr>
<tr>
<td>Subtype D</td>
<td>1 (3%)</td>
<td>7 (15%)</td>
<td>6 (14%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>12 (34%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C-like</td>
<td>0</td>
<td>2 (4%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D-like</td>
<td>0</td>
<td>2 (4%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Recombinant AD</td>
<td>0</td>
<td>2 (4%)</td>
<td>2 (5%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Recombinant AC</td>
<td>0</td>
<td>8 (17%)</td>
<td>1 (2%)</td>
<td>6 (23%)</td>
</tr>
<tr>
<td>Recombinant AB</td>
<td>0</td>
<td>0</td>
<td>1 (2%)</td>
<td>0</td>
</tr>
<tr>
<td>Recombinant CD</td>
<td>0</td>
<td>0</td>
<td>1 (2%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>CRF10_CD</td>
<td>0</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>35</td>
<td>48</td>
<td>44</td>
<td>26</td>
</tr>
</tbody>
</table>
## Observed Resistance Mutations Among the 44 pol Sequenced Samples

<table>
<thead>
<tr>
<th>Subtype</th>
<th>NRTI mutations</th>
<th>NNRTI mutations</th>
<th>Gender</th>
<th>CD4 count (cells/µL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC</td>
<td>M184V, T215F</td>
<td>K103N, Y181C</td>
<td>Female</td>
<td>83</td>
</tr>
<tr>
<td>D</td>
<td>M184V</td>
<td>K103N</td>
<td>Female</td>
<td>175</td>
</tr>
<tr>
<td>AC</td>
<td></td>
<td>Y181C</td>
<td>Male</td>
<td>39</td>
</tr>
<tr>
<td>C</td>
<td>K65R</td>
<td>Y181C</td>
<td>Female</td>
<td>374</td>
</tr>
</tbody>
</table>

- The median CD4 T-cell count was 228 cells/µL
Main Findings

• Low median CD4 T-cell counts in a supposed recently infected youth

• High prevalence of ARV resistance mutations in ARV naïve

• Could not measure effect of subtype on ARV resistance mutations

• High genetic diversity with unclassified recombinants
  – Implication on treatment
  – Implication on vaccination strategies
Conclusion

• Despite using ARVs, some patients still experience disease progression and death

• Some of the observed challenges:
  – The limited resource and skills to monitor therapy efficiency
  – The late initiation of antiretroviral therapy
  – The size of the epidemic, which precludes efficient treatment for all that need it

• Many viraemic patients are not uncovered as failing patients
  – Risk for resistance development
Conclusion

• After one year of ART, women lost their immunological advantage

• Observed behavioral factors with effect to ART include:
  – Alcohol consumption
  – Use of drugs of abuse and traditional medicine
  – Knowledge on the use of ARV

• Need for differential attention in rural compared to urban settings while rolling out ART

• The existence of diverse HIV subtypes and recombinants complicates treatment monitoring
Limitations

- Small sample size
- Patient self-reporting might result in recall bias
- Use of the routinely documented data in the ART clinic files
- We studied patients retained in care, but lacked data on patients’ LTF
Recommendations

• More comprehensive studies on ART involving more patients
  – Focusing on gender differences on adherence to ARV medication
  – Observed ART adherence difference between rural and urban settings
  – Testing the cost-efficiency of virological monitoring for treatment response
  – Follow up the observed predictors of non-adherence as described in our study

• Early diagnosis and treatment of HIV

• Monitoring of the emergence of drug-resistant HIV

• Reduce gender inequalities on accessing the health care
Thank you