TREATMENT FAILURE AND PATTERNS OF GENOTYPIC DRUG RESISTANCE MUTATIONS AMONG HAART EXPERIENCED HIV-1 PATIENTS AT KCMC

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Introduction &Background

❖Globally, there are about [31.4–35.9] million PLHIV by end of 2011 (***UNAIDS, 2012)***

❖ Sub-Saharan Africa accounts for 69% of those i.e. about 23.46 Million (***UNAIDS, 2012)***

❖ Tanzania accounts for about 1.6 -2M of PLHIV ***(NACP 4Ed , April 2012, THMIS 2012)***

❖ HIV-1 prevalence variation among regions in Tanzania

- Average 5.1% in Adult (15-49 yrs)
- Highest 15.7% (***THMIS, 2012)***

Introduction &Background

❖Access to ARV therapy for PLHIV in Tanzania has been significantly scaled up since 2004

❖About 740,040 PLHIV enrolled in ART programs (***NACP, 2012***).

- 1100 health facilities country wide

❖Over 76.2% treatment coverage (***NACP, 2012***)

❖ There is likelihood of inadequate experience of treatment outcomes

❖ More information on treatment outcome still needed

Problem statement

❖At present, laboratory tests for HIV and AIDS management in Tanzania lack drug-resistance testing & Viral load assays **(NACP., 2012)**

❖Change of a failing regimen bases on surrogate markers of treatment failure

❖ Fake ARV in Tanzania (4000 containers)-
TT-VIR 30
Lot # 0C.01.85

TFDA-CA/C.80/222/01A/47

- Stock out, inadequate of HIV care and treatment professionals
- Data on resistance pattern is scarce and weak despite its importance in the general care of HIV-infected patients and policy influence

Objectives

Broad objective

❖ To determine the prevalence of treatment failure, patterns, and factors associated with HIV-1 genotypic resistance to ARV drugs among HAART experienced HIV-1 infected patients attending at KCMC

Specific objectives

❖ To determine the prevalence of clinical, Immunological, and Virological treatment failure among HAART experienced HIV-1 infected patients attending at KCMC

❖ To determine patterns of HIV-1 genotypic resistance to ARV drugs among HAART non-respondents and treatment failure HIV-1 infected patients attending at KCMC

❖To describe factors associated with HIV-1 genotypic resistance to ARV drugs among HAART experienced HIV-1 infected patients attending clinic at KCMC

Results

Virological Treatment outcome

- 10% (13/129) study participant had undetectable VL
- 54.4% (70/129) had VL ≥50but≤400 copies/ml
- 24% (31/129) had VL ≥400 but ≤1000 copies/ml
- 11% (14/129) had VL ≥1000copies/ml
- Median VL was 285 copies/ml

Immunological Treatment outcome

- Median CD4+ T cells was 392cell/ mm^3 (IQR 203-694)at enrollment (P<0.003)
- 57% had changed at least one drug within two years due to adverse reaction
- 22% had IF based on WHO (2012 Report) criteria
- 69% of patients with IF had VL < 400 copies/ml

Results

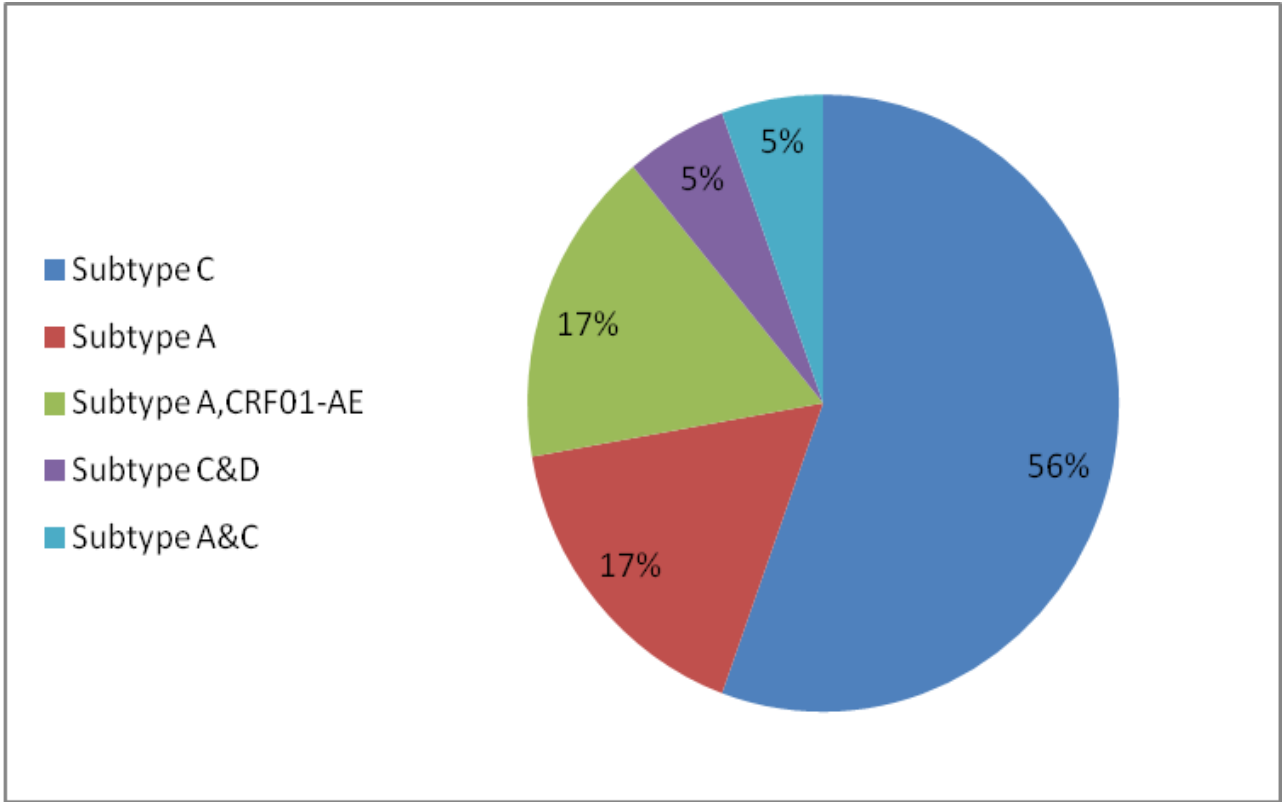

Fig.2: HIV-1 subtypes distribution in the protease and reverse transcriptase region (n=18)

Results

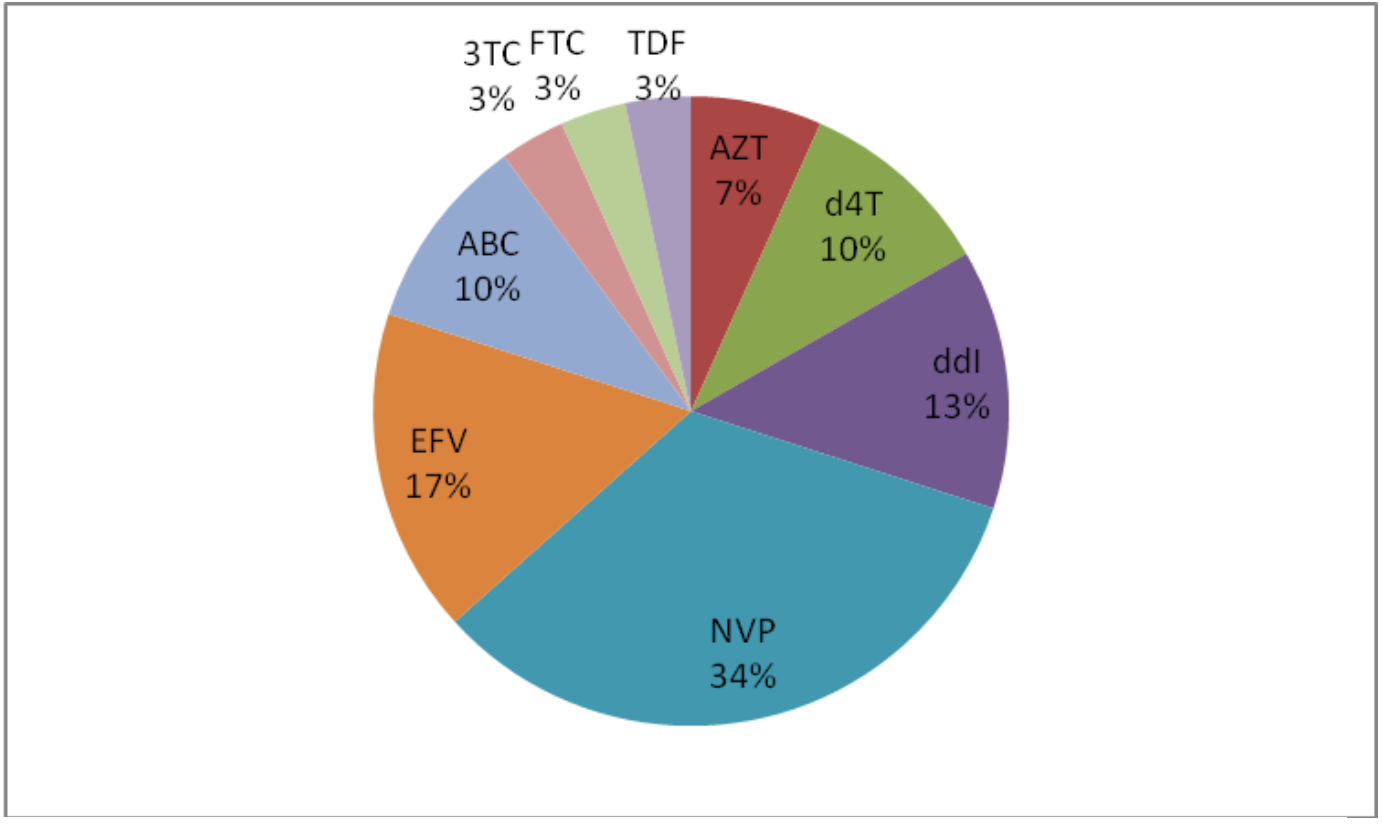

Fig.3 : Distribution of HIV-1 genotypic resistance mutation by individual ARV in the triple HAART combination (n=18)

Results

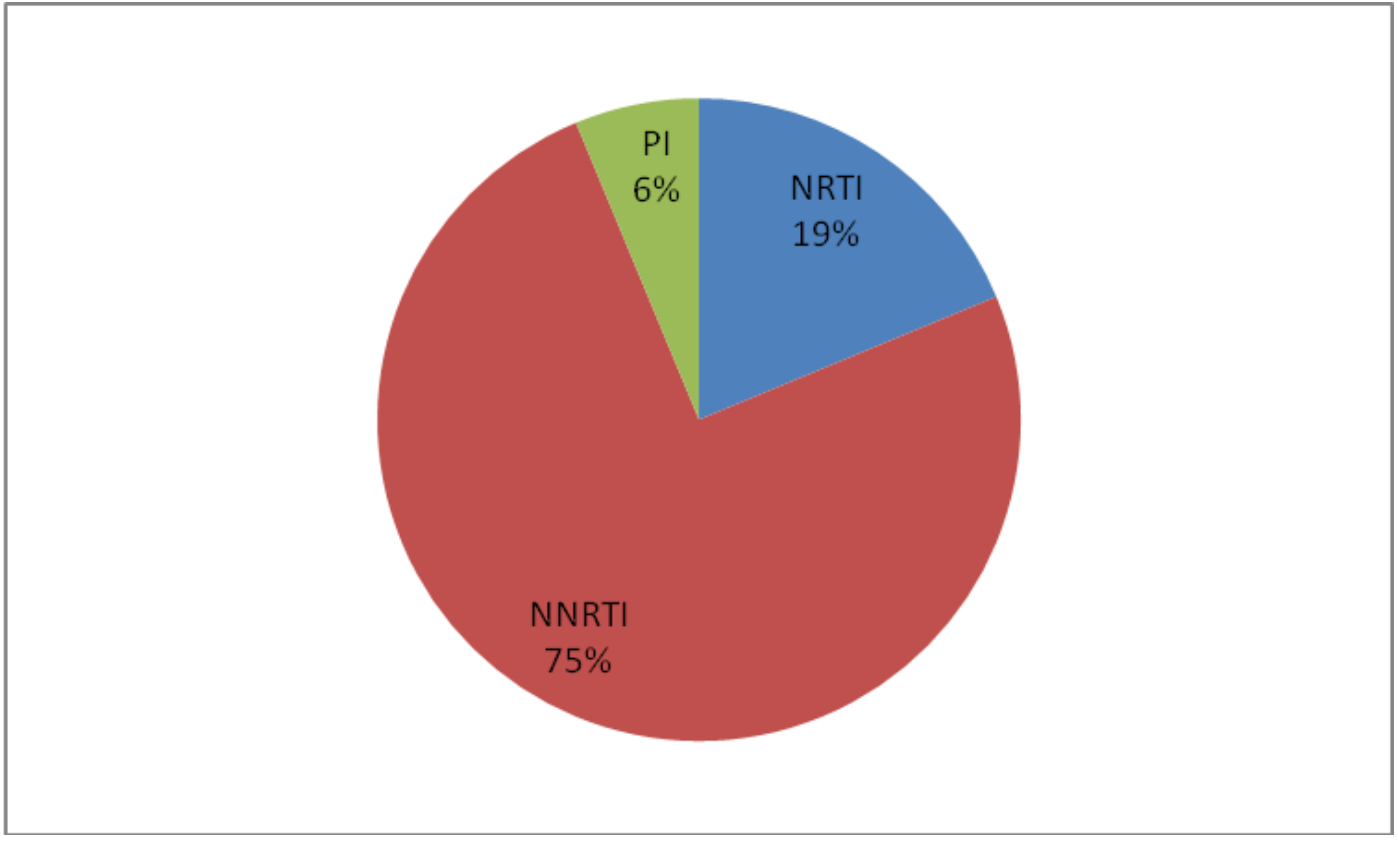

Fig.4: Distribution of HIV-1 drug resistance mutation by type of antiretroviral drug (n=18)

Patterns of resistance

1. **NNRTIs**
   - **NVP (Nevirapine)**
     - **K103N, Y181C/I**
     - **Other minor Mutations**
   - **EFV (Efavirenz)**
     - **K103N, V108I, Y181C/I, Y181F**
     - **Other Minor mutations**

Patterns of resistance (cont)

2. **NRTIs**
   - 3TC (Lamivudine), Zidovudine (AZT), Abacavir (ABC), Didanosine (ddI), Emtricitabine (FTC), Stavudine (d4T), Tenofovir (TDF)
     - T215C, M184V , T69S
     - Other minor mutations

Results

Patterns of resistance (cont)

3. **PIs**
   - **Lopinavir or Nelfinavir boosted ritonavir (LPV/r or NVF/r),**
     - **A71T**
     - **Minor mutations**

Discussion

- HIV subtype C was predominant than other subtypes (***Nyombi et al., 2008, Lau I et al., 2012)***
  - Viral factors, easy transmitted
  - Migration from Southern Africa
- The overall prevalence of genotypic HIV-1 drug resistance was 22%
  - Lack of early warning indicators for HIVDR in CTCs
  - Suboptimal ART programs
  - Limited infrastructure in RLS (***Gupta et al 2012, WHO 2012 report***))
  - Lack of Lab test, no capacity of HIVDR screening at ART initiation

Discussion

- ↑NNRTI resistance, contrast to developed countries where NRTI is the highest
  - ➢ sdNVP use in PMTCT
  - ➢ Only two options are available
  - ➢ Default regimen in Tanzania, EFV
  - ➢ Post exposure prophylaxis

- Minor drug resistance
  - ➢ Clinical relevance not fully known
  - ➢ Could lead into failure of salvage therapy

  (***Meyers T et al., 2009, Ribaudo H et al., 2010, Metzner K et al., 2011***)

Conclusion & Recommendations

Conclusion

- Prevalence of immunological failure was relatively high
- There was little correlation between virological failure and immunological failure.
- Substantial patients with HIV-1 drug resistance mutations

Recommendation

- Routine viral load testing to monitor success of ART treatment is warranted
- Routine surveillance of resistance to antiretroviral therapy is Warranted.
- Clinical studies should be conducted to see the influence of Minor mutation on long term treatment outcome