Challenge - Advanced HIV in Antiretroviral-Experienced Patients

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The forgotten 4th 90: HIV related mortality plateauing

Number of AIDS-related deaths, global, 1990–2017 and 2020 target

Source: UNAIDS 2018 estimates.
% of Advance disease in treatment experienced is increasing steadily

IeDEA-COH: Results based on 951,855 adults from 55 countries after imputation of missing data
Does not include "re-starters" after interruption

In 2015, 37% of people starting ART did so at CD4 cell count <200 cells/mm³
Amongst patients with VL ≥ 1,000 cp/mL, 82% and 61% NNRTI DR in Kinshasa and Homa Bay respectively. High levels of drug resistance among ART-experienced hospitalized patients in Kenya and DRC, C. Bossard & all, Epicentre, submitted.
From linear to circular model
Khayelitsha: Retrospective cohort study of all patients ≥10yrs on ART visiting a Khayelitsha ART clinic, 2013

Kaplan et al CROI 2017 poster 990
Most common causes of HIV related mortality (%) and CFR
Kinshasa, Conakry, Maputo, 2018

**CHK, Kinshasa, Jan-June 2018**
N= 266
- Bact. pneumonia: 2%
- Malaria: 13%
- Kaposi: 1%
- Crypto meningitis: 8%
- Cerebral toxo: 14%
- PCP: 7%
- TB: 55%

**Nsanje, Malawi, May 2016-Dec 2017, n= 734**
- Toxoplasmosis
- Oesophageal candidiasis
- PCP
- Severe bacterial infections
- Chronic diarrhoea
- Extra-pulmonary TB
- Pulmonary TB

**Donka, Conakry, 2017, n=229**
- Bact. pneumonia: 2%
- Malaria: Others: 8%
- Kaposi: Renal Failure: 4%
- Crypto M: 4%
- Cerebral toxo: 5%
- PCP: 4%
- Sepsis: 1%

**Maputo, Jose Macamo**
March-June 2018 n=481
- Bact. pneumonia: 8%
- Kaposi: 4%
- Anemia: 9%
- Gastric enteritis: 9%
- Renal Failure: 22%
- PCP: 7%
- Crypto meningitis: 5%
- Cerebral toxo: 3%
Mortality and co-morbidity IPD CHK, Kinshasa Jan-June 2018 n=266

CHK, Kinshasa, Jan-June 2018 N=266

- Bact.pneumonia 2%
- Malaria 13%
- Kaposi 1%
- Cryptomeningitis 8%
- Cerebral toxo 14%
- PCP 7%
- TB 55%

Associated co-morbidities in HIV patient who died from TB, CHK Kinshasa Jan-June 2018, n=161

- Sepsis 17%
- Renal Failure 17%
- PCP 18%
- HIVAN 7%
- Drug induced Hepatitis 4%
- Kaposi 4%
- Severe Malnutrition 6%
- Hypokalemia 4%
- Crypto meningitis 8%
- Cerebral toxo 15%
Figure 1. Mortality among patients diagnosed with tuberculosis, stratified by CD4 cell count at admission, Homa-Bay, Kenya (n = 80) and Kinshasa, Democratic Republic of Congo (n = 248).
Can we improve HIV mortality with an IPD focused strategy?

IPD mortality rates

- Kinshasa (April - Dec 2017) n=1250
- Kinshasa (Jan-June 2018) n=1214
- Nsanje (2016) n=353
- Nsanje (2017) n=243
- Homa Bay (2017) = 338

But also, high post-discharge mortality

Homa Bay, Kenya:

PHC level f/up @12 weeks after hospital discharge
234 patients with Advanced HIV, May 2016 – Dec 2017:

- 39 negative outcome (died or LTFU at PHC level) (16.7%)
- 101 no outcome (43.2%),
- 94 alive (40.2%),
Objective: identify patients with advanced disease earlier
3 levels of intervention

- **Community**
  - Adapt treatment literacy (failures, interruptions...)
  - Welcome Back Service

- **Primary Health Facility**
  - Screening package

- **Hospital**
  - Rapid assessment unit
  - Adapt referral criteria

**Where:** PHC level with CHW back up
**What:** management plan, up-referral criteria
At PHC level: comprehensive screening package

- Semi-quant CD4 LFA
- CRAG
- TB-LAM

Referral criteria: VL POC or near POC

CD4 Triage Danger signs

LAM Xpert

CrAg LFA

Referral criteria

(Δ4<100)
PHC level: triage

Pico: feasibility in overcrowded nurse based PHC clinic?
Referral hospital level
Rapid assessment unit (RAU)

Quick assessment: 25 to 35% death within 48 hours

- Patients triage -> danger signs
- POC tests: CD4, CrAg, **VL**, LAM, Creatinine, RDT, Hb, glucose, urine
- Package of medication for Advanced HIV
- Referral network and SOP’s
- Specific management algorithms
**POC diagnostic tools needed for management of advanced disease**

### Currently Available
- POC CD4
- TB-LAM
- CrAg LFA

### Challenges
- Slow uptake (e.g. TB-LAM and CrAg LFA)
- Not in national algorithms (e.g. TB-LAM)
- More costly than lab-based (e.g. POC CD4)
- Maintenance needed (e.g. POC CD4)

### Currently Lacking
- POC CD4 LFA
- PCP LFA
- Toxoplasma
- Severe Bacterial Infections

### Challenges
- Under development (e.g. CD4 LFA)
- Lack of innovation (e.g. PCP)
- Lack of validation (e.g. Toxoplasma)
- Too complex (e.g. SBI)
Advanced HIV care management: ongoing operational research

- **Modified VL algorithms to switch to 2nd line:**
  - After 1 VL > 1000 if CD4 < 100:
    - Unstable patient / stage 4
    - Failing for more than 6 months
  - Empirical switch (if no VL available within 48 hrs)

- **DTG on optimized back bone**
  - Re-challenging TLD in patient failing TLE or switch to ZLD
  - DTG in second line ART

- **Empiric TB treatment**
  - Priority for CD4 < 100
  - Decision to take at admission
  - If TB-LAM negative => clinical decision

- **Empiric treatment for other OI, if CD4 < 100**
  - High dose CTX for:
    - Toxo if neurological symptoms
    - PCP: if respiratory rate > 30 min
    - Isospora belli
  - Normal LP and neurological symptoms
    - DD Toxo/Tuberculome
Conclusion

• HIV advance disease will not disappear
• Failure and Resistance is replacing late presentation in Advance disease
• Early identification/screening is crucial -> all levels of care
  – Advance disease and OIs
  – ART experience and Failure
• Readiness to welcome back experience ART patients
• Referral system
  – Improvement of detection and case management at referral level (RAU)
• R & D : new POC diagnostics needed
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