Management of Advanced HIV Disease (AHD)

September 2022

Definition of AHD

- The WHO defines AHD as :
  - (a) For adults, adolescents, and children ≥ 5 years of age having a CD4 cell of < 200 cells/mm3 or WHO clinical stage III or IV disease
  - (b) All children Living with HIV < 5 years of age

- AHD can occur in various settings those:
  - (a) PLHIV newly presenting to care
  - (b) Returning to care after treatment interruption
  - (c) On ART who have experienced treatment failure

Impact of AHD

- PLHIV with AHD have immunosuppression with reduced ability to fight opportunistic infections (OIs) - **increased risk of morbidity and mortality**

- AHD is also associated with **increased health-care costs**, use of more health-care services and more frequent monitoring needs

Major Causes of Mortality in HIV

- Tuberculosis
  - Main cause of mortality among patients initiating ART
- Cryptococcal meningitis
- Bacterial sepsis
  - Septicaemia, pneumonia, GI infection, CNS infection, other
- Pneumocystis jirovecii pneumonia
- IRIS

Why do PLHIV Present with AHD?

ART Experienced

*Disengagement from care

*Poor adherence

*Emergence of resistance to ARV drugs

Pre-ART Late Presentation

*Inadequate awareness and health education

*Late Identification/Testing

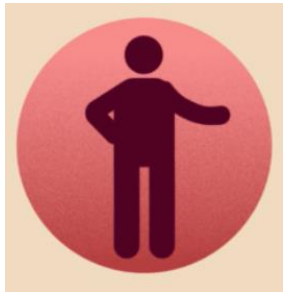
*Poor linkage to care

Screening for Advanced HIV Disease

- All PLHIV on Care should have WHO staging conducted at every visit
- **Criteria for CD4 Testing**
  - **New clients initiating ART:**
    - CD4 testing should be conducted as a baseline test for ALL PLHIV enrolled to care
  - **Patients who are treatment experienced:**
    - PLHIV ≥5 years of age and who had previously initiated ART and are reinitiating after >3 months)
    - Individuals who have documented persistent unsuppressed viral load (two viral load VL >1,000 within 3-6 months)

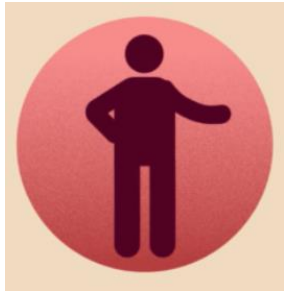
Continuous Patient Categorization

At Entry/Return to Care



- **Well**
- **Advanced HIV Disease**

After 6 Months ART



- **Established on ART**
- **NOT Established on ART**

AHD
Package of Care

- ART Initiation/Re-initiation
- OI Prophylaxis
- OI Identification/Diagnosis
- OI Management
- Follow Up/Monitoring

Package of Care for AHD - 1
Immediate ART Initiation

- **Immediate ART** initiation for all new patients /Re-initiation for those returning to care
- For patients with Pulmonary TB - initiate ART as soon as possible preferably withing 2 weeks
- Delay ART:
  - CM - 5 weeks Initiation
  - TB meningitis (TBM) – 4 to 8 weeks
- Close **monitoring** for development of immune reconstitution inflammatory syndrome **(IRIS)**

Package of Care for AHD - 2
OI Prophylaxis - Cotrimoxazole Preventive Therapy

Sub-Population	Starting/Restarting Criteria	Ending criteria
HIV exposed Infants	All infants, starting 4-6 weeks after birth	Child is confirmed HIV-negative
HIV-infected children and adolescents ≤ 15 years old	All children	Attains 15 years of age
PLHIV > 15 years old	○ Advanced HIV Disease ○ Treatment failure	○ On ART for at least 12 months, suppressed ○ Showing no signs or symptoms of WHO Clinical Stage 2,3 or 4
HIV-positive Pregnant and breastfeeding women	All	○ On ART for at least 12 months, suppressed ○ Showing no signs or symptoms of WHO Clinical Stage 2,3 or 4 ○ Not pregnant or breastfeeding

Package of Care for AHD - 2
OI Prophylaxis - TB Preventive Therapy

- TB Preventive Therapy **(TPT)** for all new patients
  - **Adults PLHIV ≥ 15 years of age:** Isoniazid and Rifapentine weekly for 3 months **(3HP)**
  - Children Living with HIV < 15 years, Pregnant women: Isoniazid daily for 6 months **(6H)**

Package of Care for AHD - 3
OI Identification/Diagnosis

- **GeneXpert Ultra**
  - for TB diagnosis for all PLHIV with presumptive TB
- **TB-LAM** in addition to GeneXpert ultra, for PLHIV with presumptive TB who:
  - Have CD4 ≤ 200 cells/mm^3 and if CD4% ≤ 25% in children < 5 years
  - Have signs of severe illness, or
  - Are currently admitted to hospital
- **Serum Cryptococcal Antigen** (sCRAG) screening:
  - for adolescents and adults with CD4 ≤ 200 cells/mm^3 or clinical suspicion of meningitis (any age)

Package of Care for AHD - 4
OI Treatment

Cryptococcal Meningitis

- Preferred Treatment:
  - **Induction** Treatment :
    - Amphotericin B 1.0 mg/kg/day + Fluconazole 1,200 mg/day for 2 weeks
    - Therapeutic Lumbar punctures on alternate days
    - Appropriate Hydration
    - Renal monitoring/Mg supplementation
  - **Consolidation Phase:** 8 weeks with Fluconazole at 800mg/day
  - **Maintenance Phase/Secondary Prophylaxis Phase:** Fluconazole 200 mg/day for at least 1 year and until CD4 count > 200 cells/mm3 for two measures 6 months apart AND VL is undetectable

Package of Care for AHD - 4
OI Treatment Cont'

TB Meningitis (TBM)

- **TB Treatment:**
  - Start on 2RHZE then 10 RH
  - Pyridoxine
- **Adjuvant corticosteroid therapy:**
  - dexamethasone in the dose of 0.4 mg/kg/day is recommended in adults (>14 years) in conjugation with antitubercular drugs
  - Reduce dose over 6–8 weeks
- **ART:**
  - Delay ART for up to 8 weeks after starting anti TB medication
  - Add dose of DTG for patients on DTG based ART (separate dose in evening)

Immune Reconstitution Inflammatory Syndrome (IRIS)

- **Definition:**
  - Paradoxical inflammatory reaction against a foreign antigen in patients who have started ART with reconstitution (improved functioning) of their immune system
- **Classification:**
  - **Unmasked IRIS:** appearance of a previously undiagnosed opportunistic infection (OI) following ART initiation (or switch to a suppressive regimen)
  - **Paradoxical IRIS:** worsening of a previously diagnosed disease after ART initiation (or switch to a suppressive regimen)
  - **Risk Factors for IRIS:** Advanced HIV Disease, Patients with a diagnosed opportunistic OI, High baseline viral load

Immune Reconstitution Inflammatory Syndrome (IRIS) Cont'

- **Diagnosis:**
  - Suspect in a patient who has **clinical deterioration weeks to months after starting ART** (or switching to a suppressive ART regimen)
  - Typically occurs within 4-8 weeks of initiation or change of ART
  - Varied clinical presentations due to multiple possible pathogens; **clinical manifestations** consistent with an inflammatory condition
  - Rule out the possibility of drug reaction, patient non-adherence to OI treatment, persistently active infection and/or drug resistance to OI treatment
  - Localized tissue inflammation can occur (without systemic manifestation)

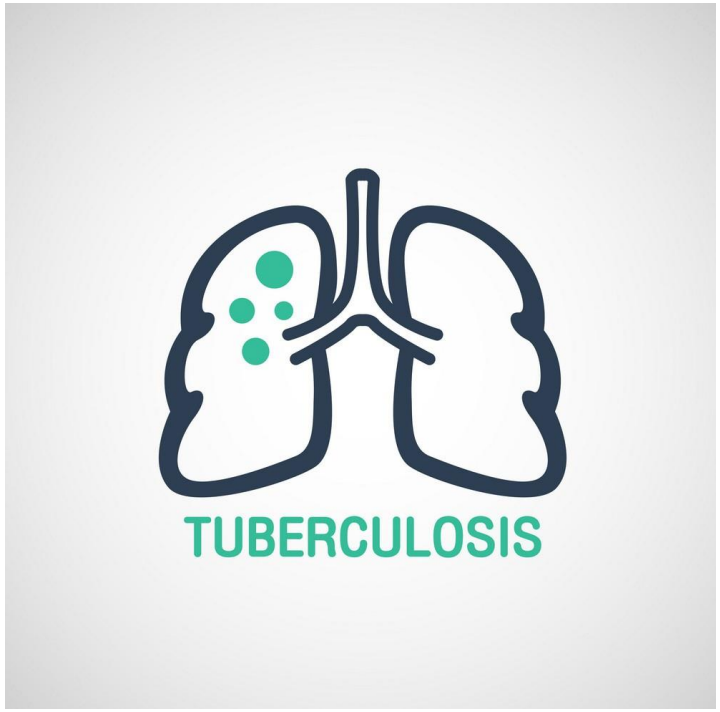
Immune Reconstitution Inflammatory Syndrome (IRIS) Management

Major Presentation

- Tuberculosis (TB)
- Mycobacterium avium complex (MAC)
- Cryptococcal meningitis
- Cytomegalovirus (CMV) retinitis
- Hepatitis B or C virus
- Progressive multifocal leukoencephalopathy (PML)
- Kaposi's sarcoma
- Cerebral toxoplasmosis
- Autoimmune diseases

- **Management - Mild IRIS**
  - Treat the OI and manage the associated symptoms
  - Treat IRIS-associated inflammation (NSAIDS, Inhaled steroids)
  - Surgical intervention (Drainage of abscesses, Excision of inflamed lymph nodes)
- **Management - Severe IRIS**
  - Treat the OI and manage the associated symptoms
  - Manage the IRIS-associated inflammation:
    - 1 to 2 mg/kg prednisone for 1 to 2 weeks, then taper (Do Not use in KS, and CM)

TB/HIV Co-Infection, Prevention &Management



Outline

- Introduction
- TB screening and diagnosis
- TB treatment
- TB preventive therapy
- ART regimens for HIV/TB patients

Background

- TB is a leading cause of morbidity and mortality among people living with HIV
- Reducing the burden of illness requires identifying TB early, providing pre-emptive and preventive treatment for TB, and providing optimal treatment for both HIV and TB
- Timely initiation of ART in combination with TB Preventive Therapy are effective ways to reduce the burden of TB in PLHIV

TB Screening and Diagnosis

TB Screening for PLHIVs

TB screening and prevention services should be offered at every clinical visit

Symptom-based TB screening using the ICF tool should be performed at every clinic visit to rule out active TB disease

Patients who screen positive (presumptive TB cases) must complete definitive diagnostic pathways and patients who screen negative should be evaluated for (TPT)

Intensified Case Finding Screening Questions

Cough of any duration (y/n)

Fever (y/n)

Noticeable weight loss/ failure to thrive/ poor weight gain (y/n)

Night sweats (y/n)

Reduced playfulness/ lethargy/ irritability (y/n)

Contact with a tb case (y/n)

- If “Yes” to any question, take a detailed history, examine the patient and do sputum examination (sputum smear or GeneXpert)
- If “No” to questions 1-5 above, consider TPT eligibility and work up for TB Preventive Therapy and repeat screening on subsequent visits (Questions 5 and 6 do not apply to adults)

TB Diagnosis

- GeneXpert is the recommended initial test for TB diagnosis.
- Where a facility has no GeneXpert, smear microscopy SHOULD BE USED as another sample is collected & referred for GeneXpert.
- TB LAM should be used where indicated among PLHIV as per guidelines.
- TB LAM SHOULD NOT be used as an alternative to GeneXpert testing.
- Chest Xray can be obtained to augment and aid deferential diagnosis

Refer to TB Screening and diagnosis algorithm

TB Diagnosis

- History taking
- Physical examination
- Investigations for Diagnosis of PTB

History Taking

- TB diagnosis begins with taking a thorough medical history.
- TB should be ruled out in any person presenting with any of the signs and symptoms of TB, and history of contact.
- The aim of history taking is to rule out other differential diagnosis with TB disease

• Differential diagnosis of pulmonary Tuberculosis

Disease	Presentation	Distinguishing From PTB
Chronic Obstructive Pulmonary Disease (chronic bronchitis /emphysema)	Exertional dyspnea, chronic cough and sputum production	Lung function tests (spirometry), imaging
Heart failure	Exertional dyspnea, chronic cough, orthopnea, edema	Imaging (CXR, echocardiogram) shows cardiomegaly, ECG, laboratory tests
Bronchiectasis	Chronic cough, daily mucopurulent sputum production	Lung function tests (spirometry), CT scan imaging
Lung abscess	Fever, cough and sputum production	Culture results, imaging usually shows infiltrates with a cavity
Lymphoma	Rapidly growing mass with fever, night sweats and weight loss	CXR CT Histopathology
Lung cancer	Cough, hemoptysis, chest pain and dyspnea	Histopathology
Sarcoidosis	Chronic cough, dyspnea, chest pain	Histopathologic detection of noncaseating granulomas
Fungal pneumonia e.g. *Aspergillus*, *Histoplasma*	Fever, chest pain, shortness of breath, cough, and/or hemoptysis	Exposure history and culture results

Physical Examination

- Physical signs of TB on respiratory examination may include: tachypnea, bronchial breath sounds, dullness on percussion, reduced air entry, fever > 37.50 C, wasting, haemoptysis and pallor
- If the patient does not have any of the signs/ symptoms above or is not found to be a presumptive TB case on further clinical review, evaluate the patient for TB preventive therapy

Investigations for Diagnosis of PTB

- GeneXpert MTB/Rif is the preferred 1st choice test for TB diagnosis and detection of Rifampicin resistance
- All persons with Presumptive TB should undergo microbiologic test to confirm diagnosis
- The choice of test is based on the following considerations:
  - When GeneXpert testing is available on site, a sputum sample should be collected and sent for GeneXpert testing.
  - When only smear microscopy is available on site, 2 sputum samples should be collected, one for smear microscopy, and the other to be transported to the GeneXpert site. If smear microscopy is positive, the patients should be started on DS TB treatment and reviewed once GeneXpert results are received. **A negative smear microscopy result does not rule out**

Investigations for Diagnosis of PTB Considerations:

- If both GeneXpert and smear microscopy are not available on site, a sputum sample should be referred to the nearest GeneXpert testing laboratory
- TB LAM should be considered for eligible PLHIV as per the diagnostic algorithm. If positive, initiate DS TB treatment and review once GeneXpert results are received. A negative TB LAM result does not rule out TB
- All adult patients newly diagnosed with TB should undergo HIV testing as per the HTS algorithm and Diabetes testing as per the Kenya Diabetes guidelines

Summary Table of Investigations

Investigation	Target	Purpose
1.GeneXpert and GeneXpert ultra	Preferred test of choice for all presumptive TB cases	For diagnosis of TB and detection RR TB
2.Smear microscopy (Fluorescent and Light microscopy)	All presumptive Pulmonary TB where GeneXpert is not available All DSTB patients for treatment follow up.	Detect TB disease. Monitoring of bacteriologically confirmed TB patients on treatment at months 2/3, 5 and 6
3. Chest X-ray	Preferred for all presumptive pulmonary and some extra pulmonary TB where accessible and affordable	A screening tool to identify those at high risk of TB disease. Supports TB diagnosis especially in children and when sputum for AFB/ GeneXpert is negative or not applicable
4. Histology	All presumptive EPTB	Tissue diagnosis in suspected EPTB e.g. TB adenitis
Other supportive tests		
Tuberculin skin test and IGRA	For detection of TB infection	Used in detection of latent TB infection

Drug Susceptible TB Treatment

TB disease category	Recommended regimen	
	Intensive phase	Continuation phase
All forms of TB except TB meningitis, bone and joint TB (osteoarticular TB)	2 RHZE	4 RH
TB meningitis Osteoarticular TB	2 RHZE	10 RH
Drug resistant TB	**Refer to a DRTB Clinical Team**	

- Follow up smears should be done for all bacteriologically confirmed pulmonary TB cases at end of month 2, 5 and 6 of TB treatment using smear microscopy
- Follow up of RR TB and DR TB should be done as per PMDT guidelines

ART in TB/HIV Co-Infection

Age	Weight	1st Line ART if TB/HIV Co-infection
Birth to 4 weeks	Any	Start anti-TB treatment immediately; start ART after 4 weeks of age, once tolerating anti-TB drugs (follow the regimen recommendations for children ≥ 4 weeks old)
> 4 weeks to < 15 years	< 30 kg	• ABC + 3TC + DTG • Increase DTG dosing frequency to twice daily for duration of rifampicin-containing TB treatment and for an additional 2 weeks after TB treatment is completed, then revert to once daily dosing
	≥ 30 kg	• Give TDF/3TC/DTG FDC morning + DTG 50mg evening for duration of rifampicin-containing TB treatment and for an additional 2 weeks after TB treatment is completed, then revert to TDF/3TC/DTG FDC once daily
≥ 15 years	Any	• Give TDF/3TC/DTG FDC morning + DTG 50mg evening for duration of rifampicin-containing TB treatment and for an additional 2 weeks after TB treatment is completed, then revert to TDF/3TC/DTG FDC once daily

TB Preventive Therapy

Eligible Populations for TB Preventive Therapy

- People living with HIV (PLHIV) : Children aged ≥ 12 months, adolescents and adults
- All household contacts of a bacteriologically confirmed PTB patient
- Prisoners and staff working in prison settings
- Health care workers and other staff in healthcare settings
- Clinical conditions
    - Patients receiving immunosuppressant's,
    - Patients receiving dialysis
    - Patients preparing for an organ transplant
    - Patients with silicosis

Indications for TPT

Target populations	TPT Regimen
• Adult PLHIV excluding patients on PI/r-based ARV regimens	Rifapentine and Isoniazid (3HP) Once weekly for three months *(12 doses)*
• Adult PLHIV on PI/r-based ARV regimens • All CALHIV aged below 15 years • Intolerance or contraindication to 3HP • Pregnant women	Isoniazid (6H) Once daily for 6 months

Follow Up of Patients on TB Preventive Therapy (TPT)

- Patients on TPT should be followed up on monthly basis and other clinic appointments harmonized.
- In case a patient don't show up, defaulter tracing should be initiated after missing appointment
- During each clinic visit, conduct the following;
  - Symptom based TB screening and update TB status
  - Assess and reinforce adherence of the patients to ascertain compliance and completion of doses
  - Assess for any adverse drug reactions and intervene appropriately

NB: If a patient screens positive for TB while on TPT, stop TPT and manage TB according to National TB guidelines

TPT Outcomes

TPT Outcome	Description
Treatment completed	An individual who has taken a full course of TPT in line with the guidelines
Lost to follow up	An individual whose TPT was interrupted for more than one month
Discontinued	An individual whose TPT was stopped due to; ❖ Adverse drug reactions ❖ Development of active TB disease during TPT treatment
Died	An individual who died in the course of TPT


THANK YOU :)