Extrapulmonary Tuberculosis (EPTB) A Tanzanian Perspective

Presented by: Dr. Kidola Jeremiah
National Institute For Medical research
Mwanza
Tanzania
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Outline

- **Definition & Common Types of EPTB** – What is EPTB and which organs it affects
- **Epidemiology** – Global and Tanzanian EPTB data (recent studies)
- **Clinical Manifestations** – Signs and symptoms of various EPTB forms
- **Diagnostic Challenges & Tools** – Difficulties in diagnosis and new advances (GeneXpert, MPT64, etc.)
- **Treatment Protocols** – Tanzania National TB guidelines & WHO recommendations
- **Special Populations** – EPTB in children patients
- **Case & Innovation** – Example case/innovation (e.g. giant rats detecting TB)
- **Improvement Strategies** – How to enhance EPTB detection and care in Tanzania

Definition of EPTB

- **Extrapulmonary TB:** TB infection outside the lungs (affecting organs such as pleura, lymph nodes, abdomen, CNS, bones, etc.). By definition, no involvement of lung parenchyma.
- **Non-contagious:** Unlike pulmonary TB, most forms of EPTB are not spread by airborne droplets (exception: laryngeal TB).
- **Common Sites:** Lymph nodes are the most frequent site (tuberculous lymphadenitis), followed by pleura (TB pleurisy), and others like spine (Pott's disease), meninges (TB meningitis), abdomen, genitourinary tract
- **Risk Factors:** EPTB occurs more often in **immunosuppressed patients** and **young children**
- In advanced HIV/AIDS, over 50% of TB cases are extrapulmonary. Prior untreated TB infection can seed other organs.

Epidemiology of EPTB

- **Global Burden:** TB remains widespread – ~10.6 million people fell ill with TB in 2021
- **Extrapulmonary TB accounts for ~15–20%** of all notified TB cases worldwide
- In 2023, about **16%** of new TB cases globally were extrapulmonary(Variation by region: e.g. ~12% in Africa, ~20–23% in Asia/Middle East)
- **Tanzania:** A high TB burden country (ranked #24 globally by incidence). In 2021, **87,415** TB cases were notified in Tanzania, of which **16,233 (19%)** were extrapulmonary.
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Epidemiology of EPTB

- In recent years EPTB proportions have been around 17–20% of TB cases

- **Trend:** The share of EPTB among TB cases in Tanzania was fairly stable (~21%) from 2015–2019, with a slight decline to 17% by 2022 (possibly due to improved pulmonary case finding).

- **Mortality:** EPTB still causes significant morbidity and mortality. Globally, TB (all forms) killed ~1.6 million people in 2021. EPTB, especially forms like TB meningitis, has high fatality if untreated

Common Types & Clinical Features of EPTB

- **Tuberculous Lymphadenitis (Lymph Node TB):** *Most common EPTB form.* Typically presents as **painless swollen lymph nodes** (often cervical nodes in the neck)
- **Pleural TB (TB Pleurisy):** TB infection of pleura causes **pleural effusion** (fluid around lungs).
- **Spinal TB (Pott's Disease):** TB of the spine/vertebrae. Causes **chronic back pain**, vertebral destruction leading to spinal deformity (gibbus) or collapse.
- **Tuberculous Meningitis:** TB infection of meninges covering the brain. Presents with **persistent headache, vomiting, neck stiffness, altered mental status**.

Common Types & Clinical Features of EPTB

- **Abdominal TB:** Can involve peritoneum (TB peritonitis with **ascites**), intestines, or abdominal lymph nodes.

- **Other EPTB Forms:** *Genitourinary TB* (e.g. TB kidney – flank pain, sterile pyuria; TB of reproductive organs can cause infertility), *Tuberculous Pericarditis* (fluid around heart, causing chest pain and tamponade risk), *Cutaneous TB* (skin lesions such as lupus vulgaris), *Disseminated (Miliary) TB* – widespread tiny lesions in multiple organs, with systemic illness (fever, night sweats, weight loss

Diagnostic Challenges in EPTB

- **Paucibacillary Nature:** EPTB lesions usually have **low bacterial load**. Smear microscopy is often *negative* (few acid-fast bacilli present). Even culture can be falsely negative in many EPTB cases due to sparse organisms.

- **Invasive Sampling Required:** Diagnosing EPTB often needs obtaining tissue or fluid from the affected site (e.g. lymph node biopsy, pleural tap, CSF lumbar puncture). These procedures can be resource-intensive and may not be readily available at all facilities.

Diagnostic Challenges in EPTB

- **Non-specific Presentation:** Symptoms of EPTB are often **vague or mimic other diseases** (e.g. TB lymphadenitis vs. lymphoma, TB spine vs. other back pain causes). Without a high index of suspicion, EPTB may be misdiagnosed or missed, leading to delays.
- **Diagnostic Delays:** It commonly takes longer to diagnose EPTB than pulmonary TB. Patients may present multiple times before TB is considered. Studies in Tanzania have shown median diagnostic delays of ~2 months for EPTB, contributing to high morbidity

Diagnostic Challenges in EPTB

- **Clinical Diagnosis vs. Confirmation:** Because of the above issues, many EPTB cases are treated **on clinical grounds without laboratory confirmation.** Up to 60% of EPTB patients in low-resource settings might not have a confirmed lab diagnosis, risking both under- and over-treatment

- **Resource Gaps:** In some regions, limited access to advanced tests (Xpert PCR, histopathology, imaging) means EPTB cases go undetected. Lack of awareness among healthcare providers can also be a barrier (if EPTB is not considered, proper tests won't be ordered).

Diagnostic Tools & Advances

- **Xpert MTB/RIF (GeneXpert PCR):** Rapid molecular test that detects *M. tuberculosis* DNA and rifampicin resistance. **WHO-endorsed for EPTB** specimens
  - Provides results in <2 hours. **High specificity** (~98%); **sensitivity** varies by specimen (~80% in lymph node tissue, ~50–70% in CSF, higher with Xpert Ultra)

- **Culture:** Gold-standard for TB detection (e.g. MGIT liquid culture). **Higher sensitivity** than smear, but **slow** (can take 2–8 weeks for growth).

Diagnostic Tools & Advances

- **Histopathology:** Examining biopsy tissue for **caseating granulomas** consistent with TB.

- **MPT64 Antigen Detection:** Newer **immunochromatographic or immunohistochemical tests** that detect the MPT64 protein secreted by *M. tuberculosis* complex.
  - In Tanzania, studies showed adding an **anti-MPT64 immunostain improved EPTB diagnosis** in both adults and children. For example, one study in Mbeya found the MPT64 test had ~90% sensitivity on tissue aspirates, outperforming routine tests

Diagnostic Tools & Advances

- **ADA (Adenosine Deaminase):** A biochemical test on fluids (pleural, ascitic CSF). **High ADA levels** in pleural fluid (>40 U/L) support TB diagnosis

- **Imaging:** Chest X-ray, Ultrasound, CT/MRI are invaluable to **localize EPTB** and guide sampling. E.g., ultrasound can detect TB pleural effusions or abdominal TB findings; MRI is very sensitive for spinal TB. **Point-of-care ultrasound** has been studied as a triage tool for EPTB in low-resource settings

Diagnostic Tools & Advances

- **Urine LAM Test:** A **lipoarabinomannan (LAM) antigen** urine dipstick, recommended for diagnosing TB in **HIV-positive patients with low CD4** counts.

- **Drug Resistance Testing:** If TB is confirmed, further molecular tests (e.g. Xpert MTB/XDR, line probe assays) or culture-based DST help detect resistance.

Treatment Protocols

- **Standard Therapy (Drug-Susceptible TB): 6-month regimen** for most forms of TB – **2 months intensive phase** (HRZE: Isoniazid, Rifampicin, Pyrazinamide, Ethambutol) followed by **4 months continuation** (HR).

- **Extended Duration for Severe EPTB:** Certain extrapulmonary sites require longer therapy. **TB Meningitis** and **TB of the bones/joints (e.g. spine)** often are treated for **9–12 months**

Special Considerations: Paediatric EPTB

- **Higher Risk in Children:** Children, especially <5 years, are more prone to severe EPTB (due to immature immune response). *Examples:* TB meningitis and miliary TB occur mostly in young kids. In Tanzania ~14% of new TB cases are in children and a substantial portion of those are extrapulmonary.

- **Diagnosis Challenges:** Young children usually cannot produce sputum. Diagnosis relies on clinical signs, chest X-ray, gastric aspirate or lymph node biopsy, **TB skin test (TST) or IGRA**, and history of TB exposure. A scoring system is often used (scoring symptoms, contact, etc.). **Xpert Ultra** can be done on gastric aspirates, CSF, etc., but yield is lower than adults. **MPT64 tests** and **ultrasound** can aid in pediatric EPTB diagnosis

Special Considerations: Paediatric EPTB

- **BCG Vaccine:** All infants should receive BCG at birth – it provides significant protection against disseminated TB and TB meningitis in early childhood. (Tanzania has high BCG coverage). Despite BCG, some children still develop EPTB if exposed, so early detection is critical

- **Common Pediatric EPTB Forms:** TB lymphadenitis is common even in older children/adolescents. TB meningitis typically in infants/toddlers. Spinal TB and abdominal TB can occur in children too.

Special Considerations: Paediatric EPTB

- **Treatment in Children:** Essentially same first-line regimen (HRZE) but doses adjusted by weight. Children generally tolerate TB drugs well; they often respond with weight gain and recovery. Ensure **nutritional support**, as many children with TB are malnourished

- **HIV Co-infection:** If the child is HIV-infected, start TB treatment first, then initiate ART within 2–8 weeks. Watch for immune reconstitution inflammatory syndrome (IRIS). Give prophylactic cotrimoxazole.

Case & Innovation – TB Detection by Giant African Rats

- **Notable Innovation – "HeroRATs":** In Tanzania, **trained Giant African Pouched Rats** are used to detect TB in sputum samples by smell. These rats have an acute sense of smell and are trained to identify the scent of TB bacteria.

- **How it Works:** Sputum samples (often those that were **negative on smear/Xpert in clinics**) are sent to APOPO's lab. Rats sniff a series of samples; when a rat detects TB, it pauses/alerts at that sample. Each sample is evaluated by multiple rats. If rats consistently indicate a sample, it is flagged as **"TB suspected"** and then rechecked using standard methods

Case & Innovation – TB Detection by Giant African Rats

- **Impact:** This **secondary screening** by rats has markedly increased case detection.

- Studies show rats can **find TB in ~40–50% of smear-negative samples** that were missed

- In Tanzania, APOPO's TB rats have analyzed over 900,000 samples and helped **detect more than 30,000 additional TB cases**

Strategies to Improve EPTB Detection & Management

- **Improve Referral Pathways:** Establish clear referral protocols for suspected EPTB.
- **Public Awareness:** Educate communities that TB is not just a "coughing disease" – it can present in many ways.

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THANK YOU ALL