



POLICY BRIEF

Tackling tuberculosis superbug requires emphasising culture-based monitoring

KEY MESSAGES

- An estimated 10.6 individuals suffered TB worldwide in 2021 including 87,415 from Tanzania. TB is a public health problem, yet only six zonal laboratories have culture facilities in Tanzania despite being a reference standard for TB monitoring.
- If monitoring is not done appropriately, clinicians fail to detect treatment failure in real time and 5 in every 100 of them develop drug resistance TB which is more difficult and expensive to treat.
- Culture based monitoring detects one out of two patients who are clinical TB negative at the second month of intensive TB therapy.
- Expansion of culture testing facilities and referral of samples to the testing laboratory will improve accuracy of TB treatment monitoring, detection of treatment failure and improve outcome.

EXECUTIVE SUMMARY

Culture is the reference standard for monitoring of tuberculosis (TB) treatment but is available in 6 zonal

referral laboratories in Tanzania and majority patients are monitored clinically or using microscopy.

We monitored resolution of TB clinical symptoms compared to culture and found that symptoms resolve in the first 2 months of treatment. Among patients who resolved their TB symptoms at month 2 of intensive TB therapy, 50% were still positive on culture. Programmatic reports indicate that 5 out of 100 patients who fail treatment develop drug resistance TB (DR-TB). Expansion of culture-based testing will improve accuracy of TB treatment, identification of treatment failure, patients at risk of DR-TB and improve outcomes.

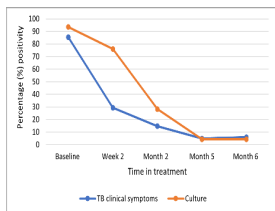
BACKGROUND

An estimated 10 million people suffer from TB and over 1 million die of the disease annually(1). In Tanzania, about 85,597 people suffered from TB in 2020 and 2,680 died in 2020(2). Although TB disease is curable, inappropriate diagnosis and

treatment as well and drug susceptibility profile of the infecting bacteria influence treatment outcome.

A minimum of six months is required to treat TB and the duration can increase to 24 months for DR-TB(3). DR-TB is a public threat to the current TB medicines. Recent epidemiological studies have indicated a global rise in DR-TB for re-treated patients from 17% in 2016 to 23% in 2022 (1). In Tanzania, of the 534 DR-TB cases reported by National Tuberculosis and Leprosy Program (NTLP) in 2019, 12% (64/534) were contributed by re-treated patients(4). To overcome the challenges of DR-TB treatment, which take longer and is 10-fold more expensive to treat compared DS-TB, it is important to monitor the progress of TB treatment using culture as recommended by the World Health Organisation (WHO)(5). In routine settings,

monitoring of TB therapy relies on assessment of resolution of TB clinical symptoms and sputum smear microscopy. Sputum smear microscopy cannot distinguish dead from viable bacilli and 45 out of 100 TB patients are smear negative(6,7). Standard culture is a reference test for monitoring but is not well established in Tanzania and majority of patients are monitored clinically or using sputum smear microscopy(4). Studies have



assessed the utility of TB clinical symptoms for monitoring in clinical trial settings (6,8) but failed to indicate how resolution of TB clinical symptoms relates with bacteriological measure of treatment response on culture

Researchers from NIMR-Mbeya Medical Research assessed the accuracy of routine examined TB clinical symptoms compared to standard culture for monitoring progress of patients on standard TB therapy in Mbeya, Tanzania. TB symptoms resolved rapidly during treatment(9)and one out of every two patients who were TB symptoms negative at the second month of TB treatment was TB positive on culture. This means, patients may stop treatment early or be declared as responding well to treatment based on clinical symptoms while they still have many TB bacilli in their lungs that will progress into relapse, resistance, or treatment failure.

Our research reproduces similar findings revealed in studies conducted in Brazil, Uganda, South Africa, Spain, Canada, and USA. In these studies, TB symptoms with

exception of cough resolved rapidly to less than 10% positivity in the first 2 months of treatment (8). Besides, at least one TB symptoms positive in follow up visits was associated with culture positivity and treatment failure (6,8)

POLICY GAPS

National and international guidelines emphasise use of sputum smear microscopy for monitoring TB treatment alongside routine examinations of TB clinical symptoms. Smear microscopy is not reliable for monitoring due to its low sensitivity and inability to discriminate live from dead bacteria during TB therapy. Culture which is the most accepted measure of treatment response is performed only when a patient is smear positive at month 2 of intensive TB therapy or at the end of treatment month 5 and 6 due to technical and

implementation challenges including costs, training needs and biosafety requirements.

POLICY OPTIONS

1. It is essential that TB culture is performed at diagnosis and months 2 and 6 of TB therapy to ensure all patients on TB treatment are monitored appropriately and treatment failure is detected in real time to overcome DR-TB.
2. The Ministry of health to uphold standards by ensuring that all patients attending routine TB treatment follow-up have access to standard culture.

IMPLEMENTATION CONSIDERATIONS

- i. Enforcing healthcare staff to request samples for culture in treatment follow visits and utilise available culture facility and existing sample referral network to

- refer TB samples to a culture laboratory.
- ii. In places where laboratory capacity is limited, arrangements should be done to refer samples to places where culture can be performed, and results be obtained timely.
 - iii. Zone laboratory should be well equipped (staff and reagents) to be able to conduct culture for all patients and referrals.
 - iv. To ensure sustainability, TB programmes should invest and allocate sufficient budget for commodities used for culture and training of healthcare laboratory scientists.

Implementation of these recommendations will help early identification of the patients failing to TB therapy

and improve treatment monitoring, early detection of DR-TB and reduce cost for management of treatment failures (10)

COMPETING INTEREST

No competing interests for the author to declare.

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GLOSSARY

TB	Tuberculosis
DR-TB	Drug resistance tuberculosis
MDR-TB	Multi-drug resistance tuberculosis
DS-TB	Drug sensitive tuberculosis
WHO	World Health Organisation
NTLP	National Tuberculosis and Leprosy Control Programme

ABOUT THE INSTITUTE

The National Institute for Medical Research is a public health research institution established by the Act of Parliament No. 23 of 1979 with the mandate to carry out, co-ordinate, monitor and control health research in the United Republic of Tanzania.

