

Innovative and Integrated Strategies for Tuberculosis Diagnosis in Developing Countries

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Abstract

Tuberculosis remains one of the leading causes of death from infectious disease worldwide. In 2023, it affected approximately 10.8 million people and caused 1.25 million deaths, with most cases concentrated in low- and middle-income countries, particularly in Africa and Asia. Despite notable advances in diagnosis over the past two decades, particularly with the introduction of rapid molecular tests, current strategies are reaching their limits in these settings due to fragile health systems, financial constraints, a lack of skilled human resources, and difficulties in maintaining equipment. This review critically analyzes the limitations of conventional and molecular tuberculosis diagnostic strategies in developing countries and explores emerging innovations, including biomarkers, point-of-care testing, artificial intelligence, assisted imaging, and community based approaches. Drawing on field experience in Africa and recent developments in diagnostic tools, we propose an integrated and sustainable strategy combining technological and organizational innovations, adapted to the realities of low-resource countries, to improve early detection, diagnostic confirmation, and management of tuberculosis patients.

Keywords

Strategies, Tuberculosis, Diagnosis, Developing Countries

1. Introduction

Tuberculosis is a chronic infectious disease caused by bacteria belonging to the

Mycobacterium tuberculosis complex (MTBC), comprising mainly *Mycobacterium tuberculosis*, but also *M. bovis*, *M. africanum*, *M. cannetii*, *M. orygis*, and *M. caprae* [1] [2]. These mycobacteria are characterized by a lipid-rich cell wall, which confers increased resistance to intracellular destruction mechanisms and allows them to persist for long periods within the host's macrophages [3]-[5].

Despite scientific and therapeutic advances made during the 20th century, tuberculosis remains a major global public health problem [1] [6]. The HIV pandemic has profoundly altered the epidemiology of the disease, increasing the risk of progression to active tuberculosis in infected individuals, while the COVID-19 pandemic has disrupted diagnostic and treatment services in many countries [7] [8]. According to the World Health Organization, 10.8 million new cases and 1.25 million deaths were reported in 2023, making tuberculosis the second leading cause of infectious mortality worldwide [2] [8] [9].

While the introduction of molecular biology tools has led to significant advances in rapid diagnosis and the detection of certain resistances, their impact remains limited in low-resource countries [10]-[13]. Economic, organizational, and structural constraints on health systems hinder equitable access to these technologies [8] [9]. In this context, it seems essential to rethink tuberculosis diagnostic strategies by favoring integrated, innovative approaches that are adapted to local realities [9]. The aim of this review is to analyze the limitations of current approaches and propose sustainable diagnostic strategies for developing countries.

2. Methodology

This narrative review is based on a critical analysis of the international scientific literature, combined with the authors' operational experience in microbiological diagnosis of tuberculosis in several resource-limited African settings. The methodological objective was to identify, evaluate, and put into perspective innovative diagnostic strategies likely to improve tuberculosis screening, diagnosis, and follow-up in developing countries, while taking into account the structural, economic, and human constraints specific to these contexts.

An in-depth literature search was conducted in the PubMed/MEDLINE, Scopus, and Web of Science databases to identify relevant publications published between January 2000 and December 2024. The search strategy combined free terms and MeSH descriptors related to tuberculosis and its diagnosis, including tuberculosis, diagnosis, molecular diagnostics, Xpert MTB/RIF, lipoarabinomannan, point-of-care testing, artificial intelligence, chest radiography, low-income countries, and sub-Saharan Africa. Boolean operators AND and OR were used to optimize the sensitivity and specificity of the search.

Publications were selected based on their scientific relevance and applicability to low- and middle-income country contexts. Original articles, systematic reviews, meta-analyses, observational studies, clinical trials, and international recommendations on tuberculosis diagnostic strategies published in English or French were included. Purely basic studies with no direct diagnostic implications were excluded, as were non-peer-reviewed documents, with the exception of strategic re-

ports and guidelines issued by the World Health Organization.

The selected articles were read in full, and data were extracted on diagnostic performance (sensitivity, specificity, predictive value), turnaround time, technical and logistical requirements, costs, and operational feasibility in resource-limited settings. Particular attention was paid to the potential impact of these tools on national tuberculosis control strategies, particularly in rural and peripheral areas.

Finally, the data from the literature were compared with the authors' field experience in reference laboratories and peripheral health facilities, enabling an integrative analysis of the strengths and limitations of existing approaches. This approach led to the proposal of an integrated and sustainable diagnostic strategy, combining conventional microbiological tools, molecular tests, biomarkers, artificial intelligence, and community strategies, formalized in the form of an algorithm adapted to the realities of low-resource countries.

3. Limitations of Conventional Diagnostic Strategies

In most low- and middle-income countries, tuberculosis diagnosis still relies heavily on conventional methods, particularly microscopy of smears stained with Ziehl-Neelsen or auramine. These techniques have the advantage of being inexpensive, simple to implement, and easily deployable on a large scale, which explains their central place in national tuberculosis control programs [2].

However, microscopy has significant limitations. Its sensitivity is low, particularly in paucibacillary patients, children, people living with HIV, and in extrapulmonary forms of tuberculosis [4] [9]. In addition, its performance is highly dependent on the quality of samples, the expertise of staff, and the existence of quality assurance systems, which are often inadequate in resource-limited settings. The presence of non-tuberculous mycobacteria in certain regions can also lead to false-positive results, compromising the clinical relevance of the diagnosis [10].

Mycobacterial culture is the gold standard for definitive diagnosis [2]. It allows microbiological confirmation, identification of MTBC species, and testing for sensitivity to anti-tuberculosis drugs. However, this method has major limitations. The slow growth rate of mycobacteria means that results can take up to six to eight weeks to come back, delaying the initiation of appropriate treatment or therapeutic adjustment in cases of resistance [2] [9].

In addition, culture requires high-level biosafety infrastructure, generally a P3 containment laboratory, to prevent the risk of nosocomial transmission [11] [12]. These technical and financial requirements exceed the capabilities of many developing countries, sometimes leading to the initiation of anti-tuberculosis treatment based solely on clinical or radiological findings, with an increased risk of diagnostic errors, treatment failure, and selection of resistant strains [10].

3.1. Molecular Tests: Contributions, Limitations, and Challenges

The introduction of molecular tests has profoundly transformed the diagnosis of tuberculosis over the past two decades. The Xpert MTB/RIF and Xpert MTB/RIF

Ultra tests have enabled rapid detection of *M. tuberculosis* and mutations associated with rifampicin resistance, with results available in less than two hours. Their deployment has contributed to reducing diagnostic delays and improving patient care in many countries [3] [8] [9].

Despite these advances, molecular tests have notable limitations. They cannot distinguish between viable and non-viable bacilli, which can lead to persistent positive results in patients who have already been treated. Their sensitivity remains low in paucibacillary forms, in children, in people living with HIV, and in extrapulmonary forms. Thus, a negative result does not formally rule out active tuberculosis in certain clinical contexts [7].

In terms of resistance, these tests target a limited number of mutations, mainly those in the *rpoB* gene [2] [13]. They do not allow for a comprehensive assessment of sensitivity profiles or the detection of resistance to all anti-tuberculosis drugs. The coexistence of sensitive and resistant bacillary populations in the same patient can also complicate the interpretation of results [2].

Next-generation sequencing technologies, including whole genome sequencing, offer promising prospects for the complete characterization of *M. tuberculosis* strains. However, their implementation remains limited in low-resource countries due to costs, infrastructure requirements, the complexity of bioinformatic analyses, and the lack of qualified human resources [14]-[18].

3.2. Emerging Innovations: Biomarkers, Artificial Intelligence, and Imaging

Biomarkers represent an interesting alternative to conventional microbiological methods. Urinary lipoarabinomannan detection tests are rapid point-of-care diagnostic tools that are particularly useful in immunocompromised patients and children. Although their sensitivity is limited in the general population, they are useful in specific clinical contexts [2] [8].

Indirect immunological diagnosis, particularly through interferon-gamma release assays (IGRA), has improved the detection of tuberculosis infection. However, these tests cannot differentiate between latent infection and active tuberculosis and cannot replace microbiological confirmation methods [19].

Artificial intelligence (AI) represents a major advance in the interpretation of complex data [20]. Machine learning algorithms applied to chest imaging enable automated detection of abnormalities consistent with pulmonary tuberculosis, providing valuable assistance in contexts where there is a shortage of qualified personnel [21]. AI also has applications in genomic data analysis, facilitating the interpretation of sequencing results [22].

3.3. Point-of-Care Diagnosis and Community Strategies

Primary health care and community strategies are an essential lever in the fight against tuberculosis in developing countries. Community health workers play a central role in screening, referral, treatment follow-up, and treatment adherence

[1] [9] [23].

The development of simple, robust diagnostic tools that can be used at the point of care, combined with appropriate training for community staff, would reduce diagnostic delays and improve access to care in rural and remote areas. The integration of digital solutions and AI assisted tools could enhance equity of access to diagnosis [9].

3.4. Towards an Integrated and Sustainable Diagnostic Strategy

The COVID-19 pandemic and recent developments in global health financing have highlighted the need to strengthen the resilience of health systems. An effective tuberculosis diagnostic strategy in low-resource countries must be integrated, combining conventional methods, technological innovations, and healthcare organization [9].

We propose an integrated diagnostic approach (see **Figure 1**), adapted to local realities, based on an algorithm combining community screening, rapid point-of-care diagnostic tools, targeted molecular tests, and judicious use of reference methods [8] [9]. Such a strategy requires strong political commitment, sustainable investment, and local ownership of innovations.

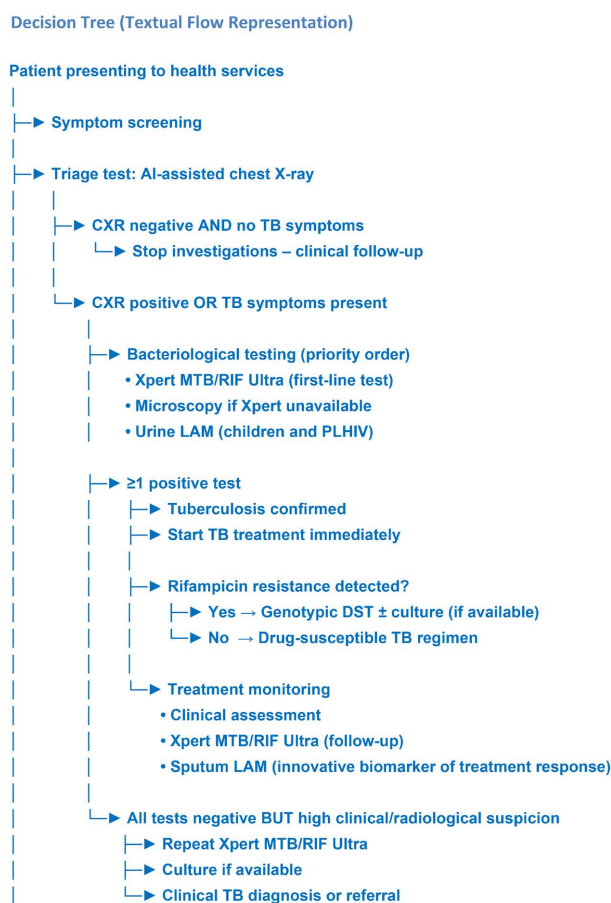


Figure 1. Innovative tuberculosis screening algorithm adapted to the context of developing countries.

4. Conclusions

Conventional tuberculosis diagnostic strategies, although essential, have shown their limitations in terms of sensitivity, speed, and accessibility in developing countries. Molecular biology tools have revolutionized diagnosis, but their impact remains constrained by economic and organizational factors.

The adoption of innovative, integrated diagnostic strategies adapted to local realities appears essential to improving tuberculosis control. By combining technological innovations, health system strengthening, and community-based approaches, it is possible to move toward earlier, more equitable, and more sustainable diagnosis, which is essential to achieving global tuberculosis control goals.

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Ethics

This study was conducted in accordance with the HELSINKI declarations on respect for human dignity.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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