

Current Trends and Advancements in Diagnostic Techniques for Tuberculosis: A Review

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Abstract

Traditional methods for diagnosing tuberculosis (TB) have relied on sputum smear tests and solid culture. These methods often have low sensitivity, take a long time to provide results, and struggle to quickly identify drug resistance. However, in the past ten years, the way we detect *Mycobacterium tuberculosis* has changed significantly. New rapid tests, like cartridge-based nucleic acid amplification tests such as GeneXpert and Truenat, as well as line probe assays, can identify active infections and genetic resistance at the same time. Additionally, we can now use non-sputum methods, measure host-response blood signatures, detect urine lipoarabinomannan (LAM), and employ next-generation sequencing (NGS), which helps diagnose TB in patients outside the lungs and in children. The use of artificial intelligence (AI) and machine learning with digital chest X-rays and automated microscopy improves screening accuracy in areas with limited resources. Despite these significant technological advances, challenges remain in applying these innovations effectively in high-burden regions. This review evaluates the clinical efficacy, implementation hurdles, and future trajectory of modern TB diagnostic stewardship.

Keywords: Tuberculosis, *Mycobacterium Tuberculosis*, Advancements, Diagnostic Techniques, Artificial Intelligence (AI).

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Introduction

Tuberculosis (TB) continues to pose a significant threat to global public health, ranking among the leading infectious diseases worldwide. Each year, millions of individuals go undiagnosed, contributing to the silent spread of this potentially deadly illness. TB is caused by the bacterium *Mycobacterium tuberculosis*, which primarily targets the lungs. However, it is important to note that TB can also disseminate to other organs, such as the kidneys, spine, and brain, resulting in a more extensive impact on the health of affected individuals. Early detection of TB is crucial not only for halting the transmission of the bacteria but also for initiating timely and effective treatment, which can save lives and prevent complications. [1,2] This highlights the ongoing need for improved screening and intervention strategies in various healthcare settings. Traditionally, for over a century, the cornerstone of TB diagnosis has been sputum smear microscopy. This technique involves

examining samples of phlegm under a microscope to identify TB bacteria. While it is cost-effective and widely accessible, it has significant drawbacks, notably its slow turnaround time, high probability of false negatives especially in cases with low bacterial loads, and its inability to detect drug-resistant strains of the disease. The gold standard for TB diagnosis has long been bacterial culture, which involves growing the bacteria from a sample. [3] However, this method requires a timeframe of four to eight weeks to yield results, which not only delays necessary treatment but also allows for the continued spread of the bacteria in the population. Recognizing these limitations, there has been a marked shift towards adopting advanced diagnostic technologies. Molecular assays, for instance, have revolutionized TB diagnosis by enabling the rapid detection of the genetic material of *Mycobacterium tuberculosis* within hours. This significant reduction in diagnostic time greatly enhances the

ability to start treatment swiftly, thereby reducing the risk of transmission. In recent updates, the World Health Organization has also advocated for alternative sampling methods for those who may struggle to provide sputum samples, such as utilizing tongue swabs or gastric aspirates. [4] Moreover, the advent of next-generation diagnostic tools is bringing about improvements in accuracy and efficiency. Techniques that incorporate advanced genetic sequencing and artificial intelligence (AI) for analyzing chest radiographs are proving instrumental in identifying both TB and associated drug-resistant strains with higher precision. The integration of these new testing methods into healthcare systems is gaining momentum, allowing for expedited results that can be communicated to patients during a single clinic visit. The ability to detect drug-resistant strains of TB promptly is critical for preventing treatment failures and decreasing mortality rates associated with the disease. Efforts to innovate and improve TB diagnostics are crucial in supporting global initiatives aimed at completely eradicating the TB epidemic and ensuring a healthier future for communities at risk. These advancements collectively represent a significant leap forward in the fight against tuberculosis, underscoring the importance of ongoing research and investment in public health infrastructures. [5,6]

Methods of Literature Search: This literature review provides a thorough analysis of key online search engines and academic databases, focusing on the functionalities of Google, Google Scholar, and PubMed. It emphasises the use of Medical Subject Headings (MeSH) alongside targeted keywords such as "Tuberculosis," "Mycobacterium tuberculosis," "Advancements," "Diagnostic Techniques," and "Artificial Intelligence (AI)." Through this exploration, the review aims to gather significant insights and relevant studies that enhance understanding of these topics. The search parameters were limited to articles published in English, Chinese, Portuguese, Spanish, and Korean, with a particular emphasis on English-language articles from the past 30 years. Initially, 95 articles were identified, and after refining the selection, 33 articles were chosen based on specific inclusion criteria, focusing solely on review articles while excluding meta-analyses and original research.

Tuberculosis: Exacting Literature Overview: Tuberculosis (TB) is a highly contagious bacterial infection that primarily affects the lungs, but can also impact other vital organs such as the brain, kidneys, and spine. The disease is caused by the bacterium *Mycobacterium tuberculosis*, a resilient organism that thrives in environments where oxygen is abundant. Transmission occurs when an individual with active pulmonary or laryngeal TB expels infectious droplets into the air through

actions such as coughing, sneezing, speaking, or even singing. To contract TB, a person generally needs to engage in close and prolonged contact with someone who is actively infected; casual interactions, such as shaking hands, hugging, kissing, or sharing utensils, do not typically lead to transmission. This makes understanding the dynamics of TB spread crucial for preventive measures. The symptoms associated with active TB can be severe and debilitating, often significantly impacting a person's quality of life. [7,8] A hallmark sign is a persistent cough lasting three weeks or longer, which may produce blood or sputum. Other debilitating symptoms include chest pain, which can be sharp or dull, and considerable feelings of weakness or fatigue, making daily activities challenging. Moreover, individuals suffering from TB may experience noticeable weight loss and a significant decrease in appetite, often accompanied by systemic symptoms such as fever, chills, and night sweats that disrupt sleep. These manifestations indicate a more advanced stage of the disease and merit immediate medical attention to prevent further complications and limit the spread of infection. Early detection and treatment are essential for managing TB effectively and ensuring better outcomes for those affected. [9,10]

Types of Tuberculosis: Latent tuberculosis (TB) occurs when the bacteria are present in the body but are kept in check by the immune system, resulting in no symptoms and making the individual non-contagious. In contrast, active TB signifies that the bacteria have multiplied, leading to illness. This form of TB is contagious, as the bacteria can be spread to others through the air when an infected person coughs or sneezes. [11]

Trends of Treatment and Prevention: Active and latent tuberculosis (TB) can be effectively treated with specific antibiotic regimens. When treating tuberculosis (TB), the course of medication typically spans several months, often lasting from six to nine months, depending on the specific strain of the bacteria and the patient's overall health. [12] It is essential for patients to adhere strictly to the prescribed treatment regimen, as incomplete courses can lead to treatment failure and the potential development of drug-resistant strains of TB. Such resistance poses a serious public health challenge and can hinder efforts to control the spread of this infectious disease. Moreover, the World Health Organization (WHO) emphasizes the importance of the Bacillus Calmette-Guérin (BCG) vaccine, which offers significant protection against the more severe forms of tuberculosis, particularly in vulnerable populations such as infants and young children. The vaccine helps in reducing the incidence of extrapulmonary TB and meningitis caused by the bacteria, thereby safeguarding the

health of those most at risk. Vaccination, combined with proper treatment, is a crucial strategy in the fight against TB globally. [13,14]

Diagnostic Trends before Modern

Advancement: Before the advent of molecular and automated diagnostic tools, the process of diagnosing tuberculosis (TB) relied heavily on various slow and non-specific methods. Ancient physicians primarily observed clinical signs such as chronic cough, blood-tinged sputum, fever, and night sweats to identify potential cases of TB. They would also utilize early stethoscopes or even direct listening to detect abnormal breath sounds in the lungs of affected patients. In the late 19th and early 20th centuries, sputum smear microscopy emerged, employing acid-fast staining techniques to identify *Mycobacterium tuberculosis* under a microscope. [15,16] However, this method was limited by its lack of sensitivity. The gold standard for TB diagnosis became bacterial culture, which involved growing the bacteria on solid media like Lowenstein-Jensen. Although reliable, this approach took an extended period of 4 to 8 weeks to yield results. The Tuberculin Skin Test (TST), the Mantoux and Pirquet methods, measured immune response to tuberculin extracts by observing skin reactions. Additionally, chest radiography became a common practice in the early 20th century, allowing for visual identification of lung cavities and scarring associated with TB. [17,18]

Recent Advancements in Tuberculosis (Tb) Diagnostics

Rapid Molecular Diagnostics: The GeneXpert MTB/RIF and Ultra tests represent a remarkable advancement in the realm of diagnostic testing for tuberculosis (TB). These cartridge-based nucleic acid amplification tests (NAATs) are engineered to swiftly detect the presence of *Mycobacterium tuberculosis*, the bacterium responsible for TB, while simultaneously identifying any resistance to rifampicin, one of the primary first-line antibiotics used in TB treatment. What sets these tests apart is their efficiency, as results can be obtained in as little as two hours, significantly hastening clinical decision-making and treatment initiation. In addition to the GeneXpert tests, the Truenat Platforms have emerged as another innovative solution in TB diagnostics. These systems utilize portable, chip-based real-time micro-PCR technology, which enables the testing of patients in decentralized environments, such as rural clinics and remote healthcare settings. [19] The World Health Organization (WHO) has endorsed these platforms, recognizing their potential to improve access to rapid TB diagnostics in areas that may lack comprehensive laboratory infrastructure. Furthermore, Loop-Mediated Isothermal Amplification (LAMP) is gaining traction as a low-

complexity alternative for DNA amplification. This method operates at a constant temperature, which eliminates the need for intricate thermal cyclers, thus simplifying the testing process. LAMP's rapid turnaround time and user-friendly design make it an attractive option for healthcare providers aiming to facilitate timely diagnosis and treatment of tuberculosis, particularly in resource-limited settings. Overall, these advancements in diagnostic technologies hold great promise for enhancing TB detection and management worldwide. [20]

Advanced Sequencing and Biomarkers: Targeted Next-Generation Sequencing (tNGS) has emerged as a highly recommended method by the World Health Organization (WHO) due to its remarkable accuracy in identifying a wide array of drug-resistance mutations directly from clinical samples. This advanced sequencing technology allows for the comprehensive analysis of genetic material, enabling healthcare professionals to understand the resistance patterns of pathogens, particularly in the context of infectious diseases like tuberculosis. In addition, urine LAM assays, such as the Abbott Determine TB LAM Ag test, have proven to be effective "rule-in" diagnostic tools for at-risk populations, with a significant emphasis on patients suffering from advanced HIV. These assays detect the presence of LAM, a biomarker associated with tuberculosis, in urine samples, thereby providing a non-invasive and rapid testing option for individuals who may not have easy access to traditional laboratory resources. Furthermore, the field of medical diagnostics is witnessing a surge in innovation with the development of emerging technologies. Blood-based mRNA expression signatures are being explored as a promising method for the early and specific detection of various diseases, leveraging the body's RNA profiles to identify pathological conditions swiftly. Additionally, CRISPR-based assays are being refined for their potential to provide highly specific and rapid responses in disease diagnostics, utilizing the precise gene-editing capabilities of the CRISPR technology to detect and analyze specific genetic sequences linked to illnesses. These advancements underscore an ongoing evolution in the realm of medical diagnostics, highlighting the integration of cutting-edge technologies aimed at improving patient outcomes through timely and accurate detection of diseases. [21,22]

Digital Health and Imaging: AI-Assisted Chest X-Rays: Advanced automated software tools designed for the interpretation of chest X-ray images are revolutionizing the detection of pulmonary abnormalities. These tools leverage artificial intelligence algorithms to analyze X-ray scans rapidly, enabling healthcare providers to identify issues such as pneumonia, tumors, and other respiratory conditions at a much faster pace.

This streamlined process is particularly beneficial in resource-constrained environments, where timely diagnoses are critical for effective triage and patient management. By optimizing the workflow,

these AI systems help healthcare professionals make informed decisions quickly, ultimately improving patient outcomes and increasing efficiency within clinical settings. [23]

Table 1: A table Representing Recent Noteworthy Research on Current Trends and Advancements in Diagnostic Techniques for Tuberculosis

Authors	Article Title	Study Method	Maintenance Method	Findings
Kerkhoff AD 2026	Tuberculosis and Other Infectious Complications in People With HIV	Review	Preventive Maintenance	Proposal only No specific study case study
Poeta P 2018	Tuberculosis in the 21th century: Current status of diagnostic methods	Review	Preventive Maintenance	No specific case study Proposal only
Alipoor SD 2024	Significance of extracellular vesicles in orchestration of immune responses in Mycobacterium tuberculosis infection	Review	Preventive Maintenance	No specific case study Proposal only
Shrivasa A 2025	Tuberculosis Diagnosis and Management: Recent Advances	Review	Preventive Maintenance	No specific case study Proposal only
Khuspe P 2026	Advances in tuberculosis diagnostics: From molecular innovations to AI-driven solutions	Review	Preventive Maintenance	Proposal only No specific study case study

Discussion

Pai M et al reviewed in their study that tuberculosis (TB) continues to pose one of the most significant challenges in global health, primarily caused by the bacterium *Mycobacterium tuberculosis*, which has adapted remarkably to survive in a variety of environments and evade detection by the immune system. TB affects millions of individuals across the globe, with a particularly profound impact in regions with limited healthcare resources. The disease is known for its stealthy nature, manifesting in various forms that can complicate diagnosis and treatment. The traditional diagnostic methods for TB, namely sputum smear microscopy and solid culture techniques, have been critical but are not without their limitations. [24,25] Gopalaswamy R et al Sputum smear microscopy can detect acid-fast bacilli in expectorated sputum, making it a cost-effective and widely accessible option. However, this technique suffers from low sensitivity, particularly in cases of paucibacillary TB, where the bacterial load is insufficient for reliable detection. This shortcoming often leads to false-negative results, prolonging the disease's diagnosis and enabling further transmission among unsuspecting individuals. Similarly, while solid culture techniques are more sensitive than sputum smear microscopy, they entail a lengthy process that can extend from several days to weeks before yielding results. This delay in confirming the presence of TB not only postpones necessary treatment but also increases the risk of transmission in communities, particularly in crowded urban areas and among vulnerable populations. [26,27] Habtamu M et al included in their study that acknowledging these diagnostic challenges, the

field of tuberculosis diagnostics is undergoing a revolutionary transformation, moving towards more rapid, decentralized, and molecular-based tests. Recently developed rapid molecular diagnostic tests, such as the GeneXpert system and TruNat, have emerged as groundbreaking tools that can detect the presence of TB and assess drug resistance within a matter of hours.

These advanced methodologies drastically reduce the time from symptom onset to diagnosis and treatment initiation, which can be critical in saving lives and controlling the spread of the disease. Furthermore, the introduction of targeted next-generation sequencing (tNGS) marks a significant advancement in TB diagnostics. [28,29] Cui X et al reported in their study that this sophisticated technology enables healthcare professionals to map complex genetic mutations that lead to resistance against both standard anti-TB medications and newer treatment options. By accurately identifying resistance patterns, clinicians can personalize treatment regimens, thus enhancing the likelihood of successful outcomes for patients. In addressing the needs of specific patient groups who face greater diagnostic challenges, alternative testing methods are being developed and continuously refined. For example, stool PCR testing has proven to be an effective option for detecting TB in pediatric populations who may struggle to produce satisfactory sputum samples. Non-invasive approaches, such as tongue swabs, are also being explored as alternatives for patients who are unable to provide quality sputum due to various health conditions. Additionally, patients with advanced HIV infection, who are at increased risk for TB and often present atypical symptoms, can benefit from

the implementation of lateral flow urine lipoarabinomannan (LF-LAM) assays. [30,31] Tu Phan LM et al reviewed in their study that these tests allow for swift diagnostic capabilities, essential for prompt treatment initiation in immunocompromised individuals. The integration of artificial intelligence (AI) into the diagnostic landscape for TB represents another promising frontier. Computer-aided detection (CAD) systems applied in digital chest radiography are significantly improving the accuracy of automated screenings. This technological advancement is particularly advantageous in remote or underserved healthcare settings, where trained radiologists may not be readily available, thus ensuring that more individuals receive timely evaluations of their respiratory health.

In summary, the collective advancements in tuberculosis diagnostics reflect a crucial and ongoing evolution that emphasizes speed, sensitivity, and specificity. These innovative methodologies are pivotal in tackling the complexities associated with TB, ultimately striving to reduce its burden on individuals as well as public health systems globally. As the battle against tuberculosis progresses, these emerging strategies are fundamental to improving diagnosis and treatment outcomes, significantly contributing to the worldwide effort to eradicate this infectious disease. [32,33]

Conclusion

The review titled "Current Trends and Advancements in Diagnostic Techniques for Tuberculosis" highlights a significant evolution in tuberculosis diagnostics. The study concluded a clear shift from traditional, slow, manual methods to rapid, automated, and precision-driven technologies. While the development of accurate diagnostic tools is progressing, the real challenge lies in effectively deploying and scaling these innovations in regions with the highest disease burden. Addressing financial constraints, infrastructural deficits, and regulatory challenges will be crucial to achieving the global objective of eradicating tuberculosis. This transition to rapid molecular assays represents a transformative change in TB diagnostics, enhancing the detection of the disease and the profiling of drug resistance on a global scale.

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