International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Emerging Rapid Diagnostic Approaches for Tuberculosis Detection in Low-Resource Settings: A Narrative Review

Rahul Yadav[1], Shivangi Yadav[2], Dr. Maitri Bajpai[3]

[1]Student, Dr. Girilal Gupta Institute of Public health, University of Lucknow
[2]Assistant Professor, Department of Allied and Healthcare, Samarpan Institute of Nursing and Paramedical Sciences, Lucknow
[3]Assistant Professor, Dr. Girilal Gupta Institute of Public health, University of Lucknow

Abstract

Background: Tuberculosis [TB] is still a big global health problem, especially in places with fewer resources. When TB isn't diagnosed quickly, it spreads more easily and leads to more deaths. That's why fast and accurate ways to diagnose TB are so important for catching the disease early and making sure people get the treatment they need.

Objectives: To review recent advances in rapid diagnostic approaches for tuberculosis detection and evaluate their significance in low-resource settings.

Sources: Relevant literature published between 2015 and 2026 was identified through PubMed, Google Scholar, Scopus, and World Health Organization reports.

Content: This narrative review provides an overview of emerging rapid diagnostic technologies for TB, including GeneXpert MTB/RIF, GeneXpert Ultra, Truenat assays, line probe assays, and point-of-care tests such as lateral-flow lipoarabinomannan assays. Recent developments in artificial intelligence-assisted radiology, biosensor technologies, and CRISPR-based diagnostics are also highlighted. The review focuses on diagnostic accuracy, accessibility, advantages, and limitations of these approaches in resource-constrained settings.

Implications: Rapid diagnostic technologies have improved early TB detection and identification of drug-resistant cases, supporting global TB control strategies. However, challenges such as high costs, limited infrastructure, and inadequate technical expertise continue to affect implementation in low-resource regions. Expanding affordable and accessible diagnostic technologies may strengthen tuberculosis control and improve public health outcomes.

Keywords: Tuberculosis; Rapid diagnostics; GeneXpert; Truenat; Point-of-care testing; Low-resource settings.

Introduction

Tuberculosis [TB] remains one of the most significant infectious diseases and continues to pose a major global public health challenge, particularly in low- and middle-income countries. Caused by Mycobacterium tuberculosis, TB primarily affects the lungs but may also involve extrapulmonary organs. Despite the availability of effective treatment, the disease continues to contribute substantially to

morbidity and mortality worldwide. According to the World Health Organization Global Tuberculosis Report 2024, approximately 10.8 million people developed TB globally, with nearly 1.25 million deaths reported annually [1]. Countries with limited healthcare resources continue to experience a disproportionately high burden due to delayed diagnosis, poor healthcare access, inadequate laboratory infrastructure, and socioeconomic inequalities.

Early diagnosis of tuberculosis is essential for timely initiation of treatment, interruption of transmission, reduction in disease progression, and prevention of drug resistance. However, conventional diagnostic approaches such as sputum smear microscopy, chest radiography, and mycobacterial culture exhibit several limitations. Sputum smear microscopy, although inexpensive and widely used, demonstrates low sensitivity, particularly among pediatric patients, HIV-positive individuals, and cases with paucibacillary disease [2]. Culture methods remain the gold standard for TB diagnosis because of their high sensitivity and ability to detect drug resistance; however, they are time-consuming and require advanced laboratory facilities, skilled personnel, and biosafety measures [3]. These limitations significantly affect TB control programs in resource-constrained settings where rapid and accessible diagnostic services are urgently needed.

The growing prevalence of multidrug-resistant tuberculosis [MDR-TB] and extensively drug-resistant tuberculosis [XDR-TB] has further complicated global TB management. Delayed identification of drug-resistant strains contributes to treatment failure, prolonged infectiousness, and increased mortality [4]. Consequently, there has been an increasing emphasis on the development of rapid, accurate, and affordable diagnostic technologies capable of detecting both drug-sensitive and drug-resistant TB. In recent years, major advances have been made in molecular diagnostics, point-of-care testing, digital technologies, and biomarker-based assays.

Molecular diagnostic methods such as GeneXpert MTB/RIF, GeneXpert Ultra, Truenat assays, and line probe assays have revolutionized TB diagnosis by enabling rapid detection of Mycobacterium tuberculosis and rifampicin resistance within a few hours [5]. These technologies have significantly improved diagnostic sensitivity and reduced turnaround time compared to conventional methods. The World Health Organization has recommended several rapid molecular diagnostic tools for use in high-burden countries due to their improved performance and operational feasibility in decentralized healthcare settings [1].

In addition to molecular diagnostics, non-sputum-based and point-of-care approaches are gaining importance in low-resource settings. Lateral flow urine lipoarabinomannan [LF-LAM] assays have demonstrated utility among HIV-positive individuals with advanced immunosuppression, while artificial intelligence-assisted chest radiography and digital health technologies are emerging as promising tools for TB screening and early detection [6]. Furthermore, advances in biosensor technology, microfluidics, and CRISPR-based diagnostic platforms may provide rapid, portable, and cost-effective alternatives for TB diagnosis in underserved populations.

Rapid diagnostic technologies play a critical role in strengthening public health interventions and achieving global TB elimination targets. Improved diagnostic accessibility in rural and resource-limited areas can facilitate early case detection, reduce community transmission, and support appropriate treatment initiation. Nevertheless, challenges including high implementation costs, technical complexity, infrastructure limitations, and inadequate trained workforce continue to hinder large-scale adoption of these technologies in low-resource settings.

Therefore, this narrative review aims to provide a comprehensive overview of emerging rapid diagnostic approaches for tuberculosis detection in low-resource settings. The review highlights recent advancements

in molecular and non-molecular diagnostics, evaluates their clinical and public health significance, and discusses implementation challenges and future perspectives for improving TB control globally.

Table 1. Limitations of Conventional Tuberculosis Diagnostic Methods

Diagnostic Method	Advantages	Major Limitations
Sputum smear microscopy	Low cost, simple, widely available	Low sensitivity, poor detection in HIV and pediatric TB
Chest X-ray	Useful for screening	Non-specific findings, cannot confirm TB
Tuberculin skin test [TST]	Useful for latent TB screening	Cross-reactivity with BCG vaccine
Culture methods	High sensitivity and drug susceptibility testing	Long turnaround time, expensive infrastructure
Histopathology	Useful in extrapulmonary TB	Invasive procedures required

Table 2. Emerging Rapid Diagnostic Technologies for Tuberculosis

Diagnostic Technology	Principle	Approximate Turnaround Time	Major Advantages	Major Limitations
GeneXpert MTB/RIF	Cartridge-based PCR molecular detection of Mycobacterium tuberculosis and rifampicin resistance	~2 hours	Rapid diagnosis, high sensitivity, simultaneous drug resistance detection	Expensive equipment and cartridges, requires stable electricity
GeneXpert Ultra	Enhanced nucleic acid amplification technology with improved sensitivity	~2 hours	Better detection in paucibacillary, pediatric, and HIV-associated TB	Higher cost and occasional false-positive results
Truenat TB	Chip-based portable real-time PCR assay	~1 hour	Portable, battery-operated, suitable for peripheral and rural settings	Limited availability and requires trained personnel
Line Probe Assay [LPA]	DNA hybridization technique for mutation detection	1–2 days	Rapid identification of multidrug-resistant TB	Requires sophisticated laboratory infrastructure

LF-LAM Assay	Detection of lipoarabinomannan antigen in urine	<30 minutes	Simple point-of-care test, useful in HIV-positive patients	Reduced sensitivity in HIV-negative individuals
AI-assisted Radiology	Artificial intelligence-based interpretation of chest X-rays	Few minutes	Rapid mass screening and reduced radiologist workload	Requires digital infrastructure and validation
CRISPR-based Diagnostics	CRISPR-mediated nucleic acid detection	<1 hour	Highly sensitive and specific, potential for point-of-care application	Still under development and limited clinical validation
Biosensor-based Diagnostics	Detection of TB biomarkers using electrochemical or optical sensors	Few minutes to 1 hour	Rapid, portable, and potentially low-cost	Limited large-scale clinical implementation

Methodology

A narrative review of the literature was conducted to evaluate emerging rapid diagnostic approaches for tuberculosis detection in low-resource settings. Relevant articles published between 2015 and 2026 were identified through electronic databases including PubMed, Google Scholar, and Scopus. Additional information was obtained from reports and guidelines published by the World Health Organization. Search terms included "tuberculosis diagnostics," "rapid diagnostic tests," "GeneXpert," "Truenat," "point-of-care TB diagnosis," "molecular diagnostics," and "low-resource settings." Original research articles, review papers, clinical studies, and international guidelines published in English were included. Studies focusing on conventional and emerging molecular, non-molecular, and digital diagnostic technologies for tuberculosis were reviewed. Articles lacking sufficient diagnostic relevance or unrelated to low-resource settings were excluded. The collected literature was critically analyzed to summarize recent advancements, diagnostic performance, implementation challenges, and public health implications of rapid tuberculosis diagnostic technologies.

Conventional Diagnostic Methods for Tuberculosis

Conventional diagnostic techniques have long served as the foundation for tuberculosis [TB] detection and management across healthcare systems worldwide. Despite the emergence of advanced molecular technologies, traditional methods continue to be widely practiced in many low-resource settings due to their affordability, availability, and ease of implementation. The most commonly used conventional diagnostic approaches include sputum smear microscopy, chest radiography, tuberculin skin testing, mycobacterial culture, and histopathological examination. However, several limitations associated with these methods have highlighted the need for rapid and more sensitive diagnostic technologies.

Sputum Smear Microscopy

Sputum smear microscopy is one of the oldest and most frequently used methods for diagnosing pulmonary tuberculosis. The technique involves staining sputum samples using Ziehl–Neelsen or fluorescent staining methods to identify acid-fast bacilli under microscopic examination. Because of its low operational cost and minimal laboratory requirements, sputum microscopy remains widely used in primary healthcare centers and national tuberculosis control programs, especially in developing countries [6].

Although smear microscopy is simple and economical, its sensitivity is relatively low, particularly among patients with low bacterial load such as children, HIV-positive individuals, and patients with extrapulmonary TB. The test generally requires a substantial concentration of bacilli in sputum for accurate detection. Additionally, smear microscopy cannot determine drug susceptibility or differentiate between viable and non-viable organisms, limiting its usefulness in monitoring treatment response [7].

Chest Radiography

Chest radiography is commonly used as an adjunctive tool in the diagnosis and screening of pulmonary tuberculosis. Radiographic abnormalities such as upper lobe infiltrates, cavitary lesions, nodules, and pleural effusions may suggest TB infection. Chest X-ray is particularly useful when sputum examination results are negative or when patients are unable to provide sputum samples [8].

Despite its utility, chest radiography lacks diagnostic specificity because similar radiological findings may occur in several pulmonary conditions including bacterial pneumonia, lung malignancies, and fungal infections. Interpretation of radiographic findings also depends heavily on the expertise of clinicians and radiologists. Furthermore, chest X-ray alone cannot confirm active TB infection or identify drug-resistant strains.

Tuberculin Skin Test

The tuberculin skin test [TST], also known as the Mantoux test, is primarily used for detecting latent tuberculosis infection. The procedure involves intradermal administration of purified protein derivative [PPD] followed by assessment of skin induration after 48–72 hours. A positive result generally indicates previous exposure to Mycobacterium tuberculosis or related mycobacterial antigens [9].

Although TST has been widely implemented for TB screening, it has important limitations. False-positive reactions may occur among individuals vaccinated with Bacillus Calmette–Guérin [BCG] or those exposed to non-tuberculous mycobacteria. Conversely, immunocompromised individuals, including patients with HIV infection, severe malnutrition, or chronic illnesses, may demonstrate false-negative results due to weakened immune responses. Moreover, the test does not distinguish latent infection from active disease.

Mycobacterial Culture

Mycobacterial culture remains the reference standard for tuberculosis diagnosis due to its superior sensitivity and ability to perform drug susceptibility testing. Culture methods involve isolation of Mycobacterium tuberculosis using solid media such as Löwenstein–Jensen medium or liquid culture systems including Mycobacteria Growth Indicator Tube [MGIT] systems [10].

Culture-based diagnosis is highly reliable and valuable for confirming active TB infection and identifying multidrug-resistant strains. However, the major drawback of culture methods is the prolonged turnaround

time resulting from the slow growth rate of Mycobacterium tuberculosis. Results may require several weeks, delaying treatment initiation and increasing the risk of transmission. In addition, culture procedures require advanced laboratory infrastructure, biosafety measures, and trained technical personnel, which are often unavailable in remote and low-resource settings.

Histopathological Examination

Histopathological examination is particularly useful in the diagnosis of extrapulmonary tuberculosis involving lymph nodes, bones, pleura, and other tissues. Biopsy specimens are examined microscopically for characteristic granulomatous inflammation and caseous necrosis associated with TB infection [11].

Although histopathology can support TB diagnosis, its findings are not entirely specific because similar granulomatous reactions may also occur in conditions such as sarcoidosis and fungal infections. The requirement for invasive biopsy procedures and specialized pathology services further limits its widespread application.

Limitations of Conventional Diagnostic Methods

Despite their continued importance, conventional TB diagnostic methods present several significant challenges. Many techniques demonstrate limited sensitivity, prolonged processing time, inability to rapidly identify drug resistance, and dependence on laboratory infrastructure. These shortcomings are particularly problematic in high-burden and low-resource settings where delayed diagnosis contributes to continued disease transmission and poor patient outcomes [12].

The limitations associated with conventional methods have accelerated the development of rapid molecular and point-of-care diagnostic technologies that offer improved sensitivity, specificity, and faster turnaround times. Emerging rapid diagnostic approaches have the potential to strengthen TB control programs by enabling early case detection and timely treatment initiation.

Table 3. Conventional Diagnostic Methods for Tuberculosis and Their Limitations

Sputum smear microscopy	Microscopic detection of acid-fast bacilli	Low cost and simple procedure	Low sensitivity and inability to detect drug resistance
Chest radiography	Imaging of pulmonary abnormalities	Useful screening tool	Non-specific radiological findings
Tuberculin skin test	Delayed hypersensitivity response to PPD	Detects latent TB infection	False-positive and false-negative results
Mycobacterial culture	Isolation of M. tuberculosis on culture media	High sensitivity and drug susceptibility testing	Long turnaround time
Histopathological examination	Microscopic tissue examination	Useful in extrapulmonary TB	Invasive and non-specific findings

The Xpert MTB/RIF assay is a fully automated molecular diagnostic test for TB disease developed in partnership among Cepheid, Inc., the Foundation for Innovative New Diagnostics [FIND], the University of Medicine and Dentistry of New Jersey [UMDNJ], and the National Institutes of Health [NIH]. It can simultaneously detect Mycobacterium tuberculosis [MTB] complex DNA and mutations associated with

rifampicin [RIF] resistance [a reliable proxy for MDR-TB] directly from sputum specimens in less than 2 hours, and it minimizes staff manipulation and biosafety risk.[4]
Xpert can detect TB, including MDR-TB, in less than 2 hours, potentially reducing the time to diagnose and treat TB.
Xpert is more sensitive than sputum smear microscopy in detecting TB, and it has similar accuracy as culture.[5-6] Moreover, its ability to detect smear-negative TB provides a significant advantage, especially for PLHIV. Importantly, its ability to detect RIF-resistant TB in less than 2 hours significantly improves the likelihood of timely treatment initiation. [Conventional culture and drug-susceptibility testing [DST] are still required to complete the drug-resistance profile and to monitor treatment.]

Rapid Molecular Tests

Rapid molecular diagnostic technologies have revolutionized tuberculosis [TB] diagnosis by enabling early and accurate detection of Mycobacterium tuberculosis and associated drug resistance. Conventional diagnostic methods such as sputum smear microscopy and culture techniques are often associated with low sensitivity and prolonged turnaround time, resulting in delayed treatment initiation and continued disease transmission. Molecular diagnostic assays based on nucleic acid amplification techniques have emerged as important alternatives because they provide faster results with improved diagnostic accuracy [13].
The increasing global burden of multidrug-resistant tuberculosis [MDR-TB] and extensively drug-resistant tuberculosis [XDR-TB] has highlighted the importance of rapid molecular testing. Early identification of drug resistance is essential for initiating appropriate treatment regimens, reducing transmission, and improving patient outcomes. Rapid molecular assays have therefore become integral components of tuberculosis control programs worldwide, especially in high-burden and low-resource settings.

GeneXpert MTB/RIF

GeneXpert MTB/RIF is among the most significant innovations in TB diagnostics. It is an automated cartridge-based nucleic acid amplification test that simultaneously detects Mycobacterium tuberculosis complex and rifampicin resistance directly from clinical specimens using real-time polymerase chain reaction [PCR] technology [13].
The assay involves automated sample preparation, DNA extraction, amplification, and detection within a closed cartridge system, thereby minimizing contamination risk and reducing the need for extensive technical expertise. Results are typically available within two hours, which represents a major improvement compared to conventional culture methods that may require several weeks.
GeneXpert MTB/RIF demonstrates significantly higher sensitivity than sputum smear microscopy, particularly among smear-negative patients and HIV-positive individuals. Studies have shown that the assay possesses high specificity and sensitivity for pulmonary tuberculosis diagnosis. Additionally, rapid detection of rifampicin resistance serves as an important marker for MDR-TB, allowing clinicians to initiate appropriate therapy at an earlier stage [13].
The introduction of GeneXpert has substantially improved TB diagnosis in high-burden countries. The World Health Organization recommended GeneXpert MTB/RIF as an initial diagnostic test for suspected pulmonary TB and rifampicin-resistant TB because of its rapidity and accuracy [16]. The assay has also

improved diagnosis among vulnerable populations such as children and HIV-positive individuals where conventional methods frequently demonstrate poor sensitivity.

Despite these advantages, GeneXpert implementation remains challenging in resource-limited settings. The high cost of cartridges and equipment, dependence on stable electricity supply, annual calibration requirements, and maintenance costs continue to affect sustainability. In rural healthcare facilities, inadequate infrastructure and interruptions in supply chains may further limit accessibility.

GeneXpert Ultra

GeneXpert Ultra is an upgraded version of the original GeneXpert assay developed to improve diagnostic sensitivity. The assay incorporates multicopy amplification targets and larger DNA reaction chambers, enabling enhanced detection of low bacterial loads [14].

The improved sensitivity of GeneXpert Ultra is particularly beneficial in paucibacillary conditions such as pediatric TB, extrapulmonary TB, and HIV-associated tuberculosis. Studies have demonstrated that GeneXpert Ultra identifies a greater number of smear-negative cases compared to the earlier GeneXpert assay. This improvement has strengthened early case detection and reduced the number of missed TB diagnoses [14].

GeneXpert Ultra maintains rapid turnaround time while improving overall diagnostic performance. However, slightly reduced specificity has been reported because of “trace-positive” results, which may occasionally detect residual DNA from previously treated infections. Nevertheless, the assay remains highly valuable in high-risk populations and resource-constrained settings.

The WHO has endorsed GeneXpert Ultra as an alternative rapid molecular diagnostic test because of its enhanced sensitivity and ability to improve TB case detection. The assay is increasingly being integrated into national tuberculosis elimination programs worldwide.

Truenat Assays

Truenat is a chip-based micro real-time PCR platform designed specifically for decentralized and low-resource healthcare environments. Developed in India, Truenat offers a portable and battery-operated molecular diagnostic system capable of functioning in peripheral laboratories and rural settings [15].

The Truenat platform consists of multiple assays including Truenat MTB, Truenat MTB Plus, and Truenat MTB-RIF Dx for rifampicin resistance detection. The assay requires minimal infrastructure and provides results within approximately one hour. Because of its portability and rapid processing time, Truenat is highly suitable for point-of-care diagnosis and community-based screening programs.

Several studies have demonstrated that Truenat possesses sensitivity and specificity comparable to GeneXpert systems for pulmonary TB diagnosis. The WHO has recommended Truenat as an initial molecular diagnostic test for TB and rifampicin resistance detection in resource-limited settings [16].

One of the major strengths of Truenat is its operational feasibility in rural healthcare systems where sophisticated molecular laboratories are unavailable. Battery-operated functionality allows testing in areas with unstable electricity supply. Furthermore, portability enables easier deployment in mobile healthcare units and remote regions.

Despite these advantages, challenges related to cartridge costs, quality assurance, maintenance, and personnel training continue to influence large-scale implementation. Sustained investment and healthcare infrastructure strengthening are necessary for maximizing the impact of Truenat technology.

Line Probe Assays

Line probe assays [LPAs] are molecular diagnostic techniques based on DNA hybridization technology that detect mutations associated with resistance to first-line and second-line anti-tubercular drugs. LPAs provide rapid diagnosis of multidrug-resistant tuberculosis by identifying mutations related to rifampicin and isoniazid resistance [17].

The procedure involves extraction of bacterial DNA, amplification using PCR, and hybridization of amplified products onto strips containing mutation-specific probes. Results are generally available within 24–48 hours, which is substantially faster than conventional culture-based drug susceptibility testing.

LPAs have demonstrated high sensitivity and specificity for detection of rifampicin resistance and are widely used in MDR-TB surveillance and management programs. Rapid identification of resistant strains facilitates timely initiation of appropriate treatment and reduces transmission of resistant organisms.

However, LPAs require sophisticated laboratory infrastructure, strict biosafety measures, and technically trained personnel. Multiple manual processing steps increase contamination risk and operational complexity. These factors restrict their use primarily to centralized reference laboratories rather than peripheral healthcare centers.

Loop-Mediated Isothermal Amplification

Loop-mediated isothermal amplification [LAMP] is an emerging nucleic acid amplification technique that amplifies DNA under constant temperature conditions without requiring thermal cycling. Compared to conventional PCR, LAMP is simpler, faster, and less equipment-dependent [18].

TB-LAMP assays can provide diagnostic results within one hour and demonstrate promising sensitivity and specificity for pulmonary TB detection. Because the technique operates at a constant temperature, it requires less sophisticated equipment and may be suitable for decentralized healthcare facilities.

The WHO has recognized TB-LAMP as a potential alternative to sputum smear microscopy in selected clinical settings, particularly where conventional molecular testing is unavailable [18]. The assay may improve access to rapid molecular diagnosis in peripheral healthcare facilities and rural communities.

Despite its operational simplicity, widespread implementation of TB-LAMP remains limited because of concerns regarding reagent stability, standardization, and integration into national TB programs.

Next-Generation Sequencing

Next-generation sequencing [NGS] has emerged as an advanced molecular diagnostic approach for comprehensive genomic analysis of Mycobacterium tuberculosis. Whole-genome sequencing enables simultaneous identification of multiple drug resistance mutations and provides detailed information regarding bacterial strain diversity and transmission patterns [19].

NGS offers substantial advantages in MDR-TB and XDR-TB management because it can rapidly detect resistance to both first-line and second-line anti-tubercular drugs. The technology also supports epidemiological surveillance and outbreak investigation.

In addition to drug resistance detection, genomic sequencing facilitates personalized treatment planning and monitoring of transmission dynamics. These applications may significantly strengthen global TB control strategies in the future.

However, NGS remains expensive and technically demanding. Implementation requires advanced laboratory infrastructure, bioinformatics expertise, quality assurance systems, and highly trained personnel. Consequently, routine use in low-resource settings remains limited at present.

Clinical Significance of Rapid Molecular Diagnostics

Rapid molecular diagnostic technologies have transformed TB control programs by enabling early diagnosis, timely treatment initiation, and rapid detection of drug-resistant strains. Molecular assays reduce diagnostic delay, improve case detection among vulnerable populations, and contribute to reduction of disease transmission within communities.

These technologies are particularly important in HIV-associated TB, pediatric TB, extrapulmonary TB, and smear-negative disease where conventional diagnostic methods often demonstrate inadequate sensitivity. Rapid molecular diagnostics also support antimicrobial stewardship by guiding appropriate therapy selection.

Integration of rapid molecular technologies into national tuberculosis elimination programs has strengthened surveillance, improved treatment outcomes, and enhanced public health interventions. However, ensuring equitable access in low-resource settings requires sustained financial investment, infrastructure development, healthcare workforce training, and effective supply chain management.

Continued research and innovation are expected to improve affordability, portability, and operational simplicity of molecular diagnostic technologies, thereby expanding their accessibility and impact in underserved populations.

Table 4. Rapid Molecular Diagnostic Tests for Tuberculosis

GeneXpert MTB/RIF	Real-time PCR detection	~2 hours	Rapid TB and rifampicin resistance detection	High cost and electricity dependence
GeneXpert Ultra	Enhanced nucleic acid amplification	~2 hours	Improved sensitivity in smear-negative TB	Slightly lower specificity
Truenat TB	Chip-based real-time PCR	~1 hour	Portable and suitable for rural settings	Cartridge and maintenance costs
Line Probe Assay	DNA hybridization	24–48 hours	Rapid MDR-TB detection	Requires advanced laboratory setup
TB-LAMP	Isothermal amplification	<1 hour	Simple and rapid procedure	Limited standardization
Next-Generation Sequencing	Whole genome sequencing	Variable	Comprehensive resistance profiling	Expensive and technically demanding

Point-of-Care Diagnostics

Point-of-care [POC] diagnostic technologies have emerged as important tools for tuberculosis [TB] detection, particularly in low-resource and rural settings where access to centralized laboratories is limited. These diagnostic approaches are designed to provide rapid results near the site of patient care, thereby reducing delays in diagnosis and treatment initiation. Point-of-care diagnostics are especially valuable in regions with high TB burden, inadequate healthcare infrastructure, and limited laboratory capacity. Early diagnosis through decentralized testing can significantly improve patient outcomes and reduce disease transmission within communities [20].

Lateral Flow Lipoarabinomannan Assay

The lateral flow lipoarabinomannan [LF-LAM] assay is a urine-based point-of-care test used for TB diagnosis, particularly among HIV-positive individuals with advanced immunosuppression. The assay detects lipoarabinomannan antigen, a glycolipid component of the mycobacterial cell wall, present in urine samples [21].

LF-LAM testing offers several advantages in resource-limited settings. The assay is inexpensive, easy to perform, requires minimal technical expertise, and provides results within approximately 30 minutes. Because urine collection is non-invasive and simple, LF-LAM testing is particularly useful among severely ill patients who may be unable to produce sputum samples.

Studies have demonstrated that LF-LAM improves TB diagnosis among HIV-positive patients with low CD4 counts and contributes to reduced mortality by facilitating early treatment initiation. Consequently, the World Health Organization recommends LF-LAM testing among hospitalized HIV-positive individuals with suspected TB [22].

However, the assay demonstrates lower sensitivity among HIV-negative individuals and patients with early-stage disease. Therefore, LF-LAM is generally used as an adjunctive diagnostic tool rather than a standalone confirmatory test.

Portable Digital Chest Radiography

Portable digital chest radiography has gained increasing importance as a point-of-care screening tool for pulmonary tuberculosis. Recent technological advancements have led to the development of lightweight, battery-operated digital X-ray systems that can be deployed in remote and underserved regions [23].

Portable radiography enables rapid TB screening in community settings, mobile clinics, prisons, refugee camps, and rural healthcare facilities. Combined with computer-aided detection software, portable digital imaging systems can facilitate large-scale screening programs with improved efficiency.

One major advantage of portable digital radiography is its ability to rapidly identify individuals requiring further microbiological confirmation. This approach is particularly useful in mass screening campaigns and active case-finding programs in high-burden settings.

Despite these benefits, challenges including equipment costs, maintenance requirements, and limited availability of trained radiology personnel may affect implementation in resource-constrained regions.

Point-of-Care Ultrasound

Point-of-care ultrasound [POCUS] is increasingly being explored as a supportive diagnostic tool for extrapulmonary and disseminated tuberculosis, particularly among HIV-positive individuals. Ultrasound examination may identify pleural effusion, abdominal lymphadenopathy, pericardial effusion, and splenic microabscesses associated with TB infection [24].

POCUS offers advantages such as portability, absence of radiation exposure, and rapid bedside assessment. In low-resource settings, ultrasound may improve clinical decision-making when access to advanced imaging modalities is limited.

However, ultrasound findings are often non-specific and operator-dependent, limiting its role as a definitive diagnostic method. Adequate training and standardization are necessary for effective utilization.

Urine-Based and Non-Sputum Diagnostics

Non-sputum-based diagnostic approaches are increasingly important because many patients, especially

children and severely ill individuals, experience difficulty producing sputum samples. Urine-based diagnostics, breath analysis, and blood biomarker assays are currently under investigation as alternative diagnostic strategies [25].

Non-invasive specimen collection improves patient compliance and facilitates screening in community settings. Emerging biomarker-based assays may further improve early detection and simplify TB diagnosis in vulnerable populations.

Role of Point-of-Care Diagnostics in Low-Resource Settings

Point-of-care diagnostic technologies have considerable public health significance in low-resource settings because they decentralize TB diagnosis and reduce dependence on centralized laboratories. Early diagnosis and immediate treatment initiation may substantially reduce disease transmission and improve treatment outcomes.

POC technologies also support active case-finding strategies and outreach programs in remote communities. Their portability and operational simplicity make them highly suitable for primary healthcare systems and rural health centers.

However, sustainable implementation requires continuous supply chains, healthcare worker training, quality assurance mechanisms, and financial investment. Strengthening healthcare infrastructure remains essential for maximizing the benefits of point-of-care diagnostics.

AI and Emerging Technologies

Artificial intelligence [AI] and emerging digital technologies are increasingly being integrated into tuberculosis diagnostics to improve screening accuracy, reduce diagnostic delays, and strengthen healthcare delivery. These technologies have gained importance because of their potential to overcome shortages of trained healthcare personnel and radiologists in low-resource settings [26].

Artificial Intelligence-Assisted Chest Radiography

AI-assisted radiology uses computer algorithms and deep learning models to analyze chest X-rays for abnormalities suggestive of tuberculosis. AI software can rapidly interpret digital chest radiographs and identify pulmonary lesions such as infiltrates, cavitations, and nodules associated with TB infection.

Several AI-based computer-aided detection systems have demonstrated diagnostic accuracy comparable to experienced radiologists [27]. AI-assisted chest radiography is particularly useful in mass screening programs, prisons, refugee camps, and rural settings where radiology expertise is limited.

The use of AI can improve efficiency, reduce workload on healthcare professionals, and support early case identification. Integration with portable digital X-ray systems further enhances accessibility in underserved regions.

However, algorithm validation, ethical concerns, infrastructure requirements, and data privacy issues remain important challenges affecting large-scale implementation.

Biosensor Technologies

Biosensors are analytical devices capable of detecting specific biological markers associated with tuberculosis infection. Electrochemical, optical, and nanotechnology-based biosensors are being investigated for rapid and sensitive detection of mycobacterial antigens and nucleic acids [28].

Biosensor technologies offer several advantages including portability, rapid results, minimal sample preparation, and potential affordability. These characteristics make them promising tools for point-of-care diagnosis in low-resource settings.

Although many biosensor platforms remain under experimental development, continued advancements may facilitate future commercialization and integration into routine TB diagnostics.

CRISPR-Based Diagnostics

Clustered Regularly Interspaced Short Palindromic Repeats [CRISPR]-based diagnostics represent an emerging molecular technology for rapid detection of infectious diseases including tuberculosis. CRISPR systems can identify specific nucleic acid sequences associated with Mycobacterium tuberculosis with high sensitivity and specificity [29].

CRISPR-based assays may provide rapid and portable diagnostic platforms suitable for decentralized healthcare settings. The technology also has potential applications in drug resistance detection.

Despite promising early results, most CRISPR-based TB diagnostics remain under clinical evaluation and require further validation before large-scale implementation.

Digital Health and Mobile Technologies

Mobile health applications and digital healthcare platforms are increasingly being utilized for TB screening, patient monitoring, and data management. Smartphone-based applications may support symptom screening, treatment adherence monitoring, and remote consultation services [30].

Digital health technologies can improve surveillance, strengthen healthcare communication, and facilitate patient follow-up in remote communities. Integration of AI with digital health platforms may further enhance TB diagnostic efficiency and accessibility.

Challenges

Despite major advances in rapid tuberculosis diagnostics, several challenges continue to affect implementation and accessibility, particularly in low-resource settings. High costs associated with molecular diagnostic equipment, cartridges, maintenance, and infrastructure remain major barriers to widespread adoption [31].

Limited laboratory infrastructure and unstable electricity supply frequently disrupt diagnostic services in rural healthcare facilities. Many advanced technologies also require trained technical personnel, biosafety measures, and quality assurance systems that may not be readily available in underserved regions.

Supply chain interruptions and inadequate maintenance services further contribute to operational difficulties. Delayed procurement of cartridges and consumables may reduce diagnostic efficiency and affect continuity of TB programs.

Diagnostic inequity remains another significant concern. Rural populations, marginalized communities, and economically disadvantaged groups often experience limited access to advanced diagnostic services. Geographic barriers and inadequate transportation infrastructure may further delay diagnosis and treatment initiation.

Emerging technologies such as AI and next-generation sequencing also face regulatory, ethical, and data privacy concerns. Validation across diverse populations and healthcare settings is necessary before large-scale implementation.

Addressing these challenges requires sustained investment, healthcare infrastructure strengthening, workforce training, international collaboration, and policy support to ensure equitable access to rapid diagnostic technologies.

Public Health Implications

Rapid diagnostic technologies have substantial public health significance because early TB detection plays a critical role in reducing transmission, improving treatment outcomes, and supporting global tuberculosis elimination efforts [32].

Early diagnosis facilitates prompt initiation of anti-tubercular therapy, thereby reducing infectiousness and preventing community spread. Rapid identification of drug-resistant strains also improves treatment selection and reduces the emergence of further resistance.

Point-of-care and decentralized diagnostic approaches are particularly important in high-burden countries where healthcare access remains limited. Improved accessibility may strengthen active case-finding programs, contact tracing, and rural healthcare delivery.

Rapid molecular diagnostics also support surveillance and monitoring of multidrug-resistant tuberculosis. Integration of digital technologies and AI-assisted screening can further improve case detection efficiency and strengthen healthcare systems.

The World Health Organization End TB Strategy emphasizes the importance of universal access to rapid diagnostics for achieving global TB elimination goals. Expanding affordable and accessible diagnostic technologies may significantly contribute to reducing TB-related morbidity and mortality worldwide.

Conclusion

Tuberculosis continues to pose a major global public health challenge, particularly in low-resource settings where delayed diagnosis contributes to ongoing transmission and poor clinical outcomes. Recent advances in rapid molecular diagnostics, point-of-care testing, artificial intelligence, and emerging technologies have significantly improved the speed and accuracy of TB detection.

Technologies such as GeneXpert, Truenat, LF-LAM assays, AI-assisted radiology, and CRISPR-based diagnostics demonstrate considerable potential for strengthening TB control programs and improving access to care in underserved populations. Rapid diagnosis facilitates timely treatment initiation, early identification of drug resistance, and reduction of disease transmission.

However, challenges including high costs, inadequate infrastructure, limited technical expertise, and accessibility barriers continue to affect widespread implementation. Sustainable investment, healthcare infrastructure development, and integration of innovative technologies into national TB programs are essential for maximizing the benefits of rapid diagnostics.

Continued research and global collaboration may further enhance diagnostic accessibility and contribute significantly toward achieving international tuberculosis elimination targets.

References

1. World Health Organization. Global tuberculosis report 2024. Geneva: World Health Organization; 2024.
2. Pai M, Behr MA, Dowdy D, Dheda K, Divangahi M, Boehme CC, et al. Tuberculosis. Nat Rev Dis Primers. 2016;2:16076.

3. Dheda K, Gumbo T, Maartens G, Dooley KE, McNerney R, Murray M, et al. The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis. Lancet Respir Med. 2017;5[4]:291-360.
4. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010;363[11]:1005-15.
5. MacLean E, Broger T, Yerlikaya S, Fernandez-Carballo BL, Pai M, Denkinger CM. A systematic review of biomarkers to detect active tuberculosis. Nat Microbiol. 2019;4[5]:748-58.
6. Steingart KR, Henry M, Ng V, Hopewell PC, Ramsay A, Cunningham J, et al. Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review. Lancet Infect Dis. 2006;6[9]:570-81.
7. Parsons LM, Somoskövi A, Gutierrez C, Lee E, Paramasivan CN, Abimiku A, et al. Laboratory diagnosis of tuberculosis in resource-poor countries. Clin Microbiol Rev. 2011;24[2]:314-50.
8. Nachiappan AC, Rahbar K, Shi X, Guy ES, Mortani Barbosa EJ Jr, Shiehmorteza M, et al. Pulmonary tuberculosis: role of radiology in diagnosis and management. Radiographics. 2017;37[1]:52-72.
9. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official American Thoracic Society/Infectious Diseases Society of America/CDC clinical practice guidelines: diagnosis of tuberculosis in adults and children. Clin Infect Dis. 2017;64[2]:111-5.
10. Siddiqi SH, Rüsch-Gerdes S. MGIT procedure manual. Geneva: Foundation for Innovative New Diagnostics; 2006.
11. Fontanilla JM, Barnes A, von Reyn CF. Current diagnosis and management of peripheral tuberculous lymphadenitis. Clin Infect Dis. 2011;53[6]:555-62.
12. Pai M, Schito M. Tuberculosis diagnostics in 2015: landscape, priorities, needs, and prospects. J Infect Dis. 2015;211[Suppl 2]:S21-8.
13. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010;363[11]:1005-15.
14. Chakravorty S, Simmons AM, Rowneki M, Parmar H, Cao Y, Ryan J, et al. The new Xpert MTB/RIF Ultra: improving detection of Mycobacterium tuberculosis and resistance to rifampin in an assay suitable for point-of-care testing. mBio. 2017;8[4]:e00812-17.
15. Nikam C, Jagannath M, Narayanan MM, Ramanabhirama V, Kazi M, Shetty A, et al. Rapid diagnosis of Mycobacterium tuberculosis with Truenat MTB: a near-care approach. PLoS One. 2013;8[1]:e51121.
16. World Health Organization. WHO consolidated guidelines on tuberculosis: module 3: diagnosis—rapid diagnostics for tuberculosis detection. Geneva: World Health Organization; 2021.
17. Nathavitharana RR, Cudahy PG, Schumacher SG, Steingart KR, Pai M, Denkinger CM. Accuracy of line probe assays for the diagnosis of pulmonary and multidrug-resistant tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2017;49[1]:1601075.
18. World Health Organization. The use of loop-mediated isothermal amplification [TB-LAMP] for the diagnosis of pulmonary tuberculosis. Geneva: World Health Organization; 2016.
19. Pankhurst LJ, Del Ojo Elias C, Votintseva AA, Walker TM, Cole K, Davies J, et al. Rapid, comprehensive, and affordable mycobacterial diagnosis with whole-genome sequencing: a prospective study. Lancet Respir Med. 2016;4[1]:49-58.

20. Lawn SD, Kerkhoff AD, Nicol MP, Meintjes G. Underestimation of the incremental yield of urine Determine TB-LAM antigen detection for diagnosis of HIV-associated tuberculosis. AIDS. 2014;28[12]:1846-8.
21. Shah M, Hanrahan C, Wang ZY, Dendukuri N, Lawn SD, Denkinger CM, et al. Lateral flow urine lipoarabinomannan assay for detecting active tuberculosis in HIV-positive adults. Cochrane Database Syst Rev. 2016;5:CD011420.
22. World Health Organization. Lateral flow urine lipoarabinomannan assay [LF-LAM] for the diagnosis of active tuberculosis in people living with HIV. Geneva: World Health Organization; 2019.
23. Qin ZZ, Ahmed S, Sarker MS, Paul K, Adel ASS, Naheyan T, et al. Tuberculosis detection from chest x-rays for triaging in a high tuberculosis-burden setting: an evaluation of five artificial intelligence algorithms. Lancet Digit Health. 2021;3[9]:e543-54.
24. Heller T, Wallrauch C, Lessells RJ, Goblirsch S, Brunetti E. Short course for focused assessment with sonography for HIV/TB: preliminary results in a rural setting in South Africa. Infection. 2010;38[5]:415-21.
25. MacLean E, Broger T, Yerlikaya S, Fernandez-Carballo BL, Pai M, Denkinger CM. A systematic review of biomarkers to detect active tuberculosis. Nat Microbiol. 2019;4[5]:748-58.
26. World Health Organization. Chest radiography in tuberculosis detection: summary of current WHO recommendations and guidance on programmatic approaches. Geneva: World Health Organization; 2016.
27. Murphy K, Habib SS, Zaidi SMA, Khowaja S, Khan A, Melendez J, et al. Computer aided detection of tuberculosis on chest radiographs: an evaluation of the CAD4TB v6 system. Sci Rep. 2020;10[1]:5492.
28. Gupta N, Renugopalakrishnan V, Liepmann D, Paulmurugan R, Malhotra BD. Cell-based biosensors for pathogen detection. Biosens Bioelectron. 2019;141:111435.
29. Ai JW, Zhou X, Xu T, Yang M, Chen Y, He GQ, et al. CRISPR-based rapid and ultra-sensitive diagnostic test for Mycobacterium tuberculosis. Emerg Microbes Infect. 2019;8[1]:1361-9.
30. Iribarren SJ, Schnall R, Stone PW, Carballo-Diéguez A. Smartphone applications to support tuberculosis prevention and treatment: review and evaluation. JMIR Mhealth Uhealth. 2016;4[2]:e25.
31. Pai M, Schito M. Tuberculosis diagnostics in 2015: landscape, priorities, needs, and prospects. J Infect Dis. 2015;211[Suppl 2]:S21-8.
32. World Health Organization. The End TB Strategy. Geneva: World Health Organization; 2015.