International Journal of Scientific Research and Engineering Development-– Volume 8 Issue 5, Sep-Oct 2025
Available at www.ijsred.com

REVIEW ARTICLE OPEN ACCESS

Tuberculosis: A Comprehensive Review of Diagnosis, Treatment, and Global Challenges

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Abstract:
Tuberculosis (TB) is a communicable disease primarily caused by *Mycobacterium tuberculosis*, affecting millions globally. Despite being preventable and curable, TB remains one of the top 10 causes of death worldwide, especially in developing nations. It primarily attacks the lungs (pulmonary TB) but can affect other parts of the body (extra pulmonary TB), including the brain, kidneys, and spine. TB spreads through airborne droplets from infected individuals, making it a public health concern. Immunocompromised individuals, such as those with HIV/AIDS, are particularly susceptible. The pathogenesis involves the bacteria evading the host immune system, leading to granuloma formation and chronic inflammation. The disease's clinical manifestations include a persistent cough, weight loss, fever, night sweats, and fatigue. Diagnosis typically includes sputum smear microscopy, culture, chest X-rays, and advanced methods like GeneXpert and PCR tests. Treatment involves prolonged antibiotic regimens, with the first-line drugs being isoniazid, rifampicin, ethambutol, and pyrazinamide. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) complicate treatment efforts. Herbal medicine is gaining interest as an adjunct or alternative therapy due to the rising resistance to conventional drugs. Several medicinal plants, such as *Ocimum sanctum*, *Curcuma longa*, and *Withania somnifera*, have shown anti-TB potential. This review aims to provide a comprehensive overview of TB, covering its etiology, pathophysiology, diagnostic tools, treatment strategies, and comparison of herbal versus allopathic treatments. It further explores the future scope in TB management, emphasizing novel therapies and preventive strategies for global eradication.

Keywords: **Tuberculosis, *Mycobacterium tuberculosis*, MDR-TB, Herbal medicine, Anti-tubercular drugs, Diagnosis, Treatment, Immune response, Pulmonary TB, Drug resistance.**

INTRODUCTION:

Tuberculosis (TB) remains a critical public health threat worldwide. It is caused by the bacterium *Mycobacterium tuberculosis* and commonly affects the lungs. TB is transmitted via airborne droplets when an infected person coughs or sneezes. The disease has been recognized for centuries, but it still causes significant morbidity and mortality. In 2023, TB claimed over 1.5 million lives globally, particularly in regions

with limited healthcare access. Despite advances in diagnostics and treatment, TB continues to challenge healthcare systems due to drug resistance, poor adherence to therapy, and co-infection with HIV (1, 2).

TB is classified into two forms: latent and active TB. In latent TB, the bacteria remain dormant in the body without causing symptoms, while active TB leads to clinical manifestations and is contagious. Approximately one-quarter of the world's population carries latent TB, and 5-10% of them may develop active TB during their lifetime. Factors such as weakened immunity, malnutrition, and co-infection with HIV increase the likelihood of progression to active disease. Understanding these dynamics is essential for controlling the spread of TB in vulnerable populations (3, 4).

The World Health Organization (WHO) has implemented global strategies to reduce TB incidence, such as the End TB Strategy, aiming for a 90% reduction in TB deaths by 2030. These efforts involve early detection, patient-centered care, and prevention programs. Nevertheless, challenges persist in under-resourced areas, including inadequate diagnostics, drug shortages, and insufficient healthcare infrastructure. Such disparities contribute to delayed diagnosis and incomplete treatment, perpetuating transmission within communities (5,6).

TB affects various organs, but pulmonary TB is the most prevalent and infectious form. Extra pulmonary TB, involving the brain (tuberculous meningitis), spine (Pott's disease), lymph nodes, and kidneys, is also common, particularly in immunocompromised patients. The clinical presentation varies with the site of infection, leading to diagnostic complexities. Common symptoms of pulmonary TB include persistent cough lasting more than two weeks, hemoptysis, fever, night sweats, chest pain, and unexplained weight loss. Early detection and treatment are crucial to prevent complications and mortality (7,8).

The pathophysiology of TB involves complex host-pathogen interactions. Once inhaled, the bacilli are phagocytosed by alveolar macrophages. However, the bacteria can evade destruction and multiply within these immune cells. This triggers a cellular immune response, leading to granuloma formation to contain the infection. Granulomas may persist without symptoms (latent TB) or break down, causing active disease. The immune system's ability to contain the bacilli is crucial in determining disease progression, which is influenced by genetic, nutritional, and environmental factors (9,10).

Diagnosis of TB requires a combination of clinical, radiological, and microbiological evaluations. Traditional methods include sputum smear microscopy and chest X-rays, while newer diagnostic tools like the GeneXpert MTB/RIF test offer rapid detection and drug resistance profiling. Culture methods remain the gold standard for confirmation but are time-consuming. Accurate and early diagnosis is essential for initiating timely treatment, improving outcomes, and limiting disease transmission (11,12).

TB treatment typically involves a 6-month regimen of first-line antibiotics: isoniazid, rifampicin, ethambutol, and pyrazinamide. However, poor adherence, incorrect

prescriptions, and substandard drugs have led to the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), which are more difficult and expensive to treat. MDR-TB requires second-line drugs and longer therapy durations, often with more severe side effects. Ensuring treatment adherence through patient education and support programs is vital for successful outcomes 13,14).

In recent years, interest in herbal medicine as an adjunct therapy for TB has grown. Various plant-based compounds possess antimicrobial, immunomodulatory, and anti-inflammatory properties. Studies have highlighted the anti-TB effects of herbs like *Azadirachta indica* (neem), *Curcuma longa* (turmeric), *Ocimum sanctum* (tulsi), and *Tinospora cordifolia* (giloy). These natural remedies may enhance immune responses, reduce side effects of conventional therapy, and combat drug-resistant strains, although further clinical validation is required(15).

The battle against TB necessitates a multidimensional approach, including public health interventions, improved diagnostics, novel drugs, and preventive vaccines. BCG, the only available TB vaccine, offers limited protection against adult pulmonary TB. Research is ongoing to develop more effective vaccines and shorter drug regimens. Public awareness, early screening, and socio-economic development are also key in mitigating TB's impact. The integration of traditional medicine and modern healthcare systems may open new avenues in TB management (16,17) .

This review aims to provide an in-depth understanding of TB, from its etiology and pathophysiology to current diagnostic and treatment strategies. It also examines the potential role of herbal therapies and contrasts them with conventional allopathic treatments. By highlighting the limitations of existing approaches and the promise of innovative solutions, this review underscores the need for sustained global efforts to eradicate TB and reduce its burden on health systems and society (18,20).

ETIOLOGY:

Tuberculosis is primarily caused by the bacterium *Mycobacterium tuberculosis*, a slow-growing, aerobic, acid-fast bacillus. It is transmitted through airborne droplets expelled by individuals with active pulmonary TB during coughing, sneezing, or talking. Once inhaled, the bacteria can settle in the lungs and initiate infection. However, not all exposed individuals develop the disease. The host's immune response plays a significant role in determining whether the infection remains latent or progresses to active TB (21,23).

Several risk factors increase the likelihood of developing TB. One of the most significant is a compromised immune system. People living with HIV are 20 to 30 times more likely to develop active TB due to reduced immunity. Other immunosuppressive conditions, such as diabetes mellitus, chronic kidney disease, and certain cancers, also elevate the risk. Additionally, malnutrition, alcohol abuse, smoking, and drug use can impair immune function, making individuals more susceptible to TB.

Socioeconomic and environmental factors also contribute to TB etiology. Overcrowded living conditions, poor ventilation, inadequate nutrition, and limited access to healthcare services facilitate the spread and persistence of TB, especially in low- and middle-income countries. Healthcare workers and individuals in close contact with TB patients, such as family members, are also at elevated risk.

Genetic susceptibility is another area of research, as some individuals may have a genetic predisposition that affects their ability to mount an effective immune response. Overall, TB etiology is multifactorial, involving the interaction of biological, environmental, and socioeconomic factors (24,25).

PATHOPHYSIOLOGY:

The pathophysiology of tuberculosis involves a complex interplay between *Mycobacterium tuberculosis* and the host's immune system. When the bacteria enter the lungs via inhalation, they are phagocytosed by alveolar macrophages. However, *M. tuberculosis* has evolved mechanisms to avoid destruction, such as inhibiting phagosome-lysosome fusion, allowing it to survive and replicate inside macrophages.

The innate immune response is the first line of defense, involving macrophages, dendritic cells, and natural killer cells. Infected macrophages release cytokines like TNF-α and IL-12, recruiting more immune cells to the site of infection. This results in the formation of granulomas — organized aggregates of immune cells that aim to contain the infection. Within the granuloma, the bacilli may persist in a dormant state, leading to latent TB.

In individuals with compromised immunity, the granulomas may break down, releasing the bacilli into surrounding tissues and airways, causing active TB. This breakdown leads to caseous necrosis - a hallmark of TB pathology. The resulting inflammation and tissue damage cause symptoms such as persistent cough, fever, weight loss, and hemoptysis.

If not contained, TB can disseminate through the bloodstream to other organs, resulting in extra pulmonary TB. Sites include the brain (tuberculous meningitis), bones (spinal TB), and genitourinary tract. The immune response to TB is double-edged: while it attempts to contain the infection, it also contributes to tissue damage and disease symptoms.

Understanding TB's pathophysiology is crucial for developing effective therapies and vaccines. Targeting the host-pathogen interactions that enable bacterial persistence offers promising avenues for innovative treatment strategies (26,28).

DIAGNOSIS:

The diagnosis of tuberculosis (TB) involves a multifaceted approach that includes clinical evaluation, radiological imaging, and microbiological testing. Early and accurate diagnosis is critical for initiating treatment, preventing transmission, and reducing mortality. Despite advances in technology, TB diagnosis remains a challenge in many resource-limited settings. The initial clinical assessment begins with a detailed history and physical examination.

Common symptoms suggestive of pulmonary TB include a persistent cough lasting more than two weeks, hemoptysis, weight loss, fever, night sweats, and fatigue. For extra pulmonary TB, symptoms depend on the affected organ and may be less specific.

Chest X-ray is a primary imaging tool used to detect lung abnormalities such as infiltrates, cavitations, and nodular lesions. However, radiographic findings alone are not definitive for TB and must be supported by microbiological confirmation.

Sputum smear microscopy is one of the oldest and most widely used diagnostic tools. It involves staining sputum samples using the Ziehl–Neelsen technique to detect acid-fast bacilli (AFB). While it is rapid and cost-effective, its sensitivity is limited, especially in HIV patients and children.

Culture remains the gold standard for TB diagnosis. Culturing *Mycobacterium tuberculosis* on Lowenstein-Jensen or liquid media can confirm the diagnosis and allow drug susceptibility testing. However, this method is time-consuming, taking several weeks for results.

Modern molecular methods have significantly improved TB diagnosis. The GeneXpert MTB/RIF assay is a rapid, automated PCR test that detects TB and rifampicin resistance within two hours. Line Probe Assays (LPA) and whole genome sequencing are also used for detecting multidrug-resistant TB (MDR-TB).

For extra pulmonary TB, additional methods such as fine-needle aspiration, biopsy, and imaging techniques like MRI or CT scans may be necessary. TB infection can also be detected using tuberculin skin test (TST) and interferon-gamma release assays (IGRAs), particularly for latent TB.

Thus, combining clinical suspicion with radiological and laboratory evidence ensures accurate diagnosis and facilitates early initiation of treatment (30,32).

TREATMENT:

The treatment of tuberculosis (TB) aims to eliminate *Mycobacterium tuberculosis* from the body, reduce transmission, and prevent the development of drug resistance. Standard treatment protocols depend on whether the patient has drug-sensitive TB, multidrug-resistant TB (MDR-TB), or extensively drug-resistant TB (XDR-TB).

For drug-sensitive TB, the World Health Organization (WHO) recommends a 6-month regimen. This consists of two phases:

- **Intensive Phase (2 months):** Isoniazid (INH), Rifampicin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB)
- **Continuation Phase (4 months):** Isoniazid and Rifampicin

These first-line drugs are highly effective when taken consistently under directly observed treatment (DOT). DOT involves health professionals supervising the intake of medication to ensure adherence.

Side effects of TB treatment can include hepatotoxicity, neuropathy, skin rashes, and gastrointestinal discomfort. Regular monitoring of liver enzymes and patient education on recognizing side effects are essential.

MDR-TB is defined as resistance to at least isoniazid and rifampicin. It requires second-line treatment for 18–24 months, involving drugs such as:

- Fluoroquinolones (e.g., levofloxacin, moxifloxacin)
- Injectable agents (e.g., amikacin, capreomycin)
- Linezolid, clofazimine, bedaquiline, and delamanid

These drugs have more adverse effects, including ototoxicity, nephrotoxicity, and bone marrow suppression, and are expensive and less accessible in low-income countries. XDR-TB, resistant to first-line and second-line drugs, requires individualized treatment regimens. Newer WHO guidelines recommend all-oral regimens, avoiding injectable, to improve patient compliance.

For latent TB infection (LTBI), isoniazid monotherapy or combination therapy with rifampicin is used for 3–9 months to prevent progression to active TB.

Supportive care includes nutritional supplementation, treatment of co-infections (especially HIV), and psychological counseling. Vaccination with Bacille Calmette-Guerin (BCG) provides protection against severe forms of TB in children but is less effective in adults.

Continued research aims to develop shorter, more effective, and less toxic drug regimens to combat TB and its resistant forms (33, 36).

HERBAL VS ALLOPATHIC MEDICINES USED FOR TB (37, 40):

Table.1: Herbal vs Allopathic medicines

Parameter	Herbal Medicine	Allopathic Medicine
Source	Plant-based compounds	Synthetic/chemical drugs
Common Drugs	*Curcuma longa* (Turmeric), *Ocimum sanctum*, *Azadirachta indica*	Isoniazid, Rifampicin, Pyrazinamide, Ethambutol
Mechanism of Action	Immunomodulatory, antimicrobial, anti-inflammatory	Bactericidal or bacteriostatic; inhibit mycolic acid synthesis etc.
Side Effects	Minimal to mild (e.g., GI upset, allergy)	Hepatotoxicity, neuropathy, rash, GI issues
Resistance Development	Low (under study)	High, especially with non-adherence (MDR-TB, XDR-TB)
Accessibility	Readily available in local regions	Depends on healthcare access, expensive in some regions
Scientific Validation	Limited clinical trials; mainly in vitro/in vivo studies	Extensive clinical research and WHO-approved guidelines
Treatment Duration	Not standardized	6 months (drug-sensitive TB), up to 24 months (MDR/XDR-TB)
Use in MDR/XDR TB	Potential adjunct therapy	Primary treatment modality
Role in TB Management	Supportive or adjunctive therapy	Primary, standardized therapy

FUTURE SCOPE OF STUDY (41,45):

The future of tuberculosis (TB) research and control strategies involves a multidisciplinary and innovative approach aimed at eradicating the disease. Several areas hold promising potential for advancement and implementation in TB diagnosis, treatment, prevention, and public health management.

One of the most critical areas for future research is the development of shorter, more effective drug regimens. Current therapies, especially for drug-resistant TB, are prolonged and associated with severe side effects. Newer drugs like bedaquiline, delamanid, and pretomanid have shown promise in treating MDR/XDR-TB, but further research is needed to optimize combinations and minimize toxicity.

Another key area is the development of a more effective vaccine than BCG. Although BCG protects against severe childhood TB, it has limited efficacy against adult pulmonary TB. Several vaccine candidates, including M72/AS01E, are in clinical trials and could revolutionize TB prevention if proven successful.

Advancements in diagnostic technologies are also crucial. Rapid molecular tests like GeneXpert have improved detection, but access remains limited in remote and under-resourced areas. Future diagnostics should be cost-effective, point-of-care, and capable of detecting both TB and drug resistance with high sensitivity and specificity.

The integration of herbal medicine into mainstream TB care is another future direction. With increasing antimicrobial resistance, herbal therapies offer complementary or alternative options. However, robust clinical trials and standardization of herbal formulations are necessary to validate their efficacy and safety.

Personalized medicine using genetic and immunological profiling may allow tailored therapies for individual patients, optimizing outcomes. Moreover, digital health solutions, including mobile apps and telemedicine, can improve adherence and follow-up, especially in remote regions.

Lastly, socio-economic improvements, public awareness campaigns, and political commitment are essential to address the social determinants of TB. Addressing poverty, malnutrition, and overcrowding will reduce the disease burden significantly.

CONCLUSION:

Tuberculosis remains one of the most persistent infectious diseases, posing a significant burden on global public health. Despite being a preventable and curable condition, TB continues to cause extensive morbidity and mortality, particularly in low- and middle-income countries. Its dual nature as both an infectious and socially rooted disease makes its control complex and multidimensional.

The causative organism, *Mycobacterium tuberculosis*, has a unique pathogenic mechanism that allows it to survive and persist in host tissues, resulting in latent or active disease. The progression from infection to disease is influenced by several factors, including immune status, nutrition,

comorbidities, and environmental conditions. TB's clinical presentation can vary, making diagnosis challenging without the aid of specialized tests.

Over the years, diagnostic methods have evolved from basic smear microscopy to advanced molecular techniques like GeneXpert and whole genome sequencing. These tools offer rapid, sensitive, and accurate diagnosis, critical for timely initiation of treatment. Treatment, while effective in most drug-sensitive cases, faces obstacles such as long duration, drug resistance, and poor compliance. The emergence of MDR-TB and XDR-TB underscores the need for continued innovation in drug development and adherence strategies.

Comparatively, herbal medicine has garnered interest as a supportive therapy. While several herbs show anti-TB potential, clinical evidence is limited. Nonetheless, integrating herbal approaches with conventional therapy could provide holistic and accessible treatment options, especially in resource-poor settings.

In conclusion, TB control requires a multi-pronged strategy encompassing early detection, effective treatment, patient education, socio-economic upliftment, and global collaboration. With sustained efforts in research, healthcare delivery, and policy implementation, the vision of a TB-free world is achievable.

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