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Review

A Comprehensive Review on Tuberculosis

Mohd Hussain Wani[1], Kulbir Singh[2], Tamheed Zahid[3], Shubam Singh[4], Ms. Tanya Sharma[5]

[1,2,3]*Student, Mewar University, Chittorgarh, Rajasthan, India*
[4]*Student, Deen Dayal Rustagi College of Pharmacy, Haileymandi, Haryana, India*
[5]*Assistant Professor, Mewar Universty, Chittorgarh, Rajasthan, India*

*Author for Correspondence: Ms. Tanya Sharma
Email: 28taney@gmail.com

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Abstract

Tuberculosis (TB) remains a global public health challenge, affecting millions of people annually. Despite advancements in diagnostics and therapeutics, the disease continues to be a leading cause of mortality, particularly in low- and middle-income countries. TB is a complex infectious disease that requires a multidisciplinary approach for effective control. This review explores the epidemiology, pathophysiology, clinical manifestations, diagnostic methods, and treatment strategies for TB. Emphasis is placed on recent advancements in molecular diagnostics, novel therapeutic approaches, and the impact of socio-economic factors on disease spread. Furthermore, the review highlights the challenges in TB control, including drug resistance, vaccine development, and the role of public health interventions in combating the disease.

Keywords: Tuberculosis, Mycobacterium tuberculosis, Drug resistance, Diagnosis, Epidemiology, Treatment strategies, Public health, Molecular diagnostics.

1. INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis, a bacterium that primarily affects the lungs but can also involve other organs such as the kidneys, bones, and central nervous system. TB has been a significant public health concern for centuries, with historical evidence suggesting its presence in human populations as early as 9000 years ago. Referred to as "consumption" in the past, TB was often fatal before the advent of antibiotics.

2. Epidemiology

Tuberculosis remains one of the most prevalent infectious diseases worldwide, ranking among the top ten causes of death. According to the World Health Organization (WHO), approximately 1.7 billion people globally have latent TB infection, meaning that nearly a quarter of the global population is harboring the bacteria without showing symptoms. The burden of TB is highest in low- and middle-income countries, particularly in South Asia, Africa, and parts of Eastern Europe. Countries such as India, China, Indonesia, the Philippines, Nigeria, Pakistan, Bangladesh, and South Africa report the highest numbers of TB cases annually, driven by factors such as high population density, malnutrition, poor healthcare infrastructure, and lack of access to medical services.

The epidemiology of TB is also shaped by socio-economic determinants. Poverty, overcrowding, and inadequate sanitation contribute to its spread, as TB is an airborne disease that thrives in conditions where individuals are in close contact. Additionally, the HIV epidemic has exacerbated TB incidence, as people with weakened immune systems are more susceptible to developing active TB. The emergence of drug-resistant TB has further complicated the disease burden, with multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) posing serious threats to global TB control efforts. The COVID-19 pandemic has also disrupted TB prevention and treatment programs, leading to increased transmission and delays in diagnosis and care.

3. Pathophysiology and Clinical Manifestations

The pathophysiology of TB begins when Mycobacterium tuberculosis is inhaled into the alveoli of the lungs. The bacteria are engulfed by alveolar macrophages, but due to their ability to evade the immune response by inhibiting phagosome-lysosome fusion, they can survive and multiply inside the host cells. This triggers an immune response that leads to the formation of granulomas, which are structures composed of infected macrophages surrounded by lymphocytes and other immune cells. These granulomas attempt to contain the infection, but in some cases, they break down, allowing the bacteria to spread to other parts of the body.

TB can manifest in different clinical forms. The most common is pulmonary tuberculosis, which primarily affects the lungs. Symptoms of pulmonary TB include a persistent cough lasting more than three weeks, hemoptysis (coughing up blood), chest pain, unexplained weight loss, fever, night sweats, and fatigue. If left untreated, pulmonary TB can cause extensive lung damage, leading to respiratory failure. Extrapulmonary TB occurs when the bacteria spread beyond the lungs to other organs such as the lymph nodes, bones, brain, kidneys, and gastrointestinal tract. TB meningitis, a severe form of the disease, affects the brain and spinal cord, leading to neurological complications. Miliary TB is a disseminated form of TB that spreads throughout the body via the bloodstream and is often fatal if not treated promptly.

4. Diagnosis of Tuberculosis

The diagnosis of tuberculosis relies on a combination of clinical assessment, microbiological testing, and imaging techniques. Conventional diagnostic methods include sputum smear microscopy, in which acid-fast bacilli (AFB) are detected under a microscope. While widely used, this method has low sensitivity, especially in patients co-infected with HIV. Chest X-ray is another commonly used diagnostic tool that can reveal lung abnormalities suggestive of TB, but it lacks specificity and cannot confirm the presence of active TB.

Molecular diagnostics have significantly improved TB detection and drug resistance screening. The GeneXpert MTB/RIF assay is a rapid molecular test that detects M. tuberculosis DNA and identifies rifampicin resistance within hours, making it a valuable tool for early diagnosis. Line probe assays are also used to detect mutations associated with drug resistance. Culture-based methods remain the gold standard for TB diagnosis, with Lowenstein-Jensen and Mycobacteria Growth Indicator Tube (MGIT) cultures allowing for bacterial growth and drug susceptibility testing. Immunological tests such as the Tuberculin Skin Test (TST) and Interferon-Gamma Release Assays (IGRAs) are used to diagnose latent TB infection rather than active disease.

5. Treatment Strategies

The treatment of tuberculosis involves a prolonged regimen of multiple antibiotics to ensure complete eradication of the bacteria and prevent drug resistance. The first-line anti-TB treatment consists of a 6-month regimen including four drugs: Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide. The intensive phase lasts for two months, followed by a four-month continuation phase with Isoniazid and Rifampicin.

For patients with multidrug-resistant TB (MDR-TB), treatment is more complex and requires second-line drugs such as fluoroquinolones (Levofloxacin, Moxifloxacin) and injectable agents (Amikacin, Capreomycin). Recently, newer drugs such as Bedaquiline and Delamanid have shown promise in improving treatment outcomes for drug-resistant TB. Extensively drug-resistant TB (XDR-TB) is even more difficult to treat, requiring prolonged therapy with limited effective drug options.

For individuals with latent TB infection, preventive therapy with Isoniazid or Rifapentine is recommended, particularly for high-risk populations such as people living with HIV, healthcare workers, and close contacts of active TB cases.

6. Challenges in TB Control

Despite progress in TB diagnosis and treatment, several challenges hinder global TB control efforts. The rise of drug-resistant TB has made treatment more complicated and costly, with MDR-TB and XDR-TB requiring prolonged regimens that often have severe side effects. Poor adherence to TB treatment contributes to the development of drug resistance, highlighting the need for patient-centered care and improved healthcare infrastructure.

Vaccine development remains a major challenge, as the Bacillus Calmette-Guérin (BCG) vaccine, currently the only licensed TB vaccine, provides limited protection, especially in adults. New vaccine candidates such as M72/AS01E have shown promise in clinical trials, but widespread implementation remains years away.

Global TB elimination efforts, including the WHO's End TB Strategy, aim to reduce TB mortality and incidence rates, but achieving these goals requires increased funding, enhanced surveillance, and improved access to healthcare services. Addressing social determinants of health, strengthening public health interventions, and investing in novel TB diagnostics and therapeutics are essential for reducing the global burden of tuberculosis.

7. Future Directions in TB Research and Control

Future efforts in TB control should focus on multiple innovative strategies to improve prevention, diagnosis, and treatment. One of the key areas of research is the development of more effective TB vaccines. The current Bacillus Calmette-Guérin (BCG) vaccine provides limited protection against pulmonary TB in adults, necessitating the need for next-generation vaccines. Several candidates, including M72/AS01E and VPM1002, are in advanced clinical trials and hold promise for better protection.

Additionally, research in host-directed therapies (HDT) aims to enhance the immune response against M. tuberculosis by modulating host pathways rather than targeting the bacteria directly. This approach could reduce the likelihood of drug resistance and improve treatment outcomes.

Another critical area is the integration of artificial intelligence (AI) and digital health technologies into TB diagnosis and management. AI-powered algorithms for chest X-ray analysis, smartphone-based diagnostic tools, and telemedicine platforms can help detect TB cases earlier and improve patient monitoring. Moreover, the development of shorter and more effective drug regimens remains a top priority, with novel anti-TB drugs such as Bedaquiline, Pretomanid, and Delamanid showing potential in reducing treatment duration and side effects.

Efforts to enhance global TB surveillance systems are also crucial. Strengthening molecular epidemiology techniques, such as whole-genome sequencing, can help track TB transmission patterns and identify drug-resistant strains early. Lastly, addressing social determinants of TB, such as poverty reduction, improved housing conditions, and better access to healthcare, will play a significant role in long-term TB control.

8. Additional Strategies for TB Control

1. Integration of Artificial Intelligence (AI) in TB Diagnosis and Treatment: AI-powered tools can improve TB diagnosis through automated analysis of chest X-rays and patient data, enhancing early detection and treatment adherence.

2. Expansion of Community-Based TB Programs: Strengthening grassroots-level interventions can enhance early detection, treatment adherence, and patient education, especially in high-burden areas.

3. Development of Shorter and More Effective Drug Regimens: Research on novel drug formulations aims to reduce treatment duration and minimize side effects, improving patient compliance.

4. Strengthening Global TB Surveillance Systems: Enhanced data collection and reporting mechanisms can improve tracking of TB trends and resistance patterns, aiding in more effective intervention strategies.

5. Addressing Social Determinants of TB: Improving access to quality healthcare, reducing poverty, and ensuring better nutrition are critical in reducing TB transmission and improving treatment outcomes.

6. Role of Next-Generation Sequencing in TB Research: Advances in next-generation sequencing (NGS) can provide deeper insights into M. tuberculosis genetic mutations, drug resistance mechanisms, and transmission dynamics. The use of NGS in real-time surveillance can help in the early detection of outbreaks and improve targeted treatment approaches.

7. Enhancing TB Control in High-Risk Populations: Special attention should be given to vulnerable groups, including migrants, prisoners, and immunocompromised individuals (such as HIV-positive patients). Tailored TB control programs, improved access to healthcare, and targeted interventions are necessary to address the specific challenges faced by these populations.

8. Strengthening Public-Private Partnerships in TB Control: Collaboration between governments, non-governmental organizations (NGOs), pharmaceutical companies, and private healthcare providers can enhance TB control strategies. Public-private partnerships (PPPs) can facilitate better resource allocation, funding for research, and improved patient access to diagnostics and treatment.
9. Promoting TB Awareness and Education Campaigns: Increasing public awareness about TB through educational programs, media campaigns, and community outreach can help reduce stigma, encourage early diagnosis, and improve treatment adherence. Public education initiatives should target both urban and rural populations, ensuring widespread dissemination of TB-related knowledge.

9. CONCLUSION

Despite significant progress, tuberculosis remains a major global health issue. Advances in diagnostics, treatment strategies, and vaccine development offer hope, but challenges such as drug resistance and healthcare accessibility hinder eradication efforts. A collaborative global approach is essential to reduce TB burden and achieve elimination targets.

Author contribution
Mohd. Hussain Wani have written the draft and revised review, editing, & rewriting & Finalized the manuscript, & Tanya sharma was responsible for editing. supervision of the manuscript. All authors approved the manuscript.

Competing interests
The authors declare no conflicts of interest.

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