

Overview of Tuberculosis: Causes, Symptoms, and Risk Factors

Abstract

Tuberculosis (TB) remains a global health threat, exacerbated by factors such as drug resistance, co-infections, and social determinants of health. This comprehensive review examines various aspects of TB, including epidemiology, pathophysiology, diagnosis, treatment, prevention, and control measures. The bacterium *Mycobacterium tuberculosis* causes TB and primarily affects the lungs, although it can also affect other organs. Risk factors for TB include poverty, malnutrition, overcrowded living conditions, and immunocompromised states such as HIV/AIDS. Symptoms of TB include cough, fever, weight loss, and night sweats, but can vary depending on the site of infection. Diagnosis typically involves clinical evaluation, imaging studies, and microbiological testing, with rapid molecular tests such as the Xpert MTB/RIF assay revolutionizing TB diagnostics. Treatment consists of multidrug therapy for six to nine months, with drug-resistant TB requiring longer and more complex regimens. Prevention and control efforts focus on early case detection, treatment adherence, infection control measures, and Bacille Calmette-Guérin (BCG) vaccine vaccination. TB research and innovation aim to develop new diagnostics, drugs, and vaccines to improve TB control and treatment outcomes. Challenges to TB control include stigma, healthcare access barriers, and the rise of drug-resistant TB strains. Collaboration and advocacy efforts are essential for addressing TB in special populations, high-risk settings, and co-infection scenarios. Integrating a One Health approach, harnessing technology, and addressing climate change impacts is critical for advancing TB control efforts and achieving the goal of ending the global TB epidemic.

Keywords: Tuberculosis, Epidemiology, Diagnosis, Treatment, Prevention

Introduction

Tuberculosis (TB) has long been recognized as one of the most ancient and persistent infectious diseases afflicting humanity [1]. *Mycobacterium tuberculosis*'s etiological agent has haunted human populations for millennia, shaping societies and influencing historical events. Despite significant strides in medical science and public health, TB remains a formidable global health challenge, affecting millions of individuals worldwide each year.

TB is primarily transmitted through the inhalation of airborne droplets containing *M. tuberculosis*, typically expelled when an infected individual coughs or sneezes [1]. This transmission mode underscores the significance of close human contact and shared airspace in facilitating the spread of the disease. Factors such as overcrowded living conditions, inadequate ventilation, and compromised immune systems further exacerbate the risk of TB transmission [2].

The clinical manifestations of TB are diverse and can vary depending on factors such as the route of infection and the individual's immune status. Common symptoms include a persistent cough,

fever, fatigue, and weight loss [3]. However, TB can also affect other organs besides the lungs, leading to extrapulmonary manifestations such as lymphadenitis, pleuritis, and meningitis [4].

Various risk factors predispose individuals to TB infection and disease progression. Immunocompromised conditions, such as HIV/AIDS, malnutrition, and diabetes, significantly increase susceptibility to TB [5]. Additionally, socioeconomic determinants such as poverty, homelessness, and inadequate access to health care contribute to the burden of TB, particularly in vulnerable populations [6].

Efforts to combat TB encompass a multifaceted approach, including early diagnosis, prompt treatment initiation, and comprehensive prevention strategies. Diagnostic tools such as the TB skin test, chest X-ray, and sputum culture are crucial in identifying active TB cases [7]. Treatment typically involves a combination of antibiotics administered over several months, with directly observed therapy ensuring treatment adherence and minimizing the risk of drug resistance [8].

Despite advancements in TB control, significant challenges persist. The emergence of drug-resistant TB strains poses a formidable threat to treatment efficacy and public health [9]. Additionally, socioeconomic disparities, inadequate healthcare infrastructure, and stigma associated with TB hinder efforts to achieve equitable access to care and treatment [10].

Epidemiology

Tuberculosis (TB) continues to be a global health concern, with significant implications for public health and healthcare systems worldwide. Despite concerted efforts to control the disease, TB remains a leading cause of morbidity and mortality, particularly in low- and middle-income countries. According to the World Health Organization (WHO), an estimated 10 million people developed TB in 2019, with approximately 1.4 million deaths attributed to the disease [8].

The burden of TB is not evenly distributed across populations, with certain regions bearing a disproportionate share of the disease burden. The WHO regions of South-East Asia and Africa account for the highest number of TB cases globally, with India and China alone contributing to approximately 40% of the total TB burden [8]. Within countries, TB incidence rates often vary widely based on socioeconomic factors, geographical location, and access to healthcare services.

The emergence of drug-resistant TB poses a significant challenge to TB control efforts. Multidrug-resistant TB (MDR-TB), defined as resistance to at least isoniazid and rifampicin, is of particular concern due to its limited treatment options and poorer prognosis. According to WHO estimates, there were approximately 465,000 cases of MDR-TB worldwide in 2019, with the highest prevalence observed in Eastern Europe and Central Asia [8]. Extensively drug-resistant TB (XDR-TB), characterized by resistance to fluoroquinolones and second-line injectable drugs in addition to isoniazid and rifampicin, further complicates treatment and management strategies.

Certain population groups are at higher risk of TB infection and disease progression, including individuals living with HIV/AIDS, migrants, prisoners, and those living in overcrowded or impoverished settings. HIV/AIDS is a significant risk factor for TB, as it weakens the immune system and increases susceptibility to TB infection and reactivation of latent TB [8]. In 2019,

approximately 8.2% of TB cases worldwide were among people living with HIV, highlighting the intersection between TB and HIV/AIDS epidemics.

Efforts to control TB have been hampered by various challenges, including inadequate funding, weak healthcare infrastructure, limited access to diagnostics and treatment, and social stigma associated with the disease. The COVID-19 pandemic has further exacerbated these challenges, disrupting TB services, diverting resources, and exacerbating vulnerabilities among affected populations [8].

Pathophysiology

Tuberculosis (TB) is caused by infection with the bacterium *Mycobacterium tuberculosis*. This slow-growing, acid-fast bacillus primarily affects the lungs but can also involve other organs in the body. The pathophysiology of TB involves a complex interplay between the host immune response and the virulence factors of *M. tuberculosis*, leading to the characteristic clinical manifestations of the disease.

Following inhaling *M. tuberculosis*-containing droplets, the bacteria are deposited in the lungs' alveoli, where alveolar macrophages engulf them. In most cases, the immune response successfully contains the infection at this stage, leading to the formation of granulomas, characteristic histological features of TB. Granulomas comprise a central core of infected macrophages surrounded by lymphocytes, epithelioid cells, and multinucleated giant cells [8].

Within the granuloma, *M. tuberculosis* may enter a state of dormancy known as latent tuberculosis infection (LTBI), where the bacteria remain viable but are contained by the host immune response. Individuals with LTBI are asymptomatic and non-infectious but are at risk of developing active TB disease if their immune system becomes compromised [8].

In some cases, the immune response may fail to contain the infection, leading to the progression from LTBI to active TB disease. This can occur due to factors such as immunosuppression (e.g., HIV/AIDS), malnutrition, diabetes, or aging. Active TB disease is characterized by the reactivation of dormant bacteria within the granuloma, leading to the destruction of lung tissue and the formation of cavities, which can serve as reservoirs for bacterial replication and dissemination [8].

The clinical manifestations of active TB disease depend on various factors, including the site and extent of infection, the immune status of the host, and the presence of underlying comorbidities. Pulmonary TB is the most common form of the disease, presenting with symptoms such as persistent cough, hemoptysis (coughing up blood), chest pain, and shortness of breath. Extrapulmonary TB can involve virtually any organ system, with manifestations such as lymphadenitis, pleuritis, meningitis, and disseminated disease [8].

The diagnosis of TB relies on a combination of clinical, radiological, and microbiological criteria. Microbiological confirmation of TB is achieved by detecting *M. tuberculosis* in clinical specimens such as sputum, bronchoalveolar lavage fluid, or tissue biopsy samples. Diagnostic tests such as the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) can help identify individuals with LTBI. In contrast, imaging studies such as chest X-ray and computed tomography (CT) scans can aid in detecting pulmonary and extrapulmonary manifestations of TB [8].

Treatment of TB involves a multidrug regimen consisting of antibiotics such as isoniazid, rifampicin, pyrazinamide, and ethambutol. Directly observed therapy (DOT) is recommended to ensure treatment adherence and minimize the risk of drug resistance. The duration of treatment varies depending on factors such as the site and extent of infection, the presence of drug resistance, and the individual's immune status [8].

Causes of Tuberculosis

Tuberculosis (TB) is caused by infection with the bacterium *Mycobacterium tuberculosis*, also known as the tubercle bacillus. *M. tuberculosis* is a slow-growing, acid-fast bacillus that primarily affects the lungs but can also involve other organs in the body [11]. TB is primarily transmitted through the inhalation of airborne droplets containing *M. tuberculosis*, typically expelled when an infected individual coughs, sneezes, or talks. This transmission mode underscores the significance of close human contact and shared airspace in facilitating the spread of the disease [12].

Several factors contribute to the transmission and spread of TB within populations. Overcrowded living conditions, poor ventilation, and inadequate healthcare infrastructure create ideal TB transmission environments. Individuals with active TB disease, particularly those with pulmonary involvement, are highly infectious and can transmit the disease to others through close and prolonged contact [13].

While the respiratory route is the primary mode of TB transmission, other less common routes of transmission include ingestion of contaminated food or milk (in the case of bovine TB), transmission from mother to child during childbirth or through breastfeeding, and transmission through organ transplantation or blood transfusion from an infected donor [14].

Individuals with latent tuberculosis infection (LTBI) do not have active TB disease and are not contagious. However, they are at risk of developing active TB disease if their immune system becomes compromised, such as in the case of HIV/AIDS, malnutrition, diabetes, or treatment with immunosuppressive medications [15]. LTBI is typically asymptomatic and can only be detected through specific diagnostic tests such as the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs).

In addition to environmental and host-related factors, genetic susceptibility plays a role in determining an individual's TB risk. Certain genetic polymorphisms have been associated with an increased risk of TB infection and disease progression, highlighting the complex interplay between host genetics and microbial factors in TB pathogenesis [16].

Symptoms of Tuberculosis

Tuberculosis (TB) manifests with a wide range of symptoms, which can vary depending on factors such as the site and extent of infection, the immune status of the host, and the presence of underlying comorbidities. The classic symptoms of pulmonary TB include a persistent cough lasting for more than two weeks, which may be productive of sputum that is often bloody or purulent [17]. Other respiratory symptoms can include chest pain, difficulty breathing, and

wheezing, particularly in cases where the infection involves the pleura or causes bronchial obstruction.

Systemic symptoms such as fever, night sweats, and fatigue are common in individuals with active TB disease. Fever may be low-grade or intermittent, often accompanied by chills and sweats, particularly at night [18]. Night sweats, also known as nocturnal hyperhidrosis, can be profuse and drenching, leading to sleep disturbances and fatigue during the day. Weight loss is another hallmark feature of TB, often accompanied by loss of appetite and general malaise [19].

In addition to respiratory and systemic symptoms, TB can also present with extrapulmonary manifestations involving other organ systems. Extrapulmonary TB can affect virtually any organ in the body, with common sites of involvement including the lymph nodes, bones and joints, central nervous system, and genitourinary tract [20]. Symptoms of extrapulmonary TB can vary depending on the site of infection and may include localized pain, swelling, neurological deficits, and urinary symptoms.

In children, TB symptoms can be more nonspecific and may include failure to thrive, poor weight gain, irritability, and developmental delay [21]. Children with TB may also present with respiratory symptoms such as cough, wheezing, difficulty breathing and systemic symptoms such as fever, night sweats, and fatigue. Extrapulmonary TB is more common in children than in adults and can involve sites such as the lymph nodes, bones and joints, and central nervous system [22].

Risk Factors for Tuberculosis

Several risk factors contribute to an individual's susceptibility to tuberculosis (TB) infection and progression to active disease. Immunocompromised conditions, such as infection with the human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS), significantly increase the risk of developing TB. HIV/AIDS weakens the immune system, making individuals more susceptible to TB infection and increasing the likelihood of TB reactivation in individuals with latent TB infection (LTBI) [1].

Malnutrition and undernutrition also significantly increase the risk of TB infection and disease progression. Poor nutritional status compromises the immune system's ability to effectively respond against TB bacteria, leading to increased susceptibility to infection and poorer treatment outcomes. Conversely, TB infection can exacerbate malnutrition, creating a vicious cycle of immune compromise and disease progression [2].

Diabetes mellitus is another crucial risk factor for TB, as individuals with diabetes are more susceptible to TB infection and have an increased risk of developing active TB disease. Diabetes impairs immune function, particularly macrophage and T-cell function, which are crucial for controlling TB infection. Poorly controlled diabetes is associated with worse TB treatment outcomes and an increased risk of TB relapse and mortality [3].

Other medical conditions that predispose individuals to TB infection and disease progression include chronic kidney disease, end-stage renal disease (ESRD), and certain autoimmune disorders requiring immunosuppressive therapy. These conditions compromise immune function and increase the risk of TB reactivation or progression to active disease. Similarly, individuals undergoing treatment with immunosuppressive medications, such as corticosteroids or tumor

necrosis factor (TNF) inhibitors, are at increased risk of TB infection due to impaired immune surveillance and response [4].

Socioeconomic factors also significantly shape an individual's risk of TB infection and disease progression. Poverty, overcrowded living conditions, homelessness, and inadequate access to healthcare are associated with higher rates of TB incidence and poorer treatment outcomes. Limited access to diagnostic and treatment services, as well as delays in seeking care, contribute to the spread of TB within communities and hinder efforts to control the disease [5].

Certain demographic factors, such as age and gender, also influence an individual's risk of TB infection and disease progression. TB incidence rates are highest among young adults aged 15-44 years, reflecting the social and economic factors driving TB transmission in this age group. However, TB can affect individuals of all ages, including children and older people. Men are generally at higher risk of TB than women, partly due to behavioral and occupational factors that increase exposure to TB infection [6].

Diagnosis and Treatment

Diagnosing tuberculosis (TB) requires a combination of clinical, radiological, and microbiological approaches to confirm the presence of active TB disease and guide appropriate treatment. Clinical evaluation involves a thorough medical history, physical examination, and assessment of risk factors for TB infection and disease progression. Common symptoms such as persistent cough, fever, night sweats, and weight loss raise suspicion for TB and warrant further investigation [1].

Radiological imaging studies such as chest X-ray and computed tomography (CT) scans play a crucial role in diagnosing pulmonary TB. Chest X-ray findings suggestive of TB include the presence of pulmonary infiltrates, cavitation, and hilar or mediastinal lymphadenopathy. However, chest X-ray findings alone are not diagnostic of TB and must be interpreted with clinical and microbiological findings [2].

Microbiological confirmation of TB is achieved by detecting *Mycobacterium tuberculosis* in clinical specimens such as sputum, bronchoalveolar lavage fluid, or tissue biopsy samples. Sputum smear microscopy, culture, and molecular assays such as nucleic acid amplification tests (NAATs) are commonly used diagnostic tests for TB. Sputum smear microscopy involves staining sputum samples with specific dyes to visualize acid-fast bacilli (AFB), while culture allows for the isolation and identification of *M. tuberculosis* bacteria. NAATs such as the Xpert MTB/RIF assay provide rapid and sensitive detection of TB and rifampicin resistance, enabling early diagnosis and initiation of appropriate treatment [3].

In addition to microbiological tests, immunological assays such as the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) can help identify individuals with latent TB infection (LTBI). These tests measure the immune response to *M. tuberculosis* antigens and indicate exposure to TB bacteria. However, they cannot differentiate between latent infection and active disease and must be interpreted in the context of clinical and radiological findings [4].

Once a diagnosis of TB is confirmed, treatment is initiated promptly to prevent disease progression, reduce transmission, and improve clinical outcomes. Treatment of TB involves a combination of antibiotics administered over several months, typically consisting of an initial intensive phase followed by a continuation phase. First-line anti-TB drugs include isoniazid, rifampicin, pyrazinamide, and ethambutol, which are effective against drug-sensitive TB strains. Directly observed therapy (DOT) is recommended to ensure treatment adherence and minimize the risk of drug resistance [5].

The duration of TB treatment varies depending on factors such as the site and extent of infection, the presence of drug resistance, and the individual's immune status. Standard treatment regimens for drug-sensitive pulmonary TB typically range from six to nine months, while treatment for extrapulmonary TB may be longer and require additional drugs such as streptomycin or fluoroquinolones [6].

In cases of drug-resistant TB, treatment regimens are more complex. They may involve second-line drugs such as fluoroquinolones, injectable agents (e.g., kanamycin, amikacin), and newer drugs such as bedaquiline and delamanid. Drug-resistant TB requires individualized treatment based on drug susceptibility testing (DST) results and close monitoring for treatment response and adverse effects [7].

Prevention and Control Measures

Preventing and controlling tuberculosis (TB) requires a multifaceted approach that addresses both biomedical and social determinants of health. Key prevention and control measures aim to interrupt TB transmission, reduce the burden of latent TB infection (LTBI), and improve access to diagnosis and treatment services for individuals with active TB disease.

One of the primary strategies for TB prevention is the identification and treatment of individuals with LTBI, particularly those at high risk of developing active TB disease. Targeted testing and treatment of LTBI can prevent disease progression and reduce the pool of individuals at risk of transmitting TB within communities. Implementation of LTBI testing and treatment programs, particularly among high-risk groups such as contacts of TB cases, healthcare workers, and individuals living with HIV/AIDS, can contribute to TB control efforts [1].

Ensuring early diagnosis and prompt treatment initiation for individuals with active TB disease is crucial for preventing transmission and improving clinical outcomes. Access to diagnostic services such as sputum smear microscopy, culture, and molecular assays should be expanded to facilitate early case detection. Treatment should be initiated promptly following diagnosis, and directly observed therapy (DOT) should be implemented to ensure treatment adherence and minimize the risk of treatment failure and drug resistance [2].

In addition to individual-level interventions, population-based measures such as TB case finding, contact tracing, and infection control play essential roles in TB control efforts. Active case-finding strategies involve targeted screening and testing of high-risk populations to identify individuals with TB disease or LTBI who may not seek care through routine health services. Contact tracing aims to identify and evaluate individuals in close contact with infectious TB cases to prevent further transmission within households and communities. Implementing infection control

measures, such as ventilation improvement, respiratory hygiene, and personal protective equipment, is crucial for preventing TB transmission in healthcare and congregate settings such as prisons and shelters [3].

Vaccination is an essential component of TB prevention and control efforts, particularly in high-burden settings where TB transmission is endemic. The Bacille Calmette-Guérin (BCG) vaccine, administered to infants soon after birth, provides partial protection against severe forms of TB, such as disseminated TB and TB meningitis in children. While the BCG vaccine is not highly effective in preventing pulmonary TB in adults, it remains an essential tool for reducing TB morbidity and mortality in children, particularly in settings with high TB incidence rates [4].

Addressing social determinants of health, such as poverty, overcrowded living conditions, and inadequate access to healthcare, is crucial for reducing the burden of TB within communities. Improving living standards, providing access to essential healthcare services, and addressing underlying social and economic disparities can contribute to TB control efforts by reducing TB transmission and enhancing treatment outcomes [5]. Table 1 provides a comprehensive overview of clinical guidelines for tuberculosis (TB) from reputable organizations, covering various aspects of TB prevention, diagnosis, treatment, and management. The table includes guidelines from organizations such as the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), European Respiratory Society (ERS), National Institute for Health and Care Excellence (NICE), American Thoracic Society (ATS), and International Union Against Tuberculosis and Lung Disease (The Union).

Key guideline topics include the treatment of drug-susceptible TB and drug-resistant TB, management of latent TB infection (LTBI), TB testing and diagnosis, TB infection control measures, and TB prevention and control strategies. Each guideline provides evidence-based recommendations for healthcare providers on best practices for TB care, including diagnostic algorithms, treatment regimens, patient-centered care approaches, and TB-HIV co-management.

Table 1: Comprehensive Clinical Guidelines for Tuberculosis

Organization	Guideline Title	Scope	Key Recommendations
World Health Organization (WHO)	Guidelines for the Treatment of Drug-Susceptible Tuberculosis	Treatment of drug-susceptible TB	Standardized treatment regimens, directly observed treatment (DOT), and combination therapy with first-line anti-TB drugs.
	Guidelines for the Management of Latent Tuberculosis Infection (LTBI)	Management of LTBI	Testing and treatment of individuals at risk for TB infection, preventive therapy with isoniazid or rifampicin

Organization	Guideline Title	Scope	Key Recommendations
	Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis	Programmatic management of drug-resistant TB	Drug susceptibility testing, individualized treatment regimens, comprehensive patient care, and support
Centers for Disease Control and Prevention (CDC)	CDC TB Treatment Guidelines	Treatment of TB	Regimens for drug-susceptible TB, management of TB-HIV co-infection, pediatric TB treatment, treatment of extrapulmonary TB
	CDC TB Testing and Diagnosis Guidelines	TB testing and diagnosis	Screening recommendations, diagnostic tests (e.g., TST, IGRA, sputum microscopy, molecular tests), contact investigation
	CDC TB Infection Control Guidelines	TB infection control measures	Environmental controls, respiratory protection, TB screening, and surveillance in healthcare settings
European Respiratory Society (ERS)	ERS/ATS Guidelines for the Management of Adult Patients with Community-Acquired Pneumonia	Management of community-acquired pneumonia (CAP)	Diagnosis and management of CAP, empirical antibiotic therapy, ICU admission criteria
	ERS/WHO TB Guidelines	TB diagnosis and treatment	Diagnostic algorithms, drug regimens for drug-susceptible and drug-resistant TB, treatment monitoring and follow-up
National Institute for Health and Care Excellence (NICE)	NICE TB Clinical Guidelines	TB diagnosis, treatment, and management	TB screening, diagnostic tests, treatment regimens, TB-HIV co-management, contact tracing
	NICE Public Health Guideline: Tuberculosis	TB prevention and control measures	Population-level interventions (e.g., TB vaccination, TB screening), TB control strategies in high-risk settings
American Thoracic Society (ATS)	ATS/CDC/IDSA Treatment of Drug-Susceptible Tuberculosis	Treatment of drug-susceptible TB	Standardized treatment regimens, DOT, patient education, and support
	ATS/CDC/IDSA Treatment of Drug-	Treatment of	Drug susceptibility testing, individualized treatment

Organization	Guideline Title	Scope	Key Recommendations
	Resistant Tuberculosis	drug-resistant TB	regimens, adjunctive surgical therapy, treatment of adverse events
	ATS/CDC/IDSA Diagnosis of Tuberculosis in Adults and Children	TB diagnosis	Diagnostic tests (e.g., TST, IGRA, sputum microscopy, molecular tests), interpretation of test results, contact investigation
International Union Against Tuberculosis and Lung Disease (The Union)	The Union Manual: Tuberculosis Diagnosis and Treatment	TB diagnosis and treatment	Diagnostic algorithms, treatment regimens, patient-centered care, TB-HIV co-management, community-based TB care

This table provides a comprehensive overview of crucial clinical guidelines for TB prevention, diagnosis, treatment, and management from reputable organizations. It offers valuable recommendations for healthcare providers involved in TB care worldwide.

Complications of Tuberculosis

Tuberculosis (TB) can lead to a wide range of complications, both pulmonary and extrapulmonary, which can significantly impact patient outcomes and quality of life. Pulmonary complications of TB include extensive lung damage, cavitation, bronchiectasis, and fibrosis, which can result in chronic respiratory symptoms such as cough, dyspnea, and hemoptysis. Progressive lung disease can lead to respiratory failure and, in severe cases, death. Extrapulmonary complications of TB involve the spread of infection to other organ systems, leading to a variety of clinical manifestations.

One of the most severe extrapulmonary complications of TB is disseminated or miliary TB, characterized by widespread hematogenous dissemination of TB bacteria to multiple organ systems. Miliary TB can affect virtually any organ, including the liver, spleen, kidneys, bones, joints, and central nervous system. Clinical manifestations of miliary TB vary depending on the organs involved and may include fever, hepatosplenomegaly, pancytopenia, renal failure, bone pain, and neurological deficits. Miliary TB is associated with high mortality rates, particularly in immunocompromised individuals, and requires prompt diagnosis and treatment to prevent life-threatening complications [1].

TB can also lead to various complications affecting the musculoskeletal system, such as tuberculous arthritis, osteomyelitis, and Pott's disease (tuberculosis of the spine). Tuberculous arthritis typically affects large weight-bearing joints such as the hip and knee, leading to joint pain, swelling, and dysfunction. Osteomyelitis is a TB infection of the bone, which can cause localized pain, swelling, and destruction of bone. Pott's disease is characterized by vertebral

collapse and spinal deformity, leading to back pain, neurological deficits, and spinal cord compression [2].

Extrapulmonary TB can also involve the central nervous system, leading to severe neurological complications such as tuberculous meningitis, tuberculoma, and spinal cord compression. Tuberculous meningitis is the most severe form of TB involving the central nervous system, characterized by inflammation of the meninges and brain parenchyma. Clinical manifestations of tuberculous meningitis include headache, fever, altered mental status, focal neurological deficits, and signs of increased intracranial pressure. Without prompt diagnosis and treatment, tuberculous meningitis can lead to neurological sequelae such as hydrocephalus, cerebral infarction, and death [3].

Other complications of TB include gastrointestinal TB, genitourinary TB, and ocular TB, which can lead to symptoms such as abdominal pain, diarrhea, hematuria, and visual disturbances. TB can also exacerbate underlying medical conditions such as HIV/AIDS, diabetes mellitus, and chronic kidney disease, leading to poorer treatment outcomes and increased morbidity and mortality. Additionally, drug-resistant TB strains, such as multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), pose significant challenges for TB treatment and management, requiring prolonged treatment regimens with second-line drugs that are often less effective and more toxic [4].

Conclusion

Tuberculosis (TB) remains a significant global health challenge, affecting millions of people worldwide and posing complex clinical, public health, and societal implications. Despite advancements in TB prevention, diagnosis, and treatment, TB continues to take a heavy toll on individuals, communities, and healthcare systems, particularly in resource-limited settings and vulnerable populations.

This comprehensive review has explored various aspects of TB, including its epidemiology, pathophysiology, clinical presentation, diagnosis, treatment, prevention, and control measures. We have examined TB's multifaceted nature, encompassing factors such as social determinants of health, TB-HIV co-infection, drug resistance, stigma, and the impact of climate change on TB transmission dynamics.

Throughout this review, we have highlighted the importance of evidence-based approaches, collaborative efforts, and innovative strategies for addressing the challenges of TB control and achieving the goal of ending the global TB epidemic. From implementing integrated TB control programs to leveraging technology and harnessing a One Health approach, there are myriad opportunities for advancing TB prevention, diagnosis, treatment, and management efforts.

Stakeholders across sectors and disciplines must come together to prioritize TB control, advocate for increased funding and resources, and address the underlying determinants of TB. By working collaboratively and adopting holistic, patient-centered approaches to TB care, we can accelerate progress toward ending the global TB epidemic and ensuring health and well-being for all.

Ultimately, ending TB requires a concerted global effort, political commitment, and sustained investments in TB research, innovation, and implementation of evidence-based interventions. Together, we can make strides towards a TB-free world where all individuals have access to

quality TB care and support, and no one is left behind in the fight against this ancient yet persistent disease.

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References

1. Alemu A, Bitew ZW, Diriba G, Gumi B. Co-occurrence of tuberculosis and diabetes mellitus, and associated risk factors, in Ethiopia: a systematic review and meta- analysis. *IJID Reg.* 2021 Oct 20;1:82-91. doi: 10.1016/j.ijregi.2021.10.004
2. World Health Organization. (2021). Global tuberculosis report 2021. <https://www.who.int/publications-detail-redirect/9789240037021>
3. Joint United Nations Programme on HIV/AIDS (UNAIDS). (2020). UNAIDS data 2020. <https://www.unaids.org/en/resources/documents/2020/unaids-data>
4. American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022 Jan 1;45(Suppl 1):S17-S38. doi: 10.2337/dc22-S002
5. Centers for Disease Control and Prevention. (2021). Tuberculosis and HIV coinfection. <https://www.cdc.gov/tb/topic/basics/tbhivcoinfection.htm>
6. Falzon D, Schünemann HJ, Harausz E, et al. World Health Organization treatment guidelines for drug-resistant tuberculosis, 2016 update. *Eur Respir J.* 2017 Mar 22;49(3):1602308. doi: 10.1183/13993003.02308-2016
7. Yorke E, Atiase Y, Akpalu J, Sarfo-Kantanka O, Boima V, Dey ID. The Bidirectional Relationship between Tuberculosis and Diabetes. *Tuberc Res Treat.* 2017;2017:1702578. doi: 10.1155/2017/1702578
8. Zeru MA. Prevalence and associated factors of HIV-TB co-infection among HIV patients: a retrospective Study. *Afr Health Sci.* 2021 Sep;21(3):1003-1009. doi: 10.4314/ahs.v21i3.7
9. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach. Geneva: World Health Organization; 2013 Jun. <https://pubmed.ncbi.nlm.nih.gov/24716260/>
10. Bruchfeld J, Correia-Neves M, Källenius G. Tuberculosis and HIV Coinfection. *Cold Spring Harb Perspect Med.* 2015 Feb 26;5(7):a017871. doi: 10.1101/cshperspect.a017871
11. Alebel A, Wondemagegn AT, Tesema C, Kibret GD, Wagnaw F, Petrucka P, Arora A, Ayele AD, Alemayehu M, Eshetie S. Prevalence of diabetes mellitus among tuberculosis patients in Sub-

- Saharan Africa: a systematic review and meta-analysis of observational studies. *BMC Infect Dis.* 2019 Mar 13;19(1):254. doi: 10.1186/s12879-019-3892-8
12. Gelaw YA, Williams G, Soares Magalhães RJ, Gilks CF, Assefa Y. HIV Prevalence Among Tuberculosis Patients in Sub-Saharan Africa: A Systematic Review and Meta- analysis. *AIDS Behav.* 2019 Jun;23(6):1561-1575. doi: 10.1007/s10461-018-02386-4
 13. Ngari MM, Rashid MA, Sanga D, Mathenge H, Agoro O, Mberia JK, Katana GG, Vaillant M, Abdullahi OA. Burden of HIV and treatment outcomes among TB patients in rural Kenya: a 9-year longitudinal study. *BMC Infect Dis.* 2023 May 30;23(1):362. doi: 10.1186/s12879-023-08347-0
 14. Chakaya JM, Harries AD, Marks GB. Ending tuberculosis by 2030-Pipe dream or reality? *Int J Infect Dis.* 2020;92S:S51–S54. doi: 10.1016/j.ijid.2020.02.021.
 15. UN. General Assembly (73rd sess. : 2018-2019). Political declaration of the high-level meeting of the general assembly on the fight against tuberculosis: resolution/adopted by the general assembly. New York: United Nations; 2018. <https://digitallibrary.un.org/record/1649568>.
 16. Enos M, Sitienei J, Ong'ang'o J, Mungai B, Kamene M, Wambugu J, Kipruto H, Manduku V, Mburu J, Nyaboke D, et al. Kenya tuberculosis prevalence survey 2016: Challenges and opportunities of ending TB in Kenya. *PLoS One.* 2018;13(12):e0209098. doi: 10.1371/journal.pone.0209098
 17. Straetmans M, Bierrenbach AL, Nagelkerke N, Glaziou P, van der Werf MJ. The effect of tuberculosis on mortality in HIV positive people: a meta-analysis. *PLoS One.* 2010;5(12):e15241. doi: 10.1371/journal.pone.0015241
 18. Gao J, Zheng P, Fu H. Prevalence of TB/HIV co-infection in countries except China: a systematic review and meta-analysis. *PLoS One.* 2013;8(5):e64915. doi: 10.1371/journal.pone.0064915
 19. Gelaw YA, Williams G, SoaresMagalhaes RJ, Gilks CF, Assefa Y. HIV prevalence among tuberculosis patients in Sub-Saharan Africa: a systematic review and meta-analysis. *AIDS Behav.* 2019;23(6):1561–1575. doi: 10.1007/s10461-018-02386-4.
 20. Endalamaw A, Ambachew S, Geremew D, Habtewold TD. HIV infection and unknown HIV status among tuberculosis patients in Ethiopia: a systematic review and meta-analysis. *Int J Tuberc Lung Dis.* 2019;23(2):187–194. doi: 10.5588/ijtld.18.0363.
 21. McHunu G, van Griensven J, Hinderaker SG, Kizito W, Sikhondze W, Manzi M, Dlamini T, Harries AD. High mortality in tuberculosis patients despite HIV interventions in Swaziland. *Public Health Action.* 2016;6(2):105–110. doi: 10.5588/pha.15.0081
 22. Masini EO, Mansour O, Speer CE, Addona V, Hanson CL, Sitienei JK, Kipruto HK, Githiomi MM, Mungai BN. Using survival analysis to identify risk factors for treatment interruption among new and retreatment tuberculosis patients in Kenya. *PLoS One.* 2016;11(10):e0164172. doi: 10.1371/journal.pone.0164172