www.ijarp.com ISSN 2456-9992 Page: 01-18

International Journal Advanced Research Publications

Review Article

Volume: 02
Issue: 05

TUBERCULOSIS: A COMPREHENSIVE CLINICAL AND SOCIAL OVERVIEW

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Article Received: 21 March 2026, Article Revised: 11 April 2026, Published on: 01 May 2026

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DOI: https://doi-doi.org/101555/ijarp.2155

ABSTRACT

Tuberculosis (TB) remains one of the most formidable challenges to global public health, persisting despite centuries of medical advancement. Caused by the bacterium Mycobacterium tuberculosis, it primarily affects the lungs but can disseminate to almost any organ system. This paper provides an extensive review of TB, covering its etiology, pathophysiology, diagnostic modalities, and current treatment paradigms. Furthermore, we explore the socio-economic factors that perpetuate the epidemic and the rising threat of multi-drug-resistant strains. In 2024, approximately 10.6 million individuals were infected globally, with India accounting for nearly 25% of the total burden. By synthesizing current clinical guidelines and epidemiological data, this overview aims to provide a holistic understanding

of the disease for students and healthcare professionals at Mewar University. Furthermore, contemporary evidence demonstrates that tuberculosis manifestations exist on a dynamic spectrum from infection to disease, rather than a binary state as previously understood. It is important to understand what causes people to move between these states in order to reduce the burden of tuberculosis and meet the goals of the END-TB Strategy set by the WHO. Vaccination, infection detection, and preventive treatment are essential components of tuberculosis prevention. But the recent rapid growth of Internet technology has made telemedicine a much more important part of treating tuberculosis. This proposal seeks to furnish a thorough examination of the diverse facets of telemedicine in the treatment of tuberculosis. It talks about functional positioning, medical qualifications, the range of applications, the management team, the operational model, the medical standards, the evaluation of medications, precautions, and risk management. It is meant to be a guide for healthcare professionals on how to use telemedicine to help people with tuberculosis.

KEYWORDS: Mycobacterium tuberculosis, Pulmonary Infection, Multi-drug Resistance (MDR-TB), Pathogenesis, BCG Vaccine, DOTS Therapy, Epidemiology, Public Health. New vaccine candidates, preventive treatment, the TB spectrum, TPT, TST, and tuberculosis control. Tuberculosis; epidemiology; diagnosis; treatment; and prevention.

1. INTRODUCTION

"A terrible disease where the struggle between the soul and body is gradual, quiet, and solemn. The outcome is certain; day by day, piece by piece, the mortal part fades and weakens. This disease sometimes advances quickly, yet it can also move at a slow pace. Regardless of the speed, it is always sure. Charles Dickens: Nicholas Nickleby. To this day, Charles Dickens' words remain true. Tuberculosis is a scourge for humanity that has existed for ages. In Dickens' time, it was referred to as consumption and had a significant social and economic impact on human life."Worldwide, mankind has seen the changing face of tuberculosis (TB). It has shifted from being an incurable disease to a curable one. When the HIV/AIDS epidemic emerged in 1981, the deadly co-infection of HIV and TB led to a global resurgence of TB. In the early 1990s, a drug-resistant TB strain caused an outbreak in New York, killing 80% of infected patients. The co-infection of HIV and TB, along with the spread of drug-resistant TB, has made the situation worse. In 1993, the WHO declared TB a global emergency. Tuberculosis has various presentations and is divided into pulmonary TB (PTB) and extrapulmonary TB (EPTB) based on clinical signs.[1]

EPTB is defined as TB that affects organs other than the lungs, such as the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, or meninges. If a patient with EPTB also has a tubercular lesion in lung tissue, that patient is categorized as having pulmonary TB, such as miliary TB. If a patient suffers from intra-thoracic mediastinal and/or hilar lymph node TB or TB pleural effusion without visible lung abnormalities on X-rays, that patient is categorized as having EPTB.WHO estimates show that in 2017, there were 10.4 million cases of TB worldwide. Two-thirds of those cases were in eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%), and South Africa (3%). EPTB makes up about 15% to 20% of all TB cases. With the HIV pandemic, the EPTB situation has become even more complex, as EPTB accounts for more than 50% of all TB cases in HIV-positive patients. Due to its various presentations, EPTB often makes early diagnosis difficult. It may show symptoms such as fever, loss of appetite, weight loss, malaise, and fatigue. [2]

In India, the only presentation may be fever of unknown origin due to its remote infection site. Tuberculosis (TB) is a serious infectious disease that mainly affects the lungs. It is caused by Mycobacterium tuberculosis. The bacteria that cause tuberculosis spread from one person to another through tiny droplets released into the air when someone coughs or sneezes. Once rare in developed countries, TB infections began to rise in 1985, partly due to the emergence of HIV, the virus that causes AIDS. HIV weakens a person's immune system, making it harder to fight TB germs. Many strains of tuberculosis resist the drugs typically used to treat the disease. People with active tuberculosis need to take several types of medications for many months to eliminate the infection and prevent antibiotic resistance.[3]

Understanding the medicalisation processes at the individual level entails observing how individuals with tuberculosis (TB) are compelled to view their bodies as medical objects, where their agency, power dynamics, and social standing are undermined by unfamiliar medical hierarchies. According to Long, Johansson, Diwan, and Winkvist (2001), a TB patient's isolated social experiences might last far longer than is medically necessary if there is no clear and predictable way out of a medicalised identity. The necessity for culturally relevant rites of permission that provide socially isolated TB patients with symbolic re-entry into their group can be brought to light through thoughtful engagement with the social and biographical effects of medicalisation. The social, historical, and cultural aspects of biomedical practice must be considered when considering medicalisation from a wider perspective. For example, medical labels have social ramifications for both the patients they affect and the physicians and researchers who use them. For instance, the term "patient" is

increasingly being used to refer to both active TB cases and LTBI cases. The need for precise cohort data and the narrowing of diagnostic and definitional categories may also contribute to the issue since the social processes that produce the facts also distort the nature of the reality they are meant to depict through processes of exclusion. [4]

One of the most important infectious illnesses in the world, tuberculosis (TB) has a considerable effect on both public health and socioeconomic development. Mycobacterium tuberculosis (Mtb) is the cause. Even with significant advancements in TB control initiatives, the disease still presents a significant obstacle, especially in environments with limited resources . According to estimates from the World Health Organization (WHO), about 10 million people get active tuberculosis (TB) each year, and the disease is thought to be responsible for about 1.5 million deaths.

Additionally, treatment and control efforts are made more difficult by the rise of drug-resistantTBstrains. Although effective TB treatment can result in a microbiological cure and clinical symptom relief, it frequently leaves behind chronic lung damage. This aftereffect, referred to as post-tuberculosis lung disease (PTLD)[5]

The host immune system's reaction to Mtb and its antigens also affects the pathophysiology of PTLD. The immune system experiences dynamic alterations as it moves from an active infection state to a quiescent state after TB treatment. On the other hand, tissue damage and chronic inflammation may result from immunological dysregulation. The pathophysiology of PTLD has been linked to altered cytokine profiles, such as increased levels of transforming growth factor-beta (TGF-β) and tumour necrosis factor alpha (TNF-α), which promote fibrogenesis and hinder tissue repair mechanisms [5]. On the other hand, anti-inflammatory cytokines including interleukin-10 (IL-10) and regulatory T cells (Tregs) contribute to tissue repair following tuberculosis (TB) inflammatory, immunological, and tissue remodelling processes.[6]

Mycobacterium tuberculosis (M. tb) is the causative agent of tuberculosis (TB), a chronic infectious disease. TB mostly affects the lungs, but it can also affect other sections of the body, such as the otorhinolaryngologic (ear, nose, and throat) regions. TB is still a serious public health concern, especially in poorer nations [1]. Inadequate treatment adherence, delayed diagnosis, and the emergence of multidrug-resistant tuberculosis (MDR-TB) are some of the reasons why the disease continues despite the availability of effective medicines. When an infected person coughs, sneezes, or speaks, airborne droplets are generated that can

spread tuberculosis from person to person. The World Health Organization (WHO) estimates that 10 million new cases and 1.4 million deaths from tuberculosis (TB) occurred worldwide in 2019. In areas with high incidence, the illness is particularly common.[7]

Despite being less frequent than pulmonary TB, otorhinolaryngologic TB symptoms are important because they can lead to serious consequences and present diagnostic difficulties. Numerous ear, nose, and throat structures can be impacted by tuberculosis (TB), resulting in a range of clinical manifestations. These symptoms frequently resemble other prevalent otorhinolaryngologic disorders, making diagnosis more difficult and postponing necessary treatment. Chronic ear discharge, nasal obstruction, hoarseness, and non-healing ulcers are examples of persistent symptoms that can result from the involvement of otorhinolaryngologic structures in tuberculosis. If not promptly and appropriately treated, these symptoms can have a substantial negative influence on a patient's quality of life and may result in consequences including airway blockage or hearing loss.[8]

554 cases of tuberculosis (TB) were reported to the Swiss Federal Office of Public Health (SFOPH) in 2017, yielding a notification rate of 6.5 cases per 100,000 people; this number is very steady. About 23% of these TB patients are Swiss, and about 77% are foreign-born; 34% of the foreign-born patients are asylum seekers (AS). According to the WHO's END TB strategy, effective TB management includes, among other things, quick diagnosis, a high cure rate, and preventing treatment failure, relapses, and interruptions prior to the planned end of treatment. Stigmatisation must be avoided and universal access to healthcare must be provided in order to ensure that TB patients are promptly diagnosed. One of the key factors influencing treatment results is adherence, which is necessary for treatment completion, TB prevention, and care. Studies conducted in Switzerland in the late 1980s revealed inadequate treatment results, with a success rate in VD County of no more than 70% for patients with comprehensive documentation (63% if patients without documentation are included). Better findings were found in a nationwide survey, however it was established that the success rate was below the expected range among several categories of foreign-born patients, such as undocumented migrants .Local research showed that the cure rate was significantly impacted by the availability of directly observed therapy (DOT) and improved training for medical personnel treating TB patients. Since then, VD County has increased its funding for TB management. Our goal is to outline the current results of the integrated medical and social approach used in VD County to manage tuberculosis.[9]

Diabetes mellitus and tuberculosis are two serious, historically widespread illnesses that have a big impact on public health. One of the most common infectious illnesses worldwide, tuberculosis (TB) has long been linked to poverty and primarily affects people with lower socioeconomic level, while it is not restricted to these groups. On the other hand, diabetes mellitus (DM), which is frequently associated with wealth, is the most common chronic non-communicable disease and affects people from all socioeconomic backgrounds. Both disorders provide significant difficulties, particularly when they coexist, affecting the course of the illness, its treatment, and general health outcomes. The combined burden of DM and TB has become a major global health concern, making preventative and treatment efforts more difficult and requiring immediate, coordinated global healthcare solutions. High-risk groups like the elderly, malnourished, and socioeconomically disadvantaged are disproportionately affected by the persistent global burden of DM and TB. The illness still poses a significant threat to world health despite ongoing, extensive efforts in TB prevention, early detection, and treatment initiatives. TB is still one of the leading causes of death in impoverished areas, accounting for up to 29% of all deaths, even though it is no longer among the top 10 causes of death in economically developed countries. HIV co-infection significantly raises the likelihood of developing active tuberculosis, making a person 12–20 times more likely to do so.3 Mortality rates remain high even in developed nations due to the compound impact of HIV. Healthcare systems are further burdened by the increasing prevalence of MDR TB, which necessitates the use of costly second-line medications and prolonged treatment periods.[10]

The factors that contributed to the co-occurrence of diabetes mellitus and tuberculosis varied and were inconsistent between studies. Sex, age, pulmonary tuberculosis, a positive sputum smear, and a family history of diabetes were the most commonly reported factors, and they were all regularly mentioned in most investigations. To evaluate the relationship between these characteristics and TB-DM, 22 research (23.4%) used statistical tools such odds ratios, relative risks, or hazard ratios, whereas 11 studies (11.7%) employed the chi-square test. Nevertheless, a sizable percentage of research (61, or 64.9%) could not identify any risk factors or related variables for the coexistence of DM and TB. The small sample sizes in many studies are probably the cause of this paucity of data. From the initiation of symptoms to clinical presentation, from clinical presentation to TB suspicion, and from clinical suspicion to TB confirmation, the diagnosis and treatment of tuberculosis are frequently delayed at multiple stages. Variability in symptom presentation, variations in host immunity, low disease knowledge, insufficient access to healthcare, and the lack of quick, accurate

diagnostic instruments are some of the reasons for these delays. Prolonged diagnostic timelines and delayed therapy commencement are largely caused by these difficulties.[11]

The increased risk of TB in individuals with DM necessitates rigorous screening to facilitate early detection and reduce transmission, morbidity, and mortality. The World Health Organization (WHO) advises tuberculosis surveillance for diabetic patients in areas with moderate to high TB prevalence. A variety of screening methods—such as clinical assessment, radiological imaging, and sputum microbiological analysis—are employed individually or in combination to identify active TB in individuals with DM. Clinical assessment is a cost-effective and time-efficient method for screening tuberculosis. Key clinical indicators suggesting pulmonary TB include fever, cough lasting more than two weeks, haemoptysis, weight loss, night sweats, and a history of exposure to an active TB case. In cases of suspected extrapulmonary TB, clinical indicators such as lymphadenopathy, fever with altered mental status, neck stiffness, and abdominal symptoms (e.g., ascites, intestinal obstruction) increase the level of suspicion. Radiological examinations, including chest X-rays and CT scans, can further aid in the diagnosis and assessment of TB.[12]

In order to achieve global TB elimination by 2050 (i.e., an incidence rate of fewer than one TB case per million population), the enormous success of the first two successful WHO programs was insufficient to drastically lower the annual TB incidence rate. The first WHO strategy's guiding principles focused on treating patients and stopping the spread of Mycobacterium tuberculosis in the community by early bacteriological case index detection and standardised therapy for infectious pulmonary variants. The widespread occurrence of TB/HIV coinfection cases and MDR-TB patients at the start of the century necessitated a more specialised and all-encompassing public health approach (the Stop TB strategy), which included DOTS components and new techniques geared to the new epidemiological environment. One of the leading causes of human suffering and mortality is still tuberculosis (TB), which is producing a pandemic of significant proportions.[13]

2. Etiology and Pathogenesis

The culprit, Mycobacterium tuberculosis, is a solely human pathogen spread primarily through inhaled aerosolized droplets. It is a slow-growing, aerobic bacillus with a thick, waxy cell wall that resists standard Gram staining. Transmission and Infection Cycle: Inhalation: TB is spread when an infected individual coughs or sneezes, releasing minute droplets. Immune Response: Once inhaled, bacteria are engulfed by alveolar macrophages. In the majority of healthy individuals, the immune system successfully contains the bacteria,

resulting in a latent TB infection. Disease Progression: Progression to active disease is most likely within the first two years of infection, though it can occur decades later if the immune system is compromised by malnutrition, HIV, or diabetes. The airborne route is the primary means of TB transmission. Tiny droplets carrying the bacteria are released into the air when a person with active pulmonary tuberculosis coughs, sneezes, laughs, sings, or even speaks. Long-term suspension of these droplet nuclei is possible, particularly in confined spaces with little ventilation. The bacteria enter the respiratory system and travel to the lungs when another person inhales these contagious droplets. Sharing food, touching surfaces, or shaking hands are not common ways for tuberculosis to spread. The risk of transmission is increased by prolonged close contact with an infected individual. Particularly at risk are family members, medical professionals, and residents in densely populated areas.[14]

3. Structure of Tuberculosis

Tuberculosis is caused by Mycobacterium tuberculosis, which is a thin bacillus with a size ranging from 2 to 4 µm in length and 0.2 to 0.5 µm in width. The bacterium does not have a flagellum and is non-spore forming. Mycobacteria have a complex cell wall that causes their pathogenicity and resistance. The cell wall is mainly composed of mycolic acids – long fatty acids giving the bacteria a hydrophobic character and making it acid-fast, resistant to drying, disinfecting, and certain types of antibiotic medications. Under the outer lipid membrane is a rigid core made of arabinogalactan bonded with peptidoglycan, ensuring mechanical stability and cell integrity. The outer part of the cell wall is composed of lipoarabinomannan (LAM) and lipoproteins, providing the ability to evade the immune response. Inside the bacterial cell wall there are ribosomes, DNA, various enzymes, and granules, but no membrane-bound organelles, characteristic of prokaryotes. A slow growth rate of Mycobacterium tuberculosis bacteria is associated with the composition of its cell wall.[15]

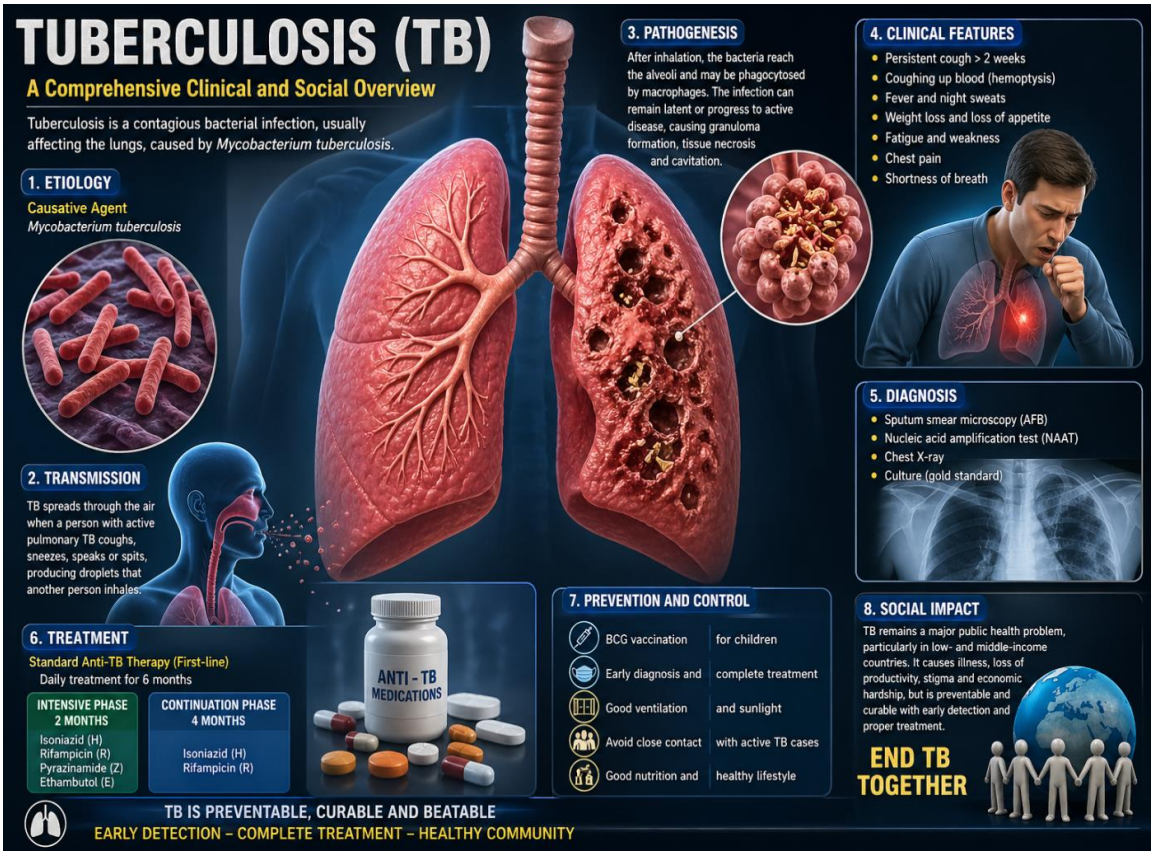

FIG 1: TUBERCULOSIS.

4. Clinical Manifestations

TB is a multisystemic infection with highly variable clinical findings. Pulmonary TB: The most common form, presenting with a persistent cough (often with hemoptysis), chest pain, and night sweats. Extrapulmonary TB: Affects organs such as the lymph nodes, gastrointestinal tract, and musculoskeletal system. Spinal involvement, known as Pott's disease, is a classic presentation. [16]

5. Diagnostic Advancements

Early detection is critical to breaking the chain of transmission.Molecular Diagnostics: Rapid molecular techniques, such as GeneXpert, have revolutionized diagnosis by detecting both the bacteria and drug resistance within hours.Imaging: Chest radiography remains a cornerstone, particularly for identifying upper-lobe infiltrates or cavitation.Biomarkers: Emerging blood-based biomarkers are currently being validated to differentiate between active and latent stages more effectively than the traditional skin tests.[17]

6. Treatment of tuberculosis:

Daily Regimen For DS-TB

RNTCP(National tuberculosis elimination programme) has provided daily regimen to PLHIV, Pediatric TB cases throughout the country and all cases of TB in 104 selected districts. In Drug Sensitive TB:For New Cases of TB, an intensive phase(IP) of 8 weeks duration will have Isoniazid(H),Rifampicin(R), Pyrazinamide(Z) and Ethambutol (E) in daily doses according to four weight groups and continuation phase(CP) having Isoniazid(H), Rifampicin(R) and Ethambutol (E)for next 16 weeks except Pyrazinamide(Z).For Previously Treated Cases: Intensive Phase:12 weeks of IP consisting of HRE with Streptomycin injection for first8 weeks only Continuation phase.Treatment period is 6e9 months of IP with Kanamycin,Levofloxacin, Ethionamide, Cycloserine, Pyrazinamide, Etham-butol, Isoniazid and 18 months of CP with Levofloxacin, Eti-onamide, Cycloserine, Ethambutol, Isoniazid on daily basis.[8:42 pm, All XDR TB patients are being treated with injection Capreo-mycin, Moxifloxacin, PAS, High dose Isoniazide, Clofazimine,Linezolid, Co-Amoxyclav for 6e12 months in intensive phase andincontinuation phase all medication except injections continue for 18 months.[18]

Following the implementation of Programmatic Management of Drug-Resistant Tuberculosis (PMDT) in 2007, an increasing number of MDR/RR-TB patients have been diagnosed and treated until 2016, For decentralization of DR TB facilities (easy accessibility, reduced patient travelling and patient satisfaction), 628 CBNAAT centres became functional by 2016 According to National Strategic Plan (NSP) 2017e25, fol-lowing are stated69

1. Decentralization of diagnosis and treatment of MDR TB at district level.
2. Recently approved WHO second line probe test.
3. Rapid molecular test for DST of second line drugs
4. Shorter MDR TB regimens
5. DST based regimens for all kinds of DR TB including ISN mono poly
6. Introduction of newer drugs such as Bedaquiline.
7. Revised recording reporting system i.e. e-NIKSHAY & Phar-macovigilance system.[19]

THERAPY:

A small number of fluoroquinolones, which are derivatives of nalidixic acid that contain fluorine, are advised for use in MDR-TB because of their strong anti-Mycobacterium action, favourable pharmacokinetics in terms of tissue and cellular distribution, and fewer side effects. 5 The use of fluoroquinolones in the treatment of tuberculosis is still debatable,

despite the fact that they have been a part of antitubercular regimens since the late 1980s, especiallyforMDR-TB.[20]

1.Moxifloxacin:

Unlike rifampicin, moxifloxacin inhibits the synthesis of proteins in bacteria that metabolise slowly. Ciprofloxacin and ofloxacin had no such impact in vitro, however moxifloxacin seemed to kill a subpopulation of tubercle bacilli that rifampicin could not kill, or rifampicin-tolerant persisters. 16. Nevertheless, it is necessary to characterise the molecular mechanisms underlying such a bactericidal effect. Moxifloxacin's anti-tubercular activity was comparable to that of isoniazid in murine models.17 In other organisms like S. pneumonia, moxifloxacin seems to be a poor substrate for efflux pumps. The heavy C-7 replacement could be the cause of this. Ciprofloxacin and other hydrophilic fluoroquinolones are excellent substrates that readily efflux out of bacteria.[21]

2.Gatifloxacin:

Preclinical research has shown that gatifloxacin has significantly higher activity and is probably cross-resistant to moxifloxine. Gatifloxacin's anti-TB activity has shown encouraging early clinical indications, with comparable (but not quite as powerful) EBA to isoniazid and identical action to moxifloxacin. The drug's profile of drug-drug interactions and toxicity is comparable to that of moxifloxacins. Similarly, children and women who are pregnant or nursing have not had the medication sufficiently tested.[22]

3.Gemifloxacin:

In several phase 3 trials, the quinolone gemifloxacin has demonstrated encouraging activity. A medication for the treatment of respiratory infections has recently been submitted for approval in the United States. Oral bioavailability is about 70% in healthy volunteers; it has a mean elimination half-life of 7.4 hours and is well tolerated. These qualities, along with its strong antibacterial activity, indicate that a once-daily dosage schedule might be appropriate. 21. The susceptibility of 250 isolates of Mycobacterium tuberculosis to ciprofloxacin, ofloxacin, levofloxacin, grepafloxacin, trovafloxacin, and gemifloxacin (SB-265805) was assessed. Ofloxacin also had good activity, with a MIC90 of 2 µg/ml, whereas levofloxacin, ciprofloxacin, and grepafloxacin demonstrated the highest activity (MIC for 90% of strains tested [MIC90] 1 µg/ml).[23]

4.Rifametane:

It is a novel semi-synthetic rifamycin with a bactericidal spectrum and potency comparable to rifampicin. However, compared to rifampicin, rifametane has a far superior pharmacokinetic profile. Forty This is demonstrated by the fact that rifametane was found to be more effective orally in TB-infected mice when its pharmacokinetics were compared to known rifamycin derivatives, such as rifampicin, even though the MIC90 values of the two compounds were the same against 20 strains of M. tuberculosis.41. The pharmacokinetics and safety of a 300 mg oral dose of rifametane against a 300 mg dose of rifampicin in male volunteers in good health.[24]

5.Aconiazide:

Aconiazide, a prodrug of isoniazid, is not carcinogenic and was created to be less hazardous than the parent medication. 49 The toxicity of isoniazid is thought to be caused by the metabolization of isoniazid into hydrazine and acetylhydrazine. It was anticipated that the acid would bind to the isoniazid metabolites and reduce toxicity since aconiazide is metabolised to isoniazid and 2-formylphenoxyacetic acid.49. It was shown to produce proportionately less isoniazid in serum in healthy people than the parent molecule. Fifty Due to issues with its commercial synthesis, the compound's advancement was postponed for a while.

However, Lincoln Diagnostics is currently submitting more toxicity data to the FDA in order to carry out clinical trials on tuberculosis patients.[25]

6.Rifalazil:

A novel semi-synthetic rifamycin called rifalazil has a longer half-life and is more effective against M. tuberculosis in vitro and in vivo than rifampicin and rifabutin. Nevertheless, bacteria that are very resistant to rifampicin exhibit cross-resistance to all rifamycins. 45 However, rifalazil's development has been halted due to serious adverse effects during the four-day Phase II experiment.[26]

7.Capuramycin:

Capuramycin analogues have strong antimycobacterial properties both in vitro and in vivo by blocking the phospho-MurNAc-pentapeptide translocase enzyme, which prevents mycobacteria from assembling their peptidoglycan.58,59 Due to their undesirable pharmacokinetic properties, a few of the strong cupuramycin analogues were not taken into consideration for additional research.For instance, RS-118641, one of the most effective anti-

MTB capuramycin analogues, exhibited MIC50 and MIC90 values of 1 and 2 mg/ml for drug-susceptible MTB strains and 0.5 and 2 mg/ml for MDR-MTB strains, respectively.[27]

DOSAGE

Delamanid is indicated as a component of an optimized background regimen for the management of multidrug-resistant Tuberculosis. In adults, the suggested dosage of this antitubercular drug is 100 mg twice daily orally (as two 50 mg tablets) in the initial 24 weeks of treatment.

The intake of this medication with meals helps achieve adequate absorption along with maintaining steady levels in the plasma. Monotherapy with delamanid is not advisable since rapid development of resistance is possible. For this reason, this medicine should always be combined with one or more effective second-line TB drugs, as directed by susceptibility patterns.The continuation of treatment with the remaining drugs of the regimen after completing the first 24 weeks depends on the clinical outcome and varies in accordance with the national program guidelines such as the former Revised National Tuberculosis Control Programme (now included under National Tuberculosis Elimination Programme).Second-line drugs that may be used as adjuncts to delamanid may include, but not limited to, fluoroquinolones, linezolid, clofazimine,[28]

DIAGNOSIS:

List of tests used in laboratory diagnosis.

Microscopy	**Culture**	**Conventional methods**	**Molecular methods**
Acid fast staining	Solid media	Rates of growth	Nucleic acid probes
Ziehl- Neelsn	Egg- based media	Pigent production	In situ hybridization
Kinyoun	Agar based media	Niacin accumulation test	Nucleic acid amplification methods
	Selective media	Nitrate reduction test	Line probe assay
Fluorochrome staining	Liquid media	Tween 80 Hydrolysis	Transcription mediated amplification
	MGIT	Catalase test	DNA sequencing
	BACTEC 460TB system	Arylsulfatase activity	Spoligotyping
	Automated continuous monitoring system	Urase activity	DNA microarray analysis
		Tyrazinamidase	CBNAAT
	HPLC(for culture confirmation and speciation.	Iron uptake	PBMC circ RNA detection
		Growth on macconckey	

M.tuberculosis bacilli must be demonstrated by a microbiological, cytopathological, or histopathological technique in order to diagnose tuberculosis.

1.Microscopy

Numerous pulmonary and extrapulmonary samples contain mycobacteria. For them to be easily visible in direct smears, there must be at least 10,000 AFB per millilitre of material.38. Reliability, reproducibility, affordability, an indicator of infectiousness, a comprehensive tool for diagnosis, tracking progress, and defining cure, and even viability in distant or tribal areas are all features of microscopy.[29]

2. Culture

Culture is the "gold standard" for a definitive diagnosis of TB. It means growing M. tuberculosis from clinical samples. Culture methods are significantly more sensitive, as they can detect fewer bacilli (10 to 100 bacilli/ml of concentrated material) and yield the necessary isolates for standard drug susceptibility testing and species identification. The sensitivity of culture for identifying M. tuberculosis varies from 0% to 80% across different extrapulmonary specimens.9,43e45 LJ media is the most common solid medium used to culture M TB. It usually takes 4 to 8 weeks for growth to be seen.46[30]

3. Molecular techniques

Clinical laboratories are moving away from the traditional, time-consuming, and boring method of identifying Mycobacteria species in culture. For example, nucleic acid probes have been developed to identify MTB, Mycobacterium avium intracellulare, M. kansasii, and M. gordonae. In clinical labs, there are four main uses.[31]

CONCLUSION:

The currently available antitubercular drugs provide treatment which involves regular administration of drug therapy for six months. However, lack of adherence to prescribed treatment regimen and combination of HIV infection, development of MDR TB, XDR TB, and recalcitrance of mycobacterium has increased the need for novel drugs with improved effectiveness. Novel therapies are required not only to decrease the treatment duration and/or decrease the number of doses taken under DOT regime but also provide improved treatments for MDR-TB cases, effective treatment of latent TB infections, and effective treatment of TB cases combined with HIV and causing minimal or no interaction with antiretroviral therapy. TB Alliance established in the year 2000 largely funded by Bill & Melinda Gates Foundation

has contributed immensely in transforming the R&D scenario in the field of tuberculosis. It is important to note that despite promising results obtained by drugs in the pipeline of TB drugs in terms of reduced treatment time, the number of such drugs is few. Tuberculosis is one of the deadliest infectious diseases and has caused death of millions of people in many years. Although there have been considerable achievements over the last decade in tackling TB burden, more needs to be done. Medical significance and physiological characteristics unique to other microorganisms have always been the focus of scientific attention. It seems that the discovery and development process of drugs and vaccines made up till now indicates that the control of TB disease progression is not an easy task and demands a strategy and a collective application of prevention, and control methods of diseases. However, with the development of novel antitubercular drugs, it seems evident that the current drug cocktail is inadequate. New therapy should be developed with minimum risk of resistance development and minimum adverse reactions from patients. At the moment, we do not have a universal drug or a set of drugs that can effectively manage all active and latent TB infections in the least possible time. The old-fashioned method of drug discovery based on the bactericidal effect, regardless of the mechanism of action or the target, may not be effective enough in finding proper candidates for treatment. Further investigations must be directed towards the identification of factors contributing to metabolic reprogramming of Mtb. Tuberculosis is still a major global health problem that affects both people's health and society as a whole. To control the disease, it is important to find it early, treat it well, and stick to the treatment plan. Social factors like poverty, malnutrition, overcrowding, and stigma keep making it worse. Vaccination, education, and better access to healthcare are all important public health strategies for prevention. To get rid of tuberculosis around the world, we need to use both medical and social methods.

Tuberculosis is still one of the most common infectious diseases in the world, causing a lot of illness and death. Every year, millions of new cases are reported, even though medicine has come a long way. For timely treatment, it is important to find the disease early through proper screening and lab tests. When done as directed, standard anti-tubercular therapy works very well. Drug-resistant tuberculosis has become a major problem for efforts to control the disease around the world. Poverty, overcrowding, bad sanitation, and malnutrition are all social factors that make diseases spread more easily. Stigma and a lack of knowledge can make it harder to get a diagnosis and treatment. It's very important to make healthcare systems stronger and make sure everyone has the same access to medicines.

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