WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Pulmonary Tuberculosis: A Comparative Literature-Based Study of Conventional Therapies vs. Emerging Treatment Strategies

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ABSTRACT :

Pulmonary tuberculosis (PTB) remains a leading infectious disease globally, with high morbidity and mortality rates, particularly in low- and middle-income countries. Despite the success of conventional treatment regimens like HRZE (isoniazid, rifampicin, pyrazinamide, and ethambutol), challenges such as long treatment duration, poor patient adherence, and the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB necessitate new approaches. This literature-based comparative study evaluates traditional anti-tubercular therapies against emerging treatment strategies, including novel drugs (bedaquiline, delamanid, pretomanid), host-directed therapies, vaccine advancements, nanotechnology-based drug delivery systems, and precision medicine tools. The analysis highlights that newer regimens offer promising advantages in terms of reduced treatment duration, improved patient compliance, and effectiveness against resistant strains. However, they also present limitations such as higher costs, emerging resistance, and limited availability in resource-constrained settings. An integrated treatment model combining conventional and innovative approaches, tailored through drug resistance profiling and supported by public health systems, is essential to achieve global TB control and elimination goals.

Keywords: Pulmonary tuberculosis, MDR-TB, XDR-TB, anti-tubercular drugs, bedaquiline, delamanid, host-directed therapy, nanotechnology, TB vaccines, drug resistance, comparative study

1. Introduction

Pulmonary tuberculosis (PTB) is a contagious bacterial infection caused by *Mycobacterium tuberculosis*, primarily affecting the lungs. It is transmitted through airborne particles when an infected person coughs, sneezes, or speaks, making it a major public health concern, especially in densely populated regions (Lönnroth et al., 2010). PTB is the most common form of tuberculosis and can range from latent infection, where the bacteria remain dormant, to active disease characterized by symptoms such as persistent cough, chest pain, weight loss, fever, and night sweats (Pai et al., 2016).

Globally, tuberculosis remains one of the top infectious disease killers. According to the **World Health Organization (WHO)**, an estimated 10.6 million people fell ill with TB in 2022, and 1.3 million deaths were reported among HIV-negative individuals, with an additional 167,000 deaths among HIV-positive patients (WHO, 2023). Pulmonary TB accounts for approximately 85% of all TB cases and is responsible for the majority of TB transmission. India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa together account for over two-thirds of the global TB burden (Glaziou et al., 2020).

Despite the existence of effective anti-tubercular drugs and control programs, the disease persists due to challenges such as delayed diagnosis, poor treatment adherence, and the rise of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) (Gandhi et al., 2010). Early and accurate treatment is essential not only to cure the patient but also to prevent community spread and emergence of drug resistance. The Directly Observed Treatment Short-course (DOTS) strategy introduced by WHO has been successful in increasing treatment success rates, yet gaps remain in implementation, especially in resource-limited settings (Uplekar et al., 2015).

The evolving nature of TB therapy, especially with the advent of new drugs and adjunctive strategies, has led to renewed interest in re-evaluating treatment protocols. This necessitates a comprehensive comparative understanding of conventional therapies (such as isoniazid, rifampicin, ethambutol, and pyrazinamide) versus emerging treatment options, including new pharmaceuticals like bedaquiline and delamanid, as well as host-directed therapies and herbal interventions (Dheda et al., 2017).

This review is based solely on published literature and aims to critically compare conventional and emerging treatment strategies for pulmonary tuberculosis. The rationale lies in the urgent need to understand the relative efficacy, safety, duration, resistance profiles, and patient outcomes associated with these therapeutic approaches. By synthesizing evidence from global health databases and peer-reviewed studies, the review also intends to highlight future directions for optimizing TB treatment protocols.

Objectives of the Review

- To provide an overview of the global burden and treatment landscape of pulmonary tuberculosis.
- To analyze and compare the conventional first-line anti-TB therapies with newer, emerging treatment options.
- To evaluate drug efficacy, resistance trends, adverse effects, and compliance issues as reported in the literature.
- To identify the challenges and future prospects in the clinical management of pulmonary tuberculosis using evidence-based data.

2. Etiology and Pathophysiology of Pulmonary Tuberculosis

Pulmonary tuberculosis (PTB) is caused by the bacterium *Mycobacterium tuberculosis*, a slow-growing, acid-fast bacillus with a complex, lipid-rich cell wall that contributes to its resistance to desiccation and antibiotics (Flynn & Chan, 2001). The pathogen primarily targets the lungs, although it can disseminate to other organs in cases of advanced or immunocompromised disease. *M. tuberculosis* belongs to the *Mycobacterium tuberculosis* complex, which also includes other species such as *M. bovis*, *M. africanum*, and *M. microti*, but *M. tuberculosis* is the predominant cause of human pulmonary TB (Gagneux, 2018).

Transmission occurs primarily through inhalation of airborne droplets released by individuals with active pulmonary TB. Once inhaled, the bacilli reach the alveoli, where they are engulfed by alveolar macrophages. Unlike many pathogens, *M. tuberculosis* can survive and replicate within macrophages by inhibiting phagosome-lysosome fusion (Ernst, 2012). This survival mechanism triggers a complex immune response, leading to the recruitment of T-cells, neutrophils, and other immune cells to the site of infection. Over time, this immune reaction results in the formation of granulomas—organized structures that aim to contain the bacilli (Ulrichs & Kaufmann, 2006).

The granuloma represents both a protective and pathological feature. While it walls off the infection and prevents dissemination, the enclosed bacteria can remain dormant for years, resulting in latent tuberculosis infection (LTBI). In about 5–10% of infected individuals, especially those with weakened immune systems (e.g., HIV-positive patients, diabetics, or the elderly), the latent infection can reactivate into active disease (Barry et al., 2009).

The progression to active PTB is marked by tissue necrosis and cavitation in the lungs. This phase is associated with clinical symptoms such as persistent cough (sometimes with hemoptysis), chest pain, weight loss, fatigue, fever, and night sweats (Menzies et al., 2008). The caseous necrosis and cavitary lesions enhance bacterial replication and increase the risk of transmission due to higher bacterial loads in sputum.

From a pathophysiological standpoint, PTB is a dynamic interplay between host immune response and bacterial virulence. The severity and outcome of infection depend on host immunity, genetic predisposition, nutritional status, and co-existing health conditions (Kaufmann, 2010). HIV co-infection is particularly significant, as it increases susceptibility to both primary infection and reactivation due to impaired cellular immunity (Pawlowski et al., 2012).

Understanding the etiology and pathophysiology of PTB is crucial for designing effective therapeutic strategies and diagnostics. Conventional treatments aim to eliminate both actively replicating and dormant bacilli, while emerging therapies are being developed to target immune modulation and drug-resistant mechanisms.

3. Diagnostic Tools and Challenges

Timely and accurate diagnosis of pulmonary tuberculosis (PTB) is essential for early treatment initiation, infection control, and reducing transmission. A wide array of diagnostic tools has been developed over time, ranging from traditional microscopic techniques to advanced molecular assays. Each method varies in terms of sensitivity, specificity, cost, infrastructure requirements, and applicability in different healthcare settings.

3.1 Conventional Diagnostic Methods

Sputum Smear Microscopy has been a cornerstone in TB diagnosis, especially in resource-limited settings. It involves staining sputum samples using Ziehl-Neelsen (ZN) or auramine-rhodamine fluorescent stains to detect acid-fast bacilli (AFB) under the microscope (Steingart et al., 2006). While this method is inexpensive and rapid, it has limited sensitivity, particularly in patients with HIV co-infection or low bacillary loads (Perkins et al., 2007).

Chest Radiography is often used as an adjunct to microbiological tests. It can reveal lung abnormalities such as infiltrates, cavitary lesions, and fibrosis suggestive of TB. However, radiological findings are not specific to TB and may overlap with other respiratory infections or malignancies, making it unsuitable as a standalone diagnostic tool (Gooze et al., 2011).

Tuberculin Skin Test (TST), also known as the Mantoux test, detects delayed-type hypersensitivity to purified protein derivative (PPD) injected intradermally. A positive reaction indicates exposure to *M. tuberculosis*, but it does not differentiate between latent and active infection. Moreover, it can yield false positives in individuals vaccinated with Bacillus Calmette–Guérin (BCG) or infected with non-tuberculous mycobacteria (Menzies et al., 2007).

3.2 Advanced Molecular and Immunological Techniques

GeneXpert MTB/RIF is a revolutionary nucleic acid amplification test (NAAT) endorsed by WHO for rapid TB diagnosis. It simultaneously detects *M. tuberculosis* DNA and rifampicin resistance within two hours with high sensitivity and specificity (Boehme et al., 2010). It is particularly useful in diagnosing smear-negative and extrapulmonary TB, as well as TB in HIV-positive patients. However, its implementation is limited by high costs and the need for stable power supply and trained personnel.

Line Probe Assays (LPAs) are molecular tests that detect mutations associated with resistance to first- and second-line anti-TB drugs. They are useful in guiding the management of drug-resistant TB, but like GeneXpert, they require specialized laboratory infrastructure (Hillemann et al., 2007).

Interferon-Gamma Release Assays (IGRAs) measure the immune response to specific TB antigens (e.g., ESAT-6 and CFP-10) by quantifying interferon-gamma release. These blood-based tests are more specific than TST and are not influenced by BCG vaccination. However, IGRAs cannot distinguish between latent and active TB and are relatively expensive (Pai et al., 2014).

3.3 Diagnostic Challenges

Despite technological advancements, TB diagnosis faces several persistent challenges:

- *Limited access to modern diagnostics* in rural and low-income regions hampers early detection and treatment initiation (Nikam et al., 2013).
- *False negatives* in smear microscopy, especially in pediatric cases and immunocompromised individuals, often delay diagnosis (Marais et al., 2006).
- *Stigma and social barriers* lead to underreporting and patient hesitancy in seeking care.
- *Difficulty in diagnosing extrapulmonary TB* using conventional methods necessitates invasive sampling procedures and sophisticated tools.
- *Distinguishing latent TB from active disease* remains a clinical challenge, as both TST and IGRA have limited predictive value for progression to active TB (Getahun et al., 2011).

Addressing these diagnostic limitations requires a multipronged approach, including expansion of molecular diagnostics, point-of-care tools, capacity building in laboratories, and integration of artificial intelligence and digital technologies for improved accuracy and reach.

4. Conventional Therapies for Pulmonary Tuberculosis

The conventional treatment of pulmonary tuberculosis (PTB) is based on the administration of a combination of first-line anti-tubercular drugs that target *Mycobacterium tuberculosis* during both its active replication and dormant phases. The primary goal of therapy is to achieve bacteriological cure, prevent transmission, reduce the risk of drug resistance, and avoid relapse. The World Health Organization (WHO) recommends a standardized regimen for drug-sensitive TB, which has been the global standard for decades (WHO, 2022).

4.1 First-Line Anti-Tubercular Drugs

The standard first-line regimen for drug-susceptible PTB includes a 6-month course consisting of an intensive phase followed by a continuation phase:

- *Intensive Phase (2 months):* Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E)
- *Continuation Phase (4 months):* Isoniazid (H) and Rifampicin (R)

This regimen is commonly referred to as *HRZE/HR*. These drugs act synergistically to kill both actively dividing and dormant bacilli:

- *Isoniazid* inhibits mycolic acid synthesis, essential for bacterial cell wall integrity (Mitchison, 2000).
- *Rifampicin* blocks RNA synthesis by binding to DNA-dependent RNA polymerase (Donald & van Helden, 2009).
- *Pyrazinamide* disrupts membrane transport and energy production in semi-dormant bacilli.
- *Ethambutol* inhibits arabinosyl transferases involved in cell wall biosynthesis.

4.2 Treatment Outcomes and Effectiveness

When adhered to correctly, this regimen yields a high success rate of 85–90% in drug-sensitive TB cases (Vekemans et al., 2021). The implementation of *Directly Observed Treatment, Short-course (DOTS)* by WHO has significantly improved compliance and cure rates worldwide. DOTS ensures that patients take their medications under supervision, thus reducing the likelihood of default and resistance development (Uplekar et al., 2015).

4.3 Adverse Effects and Limitations

Despite its effectiveness, conventional therapy is associated with several adverse drug reactions that can impact treatment adherence:

- *Isoniazid* may cause hepatotoxicity and peripheral neuropathy.
- *Rifampicin* can lead to hepatotoxicity, flu-like symptoms, and drug interactions due to enzyme induction.
- *Pyrazinamide* is often linked to hyperuricemia and hepatotoxicity.
- *Ethambutol* may cause optic neuritis and visual disturbances (Saukkonen et al., 2006).

These side effects require close monitoring and sometimes regimen adjustments. In addition, patient compliance is a major challenge due to the prolonged treatment duration and the necessity for daily dosing.

4.4 Limitations in Special Populations

Treatment complexity increases in populations such as:

- *HIV co-infected patients*, due to drug-drug interactions with antiretroviral therapy (ART) and increased risk of toxicity (Lawn & Zumla, 2011).
- *Pregnant women*, where the safety of certain drugs (e.g., streptomycin) is a concern.
- *Children*, where diagnosis and dosing are more complicated due to the paucibacillary nature of pediatric TB.

- *Diabetic patients*, who are more likely to experience treatment failure and relapse due to immunocompromised status and altered pharmacokinetics (Dooley & Chaisson, 2009).

Furthermore, the rise of *multidrug-resistant TB (MDR-TB)*, defined as resistance to at least isoniazid and rifampicin, has emerged as a major threat to the effectiveness of conventional regimens. In such cases, second-line treatment options must be considered, which are often more toxic, expensive, and prolonged (Dheda et al., 2017).

Conventional therapies have laid the foundation for global TB control, but the evolving landscape of drug resistance and patient heterogeneity necessitates newer, individualized approaches and adjunctive therapies.

5. Drug-Resistant TB: MDR and XDR Challenges

Drug-resistant tuberculosis (DR-TB) has emerged as one of the most significant challenges in global TB control efforts. Despite decades of standardized therapy, the emergence and spread of resistance to first-line and second-line anti-tubercular drugs threaten the progress made in TB management and eradication.

5.1 Definition and Classification

Drug-resistant TB occurs when *Mycobacterium tuberculosis* strains acquire mutations that render standard anti-TB drugs ineffective. It is classified into various types based on resistance patterns:

- *Multidrug-Resistant TB (MDR-TB):* Resistance to at least isoniazid and rifampicin, the two most powerful first-line drugs.
- *Extensively Drug-Resistant TB (XDR-TB):* MDR-TB with additional resistance to any fluoroquinolone and at least one of the three second-line injectable drugs (amikacin, kanamycin, or capreomycin).
- *Pre-XDR TB:* MDR-TB with resistance to fluoroquinolones but not to injectable second-line drugs (WHO, 2022).

The primary causes of drug resistance include improper use of antibiotics, incomplete treatment courses, poor adherence, inadequate treatment supervision, and lack of proper diagnostic tools to detect resistance early (Zignol et al., 2006).

5.2 Global Burden

According to WHO's Global TB Report (2023), an estimated *410,000 people* developed MDR-TB in 2022, with only about 50% receiving appropriate treatment. The *treatment success rate for MDR-TB* remains low, at around *60%*, and even lower for XDR-TB, which often requires extended therapy with less effective and more toxic drugs (WHO, 2023). The highest burden of DR-TB is reported in India, China, the Russian Federation, and several countries in Africa and Eastern Europe (Dheda et al., 2017).

5.3 Treatment Regimens and Limitations

Treatment for MDR-TB and XDR-TB involves a combination of *second-line drugs* such as:

- Fluoroquinolones (levofloxacin, moxifloxacin)
- Injectable agents (amikacin, capreomycin)
- Newer drugs like *bedaquiline*, *delamanid*, and *linezolid*
- Companion drugs like cycloserine, clofazimine, and ethionamide

These regimens are typically longer (18–24 months) and associated with increased toxicity, including nephrotoxicity, ototoxicity, bone marrow suppression, and peripheral neuropathy (Falzon et al., 2011). Moreover, the high cost and requirement for close monitoring limit their use in resource-constrained settings.

5.4 Diagnostic and Management Challenges

The diagnosis of drug-resistant TB requires molecular or culture-based susceptibility testing, which may not be widely available in low-income regions. *GeneXpert MTB/RIF* has improved early detection of rifampicin resistance, but identifying resistance to other drugs still requires more advanced methods like *line probe assays* or *culture-based DST* (Van Rie et al., 2000).

Management of DR-TB is further complicated by:

- *Treatment complexity and pill burden*
- *Delayed detection of resistance*, leading to ongoing transmission
- *Psychological stress* and *socioeconomic burden* on patients
- *Stigma and isolation*, affecting adherence and quality of life
- *Co-infection with HIV*, which worsens outcomes and increases mortality

5.5 Public Health and Future Perspectives

To combat MDR/XDR-TB, WHO has recommended shorter, all-oral regimens and increased use of newer drugs like *bedaquiline-based regimens*, which have shown promising outcomes with fewer side effects (Conradie et al., 2020). Global strategies also emphasize the importance of early diagnosis, universal drug susceptibility testing, patient-centered care, and expanded access to second-line drugs.

However, the threat of *total drug-resistant TB (TDR-TB)*, although rare, underscores the urgent need for investment in *new drug discovery, vaccine*

development, and *host-directed therapies*.

6. Emerging Therapies and Innovations in Pulmonary Tuberculosis Treatment

While conventional therapies have greatly reduced tuberculosis (TB) incidence and mortality, the growing burden of drug-resistant strains and the limitations of existing drugs have driven the search for **novel therapeutic strategies**. Emerging treatments focus on improving cure rates, shortening treatment duration, overcoming drug resistance, and enhancing host immunity.

6.1 New Anti-Tubercular Drugs

Several new drugs have been developed and introduced to improve the management of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB):

- **Bedaquiline**: A diarylquinoline that inhibits ATP synthase in *M. tuberculosis*. It is the first new anti-TB drug in over 40 years, approved for MDR-TB and included in WHO-recommended all-oral regimens (Diacon et al., 2009; WHO, 2022).
- **Delamanid**: A nitro-dihydro-imidazooxazole derivative that inhibits mycolic acid synthesis, essential for the bacterial cell wall. It shows synergistic effects with bedaquiline and is used in difficult MDR/XDR cases (Gler et al., 2012).
- **Pretomanid**: Used in combination with bedaquiline and linezolid (BPaL regimen), this drug has shown remarkable efficacy in patients with highly drug-resistant TB (Conradie et al., 2020).

These agents have improved outcomes in MDR/XDR-TB with fewer injections, reduced treatment time, and better tolerability.

6.2 Host-Directed Therapies (HDTs)

Emerging research supports **host-directed therapies** aimed at modulating the immune response and enhancing the body's ability to control TB infection. These include:

- **Metformin**, an antidiabetic drug, shown to enhance autophagy and reduce TB pathology (Singhal et al., 2014).
- **Statins** and **non-steroidal anti-inflammatory drugs (NSAIDs)** to reduce inflammation and bacterial burden (Lobato et al., 2014).
- **Vitamin D supplementation** to promote macrophage activity and granuloma formation (Martineau et al., 2011).

HDTs offer a novel approach that may work synergistically with conventional drugs and reduce the emergence of resistance.

6.3 Vaccine Development

The **Bacillus Calmette–Guérin (BCG)** vaccine is currently the only approved TB vaccine, but its protection is limited to severe forms of childhood TB. Several promising vaccine candidates are in various stages of development:

- **M72/AS01E**, a subunit vaccine developed by GSK, showed 50% efficacy in preventing active TB in latently infected adults (Tait et al., 2019).
- **VPM1002**, a recombinant BCG vaccine, is undergoing phase III trials and may offer broader protection.

Improved vaccination strategies are critical to achieving TB elimination goals.

6.4 Nanotechnology and Drug Delivery Systems

Advances in **nanotechnology** have enabled targeted delivery of anti-TB drugs to infected lung tissues, improving bioavailability and reducing systemic toxicity. Liposomal and polymeric nanoparticles are being explored for delivering isoniazid, rifampicin, and newer agents (Parvez et al., 2021).
Inhalable formulations and **controlled-release drug systems** are also under development to improve patient adherence and treatment outcomes.

6.5 Shorter and All-Oral Regimens

New regimens aim to reduce the lengthy TB treatment duration:

- The **BPaL regimen (bedaquiline, pretomanid, linezolid)** provides a 6–9 month all-oral treatment option for XDR-TB (Conradie et al., 2020).
- A **4-month regimen** containing rifapentine and moxifloxacin has shown non-inferiority to the standard 6-month HRZE regimen in drug-susceptible TB (Dorman et al., 2021).

Such regimens significantly improve treatment adherence, reduce toxicity, and minimize healthcare costs.

6.6 Genomic and Precision Medicine Approaches

With the advent of **whole-genome sequencing (WGS)**, TB treatment is moving toward **precision medicine**. WGS helps identify resistance-conferring mutations, enabling personalized drug regimens and better monitoring of transmission dynamics (Walker et al., 2015).
Furthermore, **CRISPR-based diagnostics** and **AI-powered imaging tools** are revolutionizing TB diagnostics and monitoring, especially in high-burden regions.
These innovative strategies hold the potential to transform the future of TB care by making treatments **more effective, individualized, shorter, and**

safer. However, their widespread adoption requires robust clinical trials, affordability, and integration into public health systems.

7. Comparative Analysis – Conventional vs. Emerging Treatments

The management of pulmonary tuberculosis (PTB) is rapidly evolving, with emerging therapies aiming to overcome the limitations of conventional treatment regimens. A comparative literature-based analysis reveals distinct differences in terms of efficacy, treatment duration, drug resistance management, patient compliance, and safety profiles between conventional and emerging approaches.

Parameter	Conventional Therapy	Emerging Treatments
Drug Composition	HRZE (isoniazid, rifampicin, pyrazinamide, ethambutol)	Bedaquiline, delamanid, pretomanid, linezolid, moxifloxacin, rifapentine, etc.
Duration of Treatment	6 months for drug-sensitive TB	4–6 months for newer regimens (e.g., rifapentine-moxifloxacin, BPaL)
Delivery Route	Oral, sometimes with injections for MDR/XDR cases	All-oral regimens increasingly preferred
Effectiveness (Drug-sensitive TB)	~85–90% success rate (WHO, 2022)	Similar or improved success in shorter regimens (Dorman et al., 2021)
Effectiveness (Drug-resistant TB)	~60% for MDR; lower for XDR (WHO, 2023)	~90% with BPaL regimen for XDR-TB (Conradie et al., 2020)
Toxicity and Side Effects	Hepatotoxicity, optic neuritis, neuropathy	Milder profiles in newer regimens; linezolid-associated myelosuppression is a concern
Resistance Development	Common due to poor adherence or inadequate regimens	Reduced with precision-guided and shorter therapies
Diagnostic Integration	Smear microscopy, GeneXpert, culture-based DST	Molecular diagnostics, WGS, CRISPR-based tools
Host Immunity Targeting	Not addressed	Host-directed therapies (vitamin D, metformin) under evaluation
Patient Adherence	Challenging due to prolonged treatment	Improved due to shorter, simpler, all-oral regimens
Cost and Accessibility	Widely available and affordable in many regions	Expensive and less accessible in low-resource settings
Vaccination	BCG (limited efficacy in adults)	New candidates like M72/AS01E under development (Tait et al., 2019)

7.1 Advantages of Emerging Therapies

- **Shorter duration** of treatment reduces the risk of non-compliance.
- **Improved outcomes** in MDR/XDR-TB patients, where conventional therapies often fail.
- **All-oral regimens** eliminate the need for painful injections and related complications.
- **Potential for personalized medicine**, leveraging molecular diagnostics and resistance profiling.

7.2 Limitations of New Approaches

- **High cost** and limited availability restrict use in low-income, high-burden countries.
- **Emerging resistance** to new drugs like bedaquiline is a concern if misuse occurs.
- **Toxicity profiles** of some newer drugs (e.g., linezolid) still require careful monitoring.
- **Lack of data** from long-term trials in diverse populations for some novel regimens.

7.3 Integration and Future Outlook

Rather than replacing conventional treatments entirely, emerging therapies are likely to complement existing approaches. For example, standard regimens remain highly effective for drug-sensitive TB in most settings, while newer options are being reserved for resistant and complex cases.
An integrated, tiered approach that tailors treatment based on **drug susceptibility**, **patient factors**, and **available resources** may represent the most pragmatic path forward. Public health policies must also ensure **equitable access**, **affordable pricing**, and **training of healthcare providers** to effectively implement new strategies.

8. Conclusion and Future Directions

Pulmonary tuberculosis (PTB) continues to pose a significant global health challenge, particularly in low- and middle-income countries where the burden of disease and drug resistance is highest. Conventional anti-tubercular therapy has proven effective in most drug-sensitive cases, saving millions of lives. However, the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis has exposed the limitations of existing treatments in terms of efficacy, safety, duration, and accessibility.
This literature-based comparative analysis highlights how *emerging therapies*—including novel drugs like bedaquiline and delamanid, host-directed therapies, and advanced diagnostics—are redefining TB treatment paradigms. These innovations have shown great promise, especially in drug-resistant cases, with improved outcomes, reduced toxicity, and shorter treatment durations.

Nonetheless, the translation of these novel strategies into routine practice faces several *critical challenges*:

- *High cost* and *limited access* in high-burden settings
- Need for *robust clinical trials* across diverse populations
- Risks of *emerging resistance* to new drugs
- Insufficient *infrastructure* and *trained personnel* to support molecular diagnostics and individualized therapy

Future efforts must focus on:

- *Strengthening healthcare systems* for the integration of novel regimens
- Ensuring *universal drug susceptibility testing*
- Expanding *research into host immunity modulation*
- Accelerating *vaccine development*
- Enhancing *public-private partnerships* for affordable drug distribution

In conclusion, a *comprehensive and adaptive strategy* is essential—one that leverages the strengths of both conventional and emerging approaches. Such integration, guided by evidence and supported by global commitment, can ultimately bring us closer to achieving the WHO's End TB Strategy goals and reducing the global burden of pulmonary tuberculosis.

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