Review On Tuberculosis

Priya*, Rajesh Kumar, Ajeet Pal Singh, Amar Pal Singh, Meenakshi Malhotra

St.Soldeir Institute of Pharmacy, Lidhran Campus Behind NIT (R.E.C). Jalandhar- Amritsar bypass, NH-1, Jalandhar – 144011, Punjab, India

Abstract

Tuberculosis (TB) remains a significant global health challenge, with millions of new cases reported annually. This review provides a comprehensive overview of TB, covering prevention strategies, treatment regimens, management of drug-resistant TB, and future perspectives. Prevention strategies, including vaccination with the Bacille Calmette-Guerin (BCG) vaccine, infection control measures, screening and treatment of latent TB infection (LTBI), are crucial for reducing TB transmission. Standard TB treatment involves multidrug regimens administered over several months, with adherence being paramount for successful outcomes. However, drug-resistant TB, including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), poses significant challenges, requiring individualized treatment regimens and close monitoring. Future perspectives include ongoing research into novel TB drugs, shorter treatment regimens and improved diagnostics. Despite challenges, continued efforts in TB prevention, treatment and research are essential for reducing the global burden of this infectious disease.

Keywords: Tuberculosis, Global, Bacille Calmette-Guerin (BCG), Treatment, Prevention, Adherence.

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by the bacterium Mycobacterium tuberculosis(M.tb). It primarily affects the lungs but can also affect other parts of the body, such as the brain, kidney and spine. TB remains a significant global health threat, with an estimated 10 million new cases and 1.5 million deaths annually worldwide.

TB has been a part of human history for millennia, with evidence of its presence found in ancient Egyptian mummies and in writings dating back to Hippocrates. Despite advances in medicine and public health, TB continues to disproportionately affect low- and middle-income countries, where factors such as poverty, overcrowding and limited access to healthcare contribute to its persistence.

The emergence of drug-resistant strains of M.tb, coupled with challenges in diagnosis and treatment, further complicates efforts to control TB. Additionally, the intersecting epidemics of TB and HIV/AIDS present unique challenges, as HIV weakens the immune system, increasing the risk of TB infection and progression to active disease.

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Efforts to control TB have been hindered by various factors, including insufficient funding, inadequate healthcare infrastructure and stigma associated with the disease. However, initiatives led by organizations such as the World Health Organization (WHO) and global partnerships like the Stop TB Partnership have made significant strides in TB prevention, diagnosis, and treatment.

Despite these efforts, TB remains a pressing public health issue, underscoring the need for continued research, advocacy and investment in TB control programs. This review aims to provide a comprehensive overview of tuberculosis, encompassing its epidemiology, etiology, pathogenesis, clinical features, diagnosis, treatment, prevention, and global efforts in combating the disease.
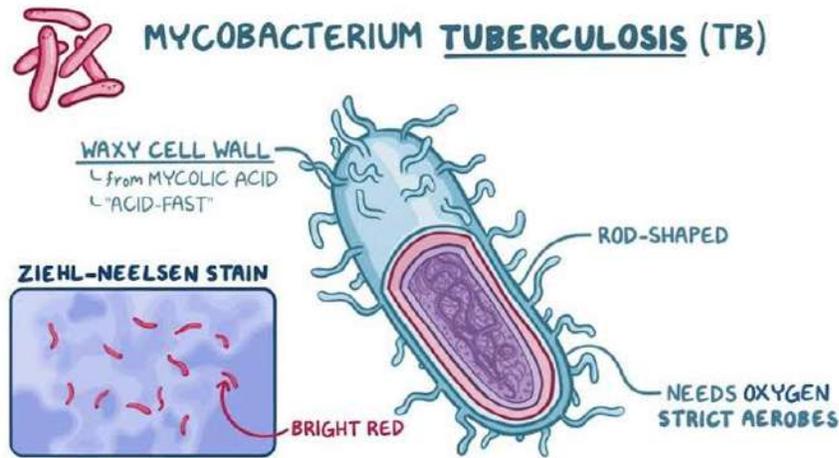

Figure 1: Structure of Mycobacterium Tuberculosis

Epidemiology

Epidemiology is the study of the distribution and determinants of health-related events within populations and the application of this study to the control of health problems. In the case of tuberculosis(TB), epidemiological data provide crucial insights into the prevalence, incidence and distribution of the disease across different and geographic regions. Understanding TB epidemiology involves analysing factors such as demographic characteristics, socioeconomics status, geographic location, and risk factors associated with TB transmission.
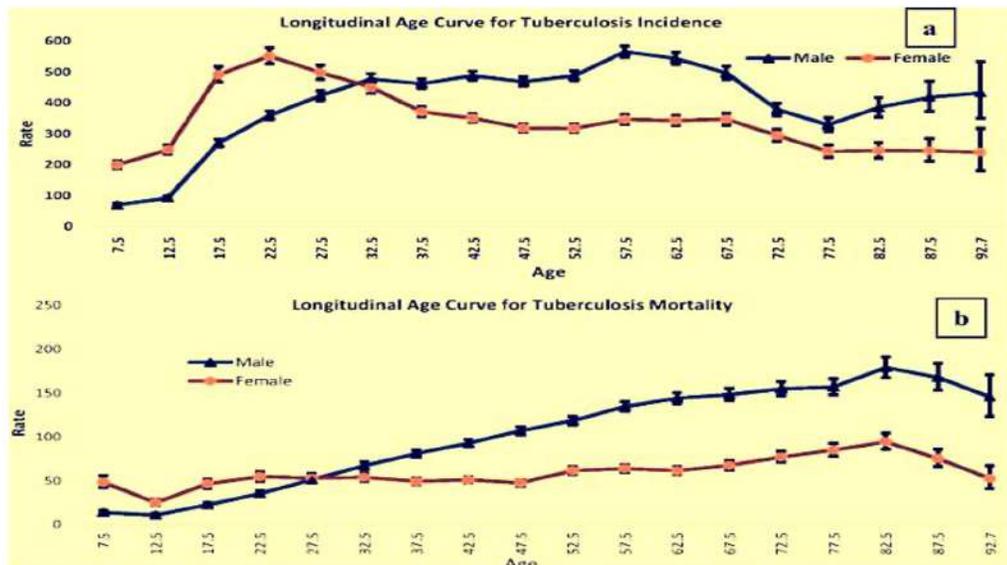

Figure 2: Trends in incidence and mortality of tuberculosis in India over pass three decades: a joint and age-period-cohort analysis

Key epidemiological indicators for TB include:

- Incidence rate: The number of new TB cases occuring in a defined population over a specified time period.
- Prevalence rate: The proportion of individuals in a population who have TB at a given point in time.
- Mortality rate: The number of deaths attributed to TB within a population over a specified time period.
- Case fatality rate: The proportion of diagnosed TB cases that in death.

TB epidemiology also involves identifying high-risk populations, such as individuals with HIV/AIDS, diabetes or other immunocompromising conditions, as well as groups with increased exposure to TB due to factors like overcrowded living conditions, poor ventilation, and limited access to healthcare.

Analysing TB epidemiological data helps public health officials and policymakers develop targeted interventions and allocate resources effectively to control the spread of TB. These interventions may include active case finding, contact tracing, targeted screening programs and efforts to address social determinants of health that contribute to TB transmission.

By understanding the epidemiology of TB, public health efforts can be tailored to address specific challenges and priorities in different communities, ultimately contributing to the global goal of TB elimination.

ETIOLOGY AND PATHOGENESIS OF TUBERCULOSIS

Tuberculosis(TB) is an infectious disease caused by the bacterium Mycobacterium tuberculosis(M. tuberculosis).The etiology of TB lies in the ability of M. tuberculosis to evade the host immune system and establish within the human body.

Etiology:

❖ **Mycobacterium tuberculosis:**
- Gram-positive, acid-fast bacillus.
- Slow-growing bacterium with a waxy cell wall composed of mycolic acids, contributing to its resistance to environmental stressors and immune defences.
- Infection primarily occurs through inhalational of aerosolized droplets containing M. tuberculosis, typically from individuals with active pulmonary TB.

Pathogenesis:

❖ **Inhalational and Phagocytosis:**
- Upon inhalation, M. tuberculosis reaches the alveoli of the lungs.
- Alveolar macrophages phagocytose M. tuberculosis, initiating the host immune response.

❖ **Intracellular Survival:**
- Instead of being destroyed, M. tuberculosis survives and replicates within macrophages.
- Bacterial factors such as cell wall components and virulence factors contribute to intracellular survival.

❖ **Granuloma Formation:**
- As the infection progresses, immune cells, including macrophages and T lymphocytes, form organized structures called granulomas around infected macrophages.
- Granulomas serve as a site of containment and immune response against M. tuberculosis.

❖ **Immune Response:**
- Macrophages release pro-inflammatory cytokines and chemokines, recruiting additional immune cells to the site of infection.
- T lymphocytes play a crucial role in controlling TB infection, activating macrophages and directly killing infected cells.

❖ **Latent Tuberculosis Infection(LTBI) and Reactivation:**
- In some individuals, the immune response is sufficient to contain M. tuberculosis within granulomas, leading to latent TB infection.
- Factors such as immunosuppression, malnutrition and comorbidities like

HIV/AIDS can increase the risk of TB reactivation, leading to active TB disease.

Conclusion:

Understanding the etiology and pathogenesis of tuberculosis is crucial for developing effective diagnostic, treatment, prevention strategies. By elucidating the mechanism by which M. tuberculosis evades host immunity and establishes infection, researchers can identify potential targets for drug development and vaccine design, ultimately aiding in the global efforts to control and eliminate tuberculosis.
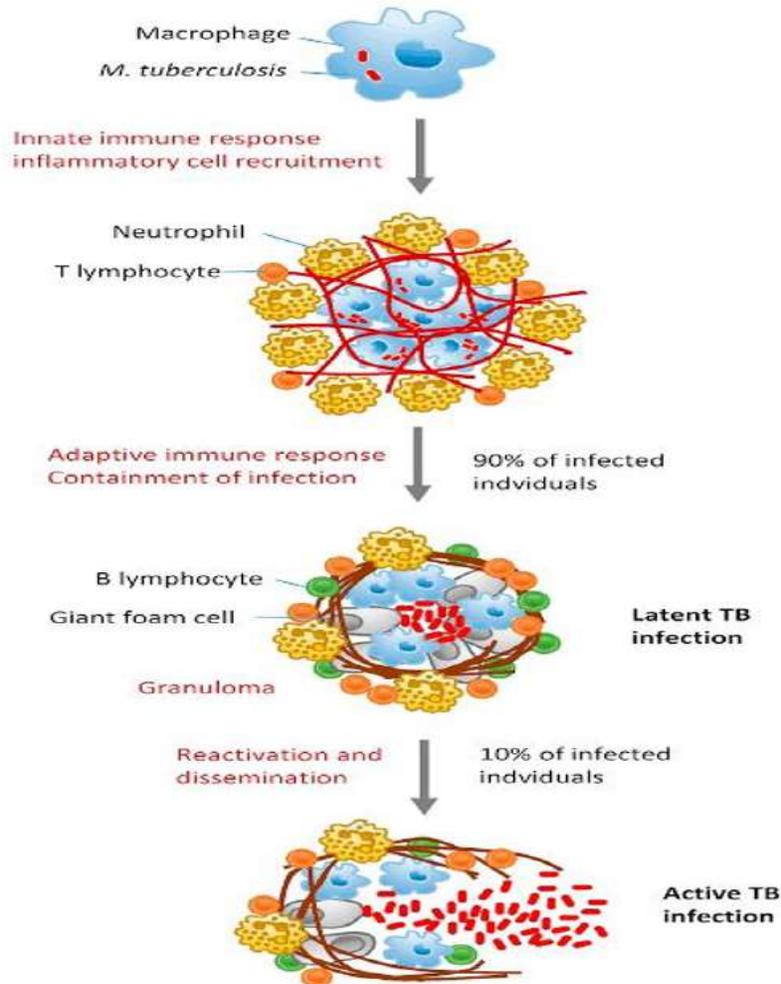

Figure 3: Tuberculosis Pathogenesis and Disease Progression Clinical Features of Tuberculosis

Clinical features of tuberculosis (TB) can vary depending on factors such as the site of infection, the immune status of the individual and whether the TB infection is latent or active. Here are the key clinical features associated with TB:

1. Pulmonary TB:
- Persistent cough lasting more than two weeks, sometimes accompanied hemoptysis (coughing up blood).
- Chest pain, often pleuritic in nature (worsening with deep breathing or coughing).
- Fever, often low-grade but may be higher in severe cases.
- Night sweats, particularly drenching sweats that disrupt sleep.
- Fatigue and malaise, with a general feeling of being unwell.

- Weight loss and loss of appetite, leading to unintentional weight loss.
- Breathlessness or shortness of breath, especially with excretion.

2. **Extrapulmonary TB:**

Depending on the site of infection, extrapulmonary TB can present with various symptoms:

- Lymph nodes (cervical, axillary or mediastinal): Swelling and pain in the affected area.
- Pleura (pleural TB): Pleuritic chest pain, pleural effusion (fluid buildup in the pleural space) and breathlessness.
- Bones and joints (skeletal TB): Pain, swelling and limited range of motion in the affected joint or bone.
- Central nervous system (CNS TB): Headache, confusion, focal neurological deficits, seizures and altered mental status.

- Genitourinary system (genitourinary TB): Dysuria, frequency, hematuria, flank pain, and renal failure in severe cases.
- Gastrointestinal system (gastrointestinal TB): Abdominal pain, diarrhoea, weight loss, and features of bowel obstruction or perforation.
- Skin and soft tissue (cutaneous TB): Skin lesions such as nodules, ulcers or abscesses that may be painless or mildly tender.

3. **Disseminated TB:**

- Disseminated TB occurs when the infection spreads beyond the lungs to other organs and tissues in the body.
- Symptoms may include fever, night sweats, weight loss, fatigue, and symptoms related to involvement of specific organs (e.g., CNS symptoms in miliary TB).
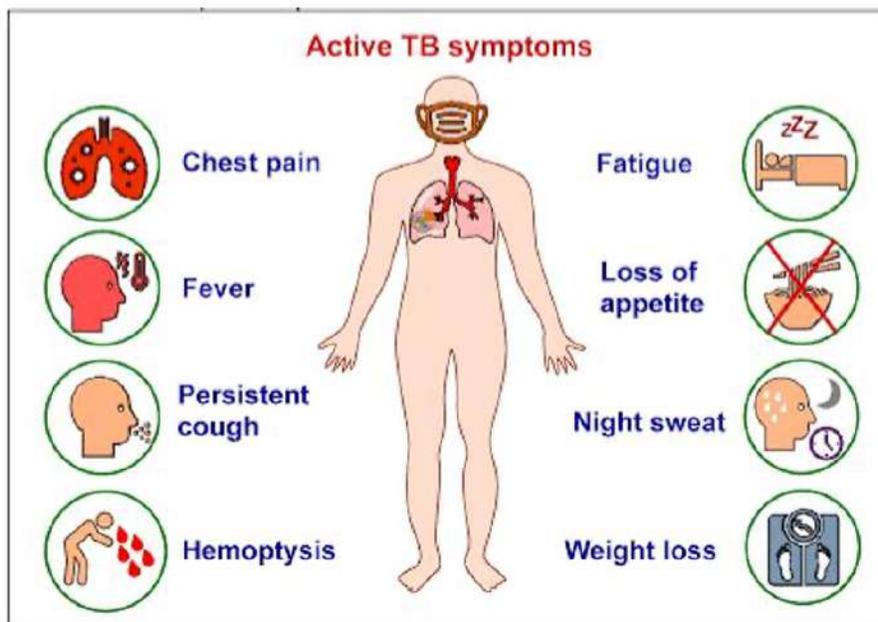

Figure 4: Symptoms Of Active Tuberculosis (TB)

4. **Children and Immunocompromised Individuals:**

- Children and immunocompromised individuals, such as those living with HIV/AIDS, may present with atypical or nonspecific symptoms.

- Symptoms may be milder or absent in children, making diagnosis challenging.
- Immunocompromised individuals are at higher risk of developing severe forms of TB, including disseminated and extrapulmonary TB.

It's important to note that the clinical presentation of TB can be variable and nonspecific, leading to delays in diagnosis and treatment initiation. Healthcare providers should maintain a high index of suspicion for TB, especially in high index od suspicion for TB, especially in high-burden settings or in individuals with risk factors for TB and promptly evaluate and manage suspected cases to prevent transmission and improve outcomes.

DIAGNOSIS OF TUBERCULOSIS

Certainly! When diagnosing tuberculosis (TB), healthcare professionals utilize various methods to accurately detect the presence of Mycobacterium tuberculosis bacteria or assess the body's immune response to TB infection.

Here's an explanation:

1. **Medical History and Physical Examination:**
- Healthcare providers assess the patient's medical history, including any known exposure to TB, previous TB infection and presenting symptoms.
- Physical examination helps identify clinical signs suggestive of TB, such as persistent cough, fever, weight loss and night sweats.
2. **Imaging Tests:**
- Chest X-ray is commonly used to detect abnormalities in the lungs, such as infiltrates or cavities, suggestive of TB infection.
- Computed tomography (CT) scan provides detailed images that help evaluate lung involvement and detect extrapulmonary TB.

Figure 5: The rapid diagnosis of drug-resistant and drug sensitive tuberculosis using mass spectrometry and machine learning.

3. **Laboratory Tests:**
- **Sputum Culture:** A gold standard test that involves culturing sputum samples to identify the presence of Mycobacterium tuberculosis bacteria
- **Nucleic Acid Amplification Tests (NAATs):** Rapid molecular tests that detect TB DNA/RNA, providing quick diagnosis, especially in cases of drug-resistant TB.

- **Tuberculin Skin Test (TST) or Interferon-Gamma Release Assays(IGRAs):**These tests indirectly measure the body's immune response to TB infection.
4. **Additional Tests:**
5. **Molecular Tests (e.g., Xpert MTB/RIF):** This rapid molecular assay detects TB DNA and simultaneously assesses rifampicin resistance, aiding in early diagnosis and treatment initiation.

6. <u>**Clinical Evaluation:**</u>
- Healthcare providers integrate findings from medical history, physical examination, imaging and laboratory tests to make a clinical diagnosis of TB and initiate appropriate treatment.
- The healthcare provider will evaluate the patient's symptoms, risk factors, and test results to confirm or rule out TB.

7. <u>**Management:**</u>
- If TB is diagnosed, prompt initiation of treatment with antibiotics is crucial to prevent disease progression and transmission.

By employing these diagnostic methods, healthcare professionals can accurately diagnose TB, enabling timely initiation of treatment and effective management of the disease.

TREATMENT OF TUBERCULOSIS

Tuberculosis(TB) remains a significant global health threat, causing considerable morbidity and mortality worldwide. Despite advancements in medical science, TB treatment remains complex due to drug resistance and co-infections with HIV. This review aims to provide a comprehensive overview of TB treatment strategies, including drug regimens, adherence, management of drug-resistant TB and future perspectives.

TREATMENT REGIMENS:

Standard TB treatment typically involves a combination of drugs administered over several months. The first-line drugs include isoniazid(INH), rifampicin(RIF), pyrazinamide(PZA) and ethambutol(EMB), collectively known as the "first-line drugs". The most widely used regimen is 2-month intensive phase with all four drugs followed by a 4-month continuation phase with INH and RIF. This regimen, known as "2HRZE/4RH", has been effective in treating drug-sensitive TB.

ADHERENCE:

Adherence to treatment is crucial for successful TB management. Patients must adhere strictly to the prescribed regimen to prevent drug resistance and treatment failure. Healthcare providers play a pivotal role in educating patients about the importance of adherence and addressing and any barriers to adherence, such as medication side effects or socioeconomic factors.

MANAGEMENT OF DRUG-RESISTANT TB:

Drug-resistant TB poses a significant challenge to TB control efforts. Multidrug-resistant TB (MDR-TB) is resistant to both INH and RIF, while extensively drug-resistant TB (XDR-TB) is resistant to additional second-line drugs. Treatment of drug-resistant TB requires longer durations of therapy, often with more toxic and less effective drugs. Individualized treatment regimens based on drug susceptibility testing (DST) results are essential for managing drug-resistant TB. Additionally, adherence support and close monitoring for adverse effects are crucial in this population.

SECOND-LINE DRUGS:

Second-line drugs used in the treatment of drug-resistant TB include fluoroquinolones (e.g., moxifloxacin), injectable agents (e.g., kanamycin, capreomycin), and other agents (e.g., linezolid, bedaquiline, delamanid). These drugs have varying degrees of efficacy and potential side effects, highlighting the importance of careful selection and monitoring by experienced healthcare providers.

ADVERSE EFFECTS AND MONITORING:

TB medications can cause various adverse effects, ranging from mild gastrointestinal symptoms to severe hepatotoxicity, peripheral neuropathy and QT interval prolongation. Regular monitoring of patients during treatment is essential to detect and manage adverse effects promptly. Liver function tests, renal function tests and opthalmologic examinations are

commonly performed to monitor for drug toxicity.

PAEDIATRIC TB TREATMENT:

TB treatment in children requires special considerations due to differences in pharmacokinetics, dosing, and formulations compared to adults. Paediatric TB regimens often include fixed-dose combination formulations to simplify administration and improve adherence. Careful monitoring of growth, development, and potential drug interactions in essential in paediatric TB management.

PREGNANCY AND TB TREATMENT:

TB treatment during pregnancy presents unique challenges, as certain TB medications may pose risks to the developing foetus. However, untreated TB carries significant risks for both the mother and the unborn child. Healthcare providers must weigh the risks and benefits of TB treatment in pregnant women and carefully select the safest drug regimen.

FUTURE PERSPECTIVES:

Despite progress in TB treatment, challenges remain, including the emergence of drug resistance, co-infection with HIV, and the need for shorter, more effective treatment regimens. Ongoing research focuses on developing novel TB drugs, optimizing treatment duration and improving diagnostics to facilitate early detection and treatment initiation.

CONCLUSION:

Effective TB treatment requires a multidimensional approach, encompassing standard drug regimens, adherence support, management of drug-resistant TB and special considerations for vulnerable populations. Continued efforts to improve TB treatment strategies are essential to reduce the global burden of this infectious disease.

PREVENTION FOR TUBERCULOSIS

Tuberculosis(TB) remains a significant global health concern, with millions of new cases reported each year. While treatment of active TB is essential, prevention strategies play a crucial role in reducing the burden of the disease. This review aims to provide an overview of prevention strategies for TB, including vaccination, infection control measures, and targeted interventions for high-risk populations.

VACCINATION:

The Bacille Calmette-Guerin (BCG) vaccine is the only licensed vaccine for TB prevention. Administered primarily to infants in TB-endemic countries, BCG vaccination provides variable protection against severe forms of TB, such as disseminated and meningeal TB, in children. However, its efficacy against pulmonary TB, the most common form of the disease, is limited and varies widely across different populations. Despite its limitations, BCG vaccination remains an essential components of TB control programs, particularly in high-burden settings.

INFECTION CONTROL MEASURES:

Preventing the transmission of TB in healthcare settings and congregate settings, such as prisons and homeless shelters, is crucial for TB control. Infection control measures include administrative controls (e.g., early identification and isolation of infectious individuals), environmental controls(e.g., adequate ventilation), and personal protective equipment (e.g., respirators for healthcare workers). Implementation of comprehensive infection control measures can reduce the risk of TB transmission in high-risk settings.

SCREENING AND TREATMENT OF LATENT TB INFECTION (LTBI):

Identifying individuals with latent TB infection (LTBI) and providing preventive treatment is a key strategy for TB prevention. LTBI refers to the presence of M. Tuberculosis in the body without active disease. Screening for LTBI involves targeted testing of high-risk populations, such as close contacts of TB cases, healthcare workers and immigrants from TB-endemic regions. Treatment of LTBI with

isoniazid (INH) or rifampicin (RIF) reduces the risk of progression to active TB disease and is recommended for individuals at high risk of developing TB.

TARGETED INTERVENTIONS FOR HIGH-RISK POPULATIONS:

Certain populations face an increased risk of TB due to social determinants of health, such as poverty, overcrowded living conditions and limited access to healthcare. Targeted interventions aimed at addressing these underlying factors can contribute to TB prevention efforts. Examples include improving housing conditions, enhancing access to healthcare services, and providing social support to marginalized populations.

CONTACT TRACING AND CASE MANAGEMENT:

Prompt identification and treatment of TB cases, along with contact tracing to identify individuals exposed to TB, are essential components of TB control. Contact tracing involves identifying and evaluating individuals who have had prolonged close contact with a TB case and providing appropriate testing and treatment if indicated. Effective case management, including directly observed therapy (DOT) for active TB cases, ensures optimal treatment outcomes and reduces the risk of ongoing transmission.

CONCLUSION:

Prevention strategies play a critical role in reducing the global burden of tuberculosis. Vaccination with the BCG vaccine, implementation of infection control measures, screening and treatment of latent TB infection, targeted interventions for high-risk populations, and comprehensive case management are essential components of TB prevention efforts. Continued investment in the strategies, along with research into new preventive interventions, is crucial for achieving TB elimination goals.

GLOBAL EFFORTS AND CHALLENGES FOR TUBERCULOSIS ERADICATION

Tuberculosis (TB) remains a significant global health challenge, affecting millions of people every year despite being a preventable and treatable disease. This essay explores the global efforts and challenges in combating tuberculosis, highlighting the progress made, persistent obstacles, and strategies for achieving the goal of eradication.

GLOBAL BURDEN OF TUBERCULOSIS:

Tuberculosis continues to be one of the top infectious disease killers worldwide, causing immense suffering and economic burden, particularly in low- and middle-income countries. According to the World Health Organization(WHO), an estimated 10 million people fell ill with TB in 2020, with around 1.5 million succumbing to the disease. Moreover, TB disproportionately affects vulnerable populations, including those living with HIV, malnourished individuals, and people in overcrowded and impoverished settings.

GLOBAL EFFORTS:

Over the years, significant progress has been made in tackling tuberculosis through coordinated global efforts. Key initiatives include the WHO's End TB Strategy, which aims to reduce TB deaths by 95% and cut new cases by 90% between 2015 and 2035. Additionally, the Global Fund to Fight AIDS, Tuberculosis and Malaria, along with other international partnerships and funding mechanisms, plays a crucial role in supporting TB prevention, diagnosis and treatment programs in various countries.

DIAGNOSTIC AND TREATMENT ADVANCES:

Advancement in TB diagnostics and treatment have revolutionized the approach to managing the disease. Rapid molecular tests like GeneXpert have improved the early detection of TB and drug-resistant strains, enabling timely initiation of appropriate treatment. Furthermore, the development of shorter, more effective drug regimens, such as the use of bedaquilline and

delamanid for multidrug-resistant TB, has increased treatment success rates and reduced the burden of long-term therapy.

VACCINATION EFFORTS:

The Bacillus Calmette-Guerin (BCG) vaccine remains the only licensed vaccine for TB prevention, although its efficacy varies widely. Efforts to develop novel TB vaccines and viral vector-based candidates, are ongoing, with several candidates in various stages of clinical trials. A highly efficacious TB vaccine could significantly contribute to the global TB control efforts by preventing new infections.

CHALLENGES:

Despite progress, numerous challenge hinder the global efforts to eradicate tuberculosis.

DRUG RESISTANCE:

The emergence of drug-resistant TB poses a significant threat to TB control efforts, as treatment becomes more complex, expensive, and less effective. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) require prolonged and often toxic treatment regimens, leading to lower treatment success rates and higher mortality.

LIMITED ACCESS TO HEALTHCARE:

Many TB-affected regions face challenges related to limited access to healthcare services, including diagnostic facilities, trained healthcare personnel, and essential medications. Barriers to access, such as geographic remoteness, poverty, stigma and discrimination, prevent individuals from seeking timely diagnosis and treatment, exacerbating the spread of TB within communities.

CO-INFECTION WITH HIV:

The intersection of TB and HIV/AIDS presents a formidable challenge, particularly in regions with high HIV prevalence. HIV weakens the immune system, increasing the risk of TB infection and progression to active disease. Conversely, TB can accelerate the progression of HIV infection to AIDS. Integrated TB/HIV services are essential for optimizing outcomes and reducing mortality among co-infected individuals.

STIGMA AND DISCRIMINATION:

Stigma associated with TB remains a significant barrier to care, leading to delayed diagnosis, treatment non-adherence, and social isolation for affected individuals and their families. Addressing misconceptions and reducing stigma through community engagement and education is crucial for promoting early diagnosis and treatment adherence.

FUNDING SHORTFALLS:

Despite the availability of effective interventions, funding gaps persist in TB control programs, particularly in low-resource settings. Limited financial resources hinder the scale-up of essential resources hinder the scale-up of essential services, including TB prevention, diagnosis and treatment, thereby impeding progress towards TB eradication goals.

CONCLUSION

Tuberculosis (TB) remains a formidable global health threat, with millions of new cases reported each year. Despite concerted efforts to control the disease, challenges persist, including drug resistance, co-infection with HIV and socioeconomic factors that hinder access to care. However, progress has been made in various aspects of TB prevention, treatment and research.

Prevention efforts are critical for reducing TB transmission and include vaccination with the Bacille Calmette-Guerin (BCG) vaccine, implementation of infection control measures, screening and treatment of latent TB infection (LTBI) and targeted interventions for high-risk populations. While the BCG vaccine provides some protection against severe forms of TB in children, its efficacy against pulmonary TB, the most common form of the disease, is limited. Therefore, ongoing research into new TB

vaccines with improved efficacy is essential for achieving TB elimination goals.

Infection control measures, including early identification and isolation of infectious individuals, adequate ventilation in healthcare settings, and appropriate use of personal protective equipment, are crucial for preventing TB transmission in high-risk environments. However, resource constraints and competing priorities in low- and middle-income countries often limit the implementation of comprehensive infection control measures, highlighting the need for continued advocacy and investment in TB control efforts.

Screening and treatment of LTBI play a crucial role in TB prevention by reducing the risk of progression to active TB disease. Targeted testing of high-risk populations, such as close contacts of TB cases and healthcare workers, followed by provision of preventive treatment with isoniazid (INH) or rifampicin (RIF), can significantly impact TB incidence. However, challenges related to adherence to treatment and access to healthcare services remain barriers to the effective implementation of LTBI screening and treatment programs.

Treatment of active TB disease involves multidrug regimens administered over several months, with adherence being a cornerstone of successful treatment outcomes. While standard TB treatment regimens have been effective in treating drug-sensitive TB, the emergence of drug-resistant TB, including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), poses significant challenges. Individualized treatment regimens based on drug susceptibility testing (DST) results, along with close monitoring for adverse effects, are essential for managing drug-resistant TB.

Future perspectives in TB research hold promise for improving prevention, diagnosis, and treatment of the disease. Ongoing efforts to develop new TB vaccines, optimize treatment regimens, and improve diagnostics are critical for accelerating progress towards TB elimination.

Additionally, addressing social determinants of health, such as poverty, malnutrition, and inadequate housing, is essential for reducing TB incidence and achieving health equity.

In conclusion, TB remains a complex and challenging global health issue, but progress has been made in various aspects of TB prevention, treatment, and research. Continued investment in TB control efforts, along with a multisectoral approach that addresses both biomedical and social determinants of health, is essential for reducing the global burden of this infectious disease and achieving the goal of TB elimination.

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