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An overview on present scenario and future direction of tuberculosis

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Abstract

Mycobacterium tuberculosis is the bacteria that cause tuberculosis. Although the lungs are the main organ affected by this bacterium, it can also damage the kidneys, spine, and brain. When an infected individual coughs, sneezes, speaks, or sings, the infection spreads through the air and becomes highly contagious. The disease is becoming more common in many parts of the world, and the prevalence of drug-resistant T.B. also is increasing worldwide. It covers the symptoms, types, diagnosis, treatment, prevention and immunization of tuberculosis along with epidemiology. The review also examines new drug protocols, statics and public health efforts all over globe. Also the covers future efforts for control and eradication of various type of tuberculosis with new drug regimen. Challenge to T.B. control includes stigma healthcare access barrier, and the rise of drug resistant T.B. strains. Collaboration and advocacy efforts are essential for addressing T.B. in strait of population which is affected by T.B., high risk setting and co-infection scenario. One health approach harnessing technology and addressing climate change impacts is critical for advancing T.B. control efforts and achieving. So well targeted public healthcare efforts along with increasing awareness about the disease and its pathologenisis and newly added medications. Persistent political commitment, resource mobilization, and international solidarity are necessary in the fight against tuberculosis. Together, we can overcome the obstacles presented by tuberculosis (TB) and get closer to a world free of this age-old illness by emphasizing evidence-based interventions.

Keyword: Tuberculosis; Public Healthcare; Drug Resistant. Epidemiology; Contagious

1. Introduction

One major worldwide health concern that still exists is tuberculosis (TB), especially in low- and middle-income nations. Globally, tuberculosis (TB) continues to be the primary cause of morbidity and mortality, although progress in detection and treatment. Control attempts are complicated by the causal pathogen, Mycobacterium TB, continuing to elude immune responses. The problem is made worse by the rise of drug-resistant pathogens and socioeconomic in equality. Notable successes have resulted from efforts to stop the TB epidemic, such as enhanced diagnosis, treatment plans, and preventive measures. Nonetheless, obstacles continue to exist, impeding the advancement of the World Health Organization's End TB Strategy objectives. This study examines the state of the art and potential directions for tuberculosis control; with a focus on scientific advancements, diagnosis, treatment, prevention, and epidemiology. It attempts to educate stakeholder's engaged in TB control efforts and provide pathways for future action to successfully combat TB by analyzing current literature and new findings.

1.1. Symptoms

The symptoms and signs of tuberculosis may be changes if infection is latent or active. When a person has a latent tuberculoses infection, the bacteria are still there but are not generating symptoms, and they are not communicable. On the other hand, signs of active TB disease could be:

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- Persistent cough that doesn't go away after three weeks
- Spitting up sputum or blood
- Chest ache
- Weakness and exhaustion
- Sweating at night and fever
- Appetite decline
- Other body parts may also be affected by TB, resulting in symptoms unique to those regions

1.2. Diagnosis

A physical examination, a medical history, and laboratory tests are usually used to diagnose tuberculosis. Typical diagnostic examinations consist of:

- A tiny amount of TB antigen is injected under the skin during a tuberculin skin test (TST), and the results are usually seen within 48 to 72 hours.
- Interferon-gamma release assays (IGRAs): By assessing the immune system's reaction to antigens unique to tuberculosis, these blood tests identify the existence of tuberculosis infection.
- Chest X-ray: Imaging tests may identify lung abnormalities that point to a tuberculosis infection. Sputum culture: To determine whether TB bacteria are present, a sample of sputum must be obtained and cultured.
- The tuberculin skin test (TST): TB protein (antigen) into the skin, usually on the forearm. An in duration is a raised, red lump that is found at the injection site that is examined by a healthcare provider 48 to 72 hours later.

A positive reaction is indicated by the size of the in duration, which is assessed. If the in duration exceeds a threshold, it suggests that the TB bacterium was exposed. It's crucial to remember that a positive TST does not always signify an active illness; rather, it just suggests TB infection.

Interferon-Gamma Release Assays (IGRAs): Blood tests known as interferon-gamma release assays, or IGRAs, are used to measure how the immune system reacts to particular TB antigens. The absence of these antigens in the Bacillus Calmett-Guerin (BCG) vaccine and the majority of non tuberculous mycobacterial owers the possibility of false-positive results in those who have received the vaccination or who have been exposed to other mycobacterial diseases.

IGRAs are thought to be more accurate than TST readings, and they are especially helpful for people who have had the BCG vaccination or are not likely to return for a TST reading.

Chest X-ray: A popular imaging test used to identify lung abnormalities that can point to a tuberculosis infection is a chest X-ray. In filtrates, nodules, cavities, or consolidations indicative of active tuberculosis disease are a few examples of these anomalies.

Although a chest X-ray is useful in detecting pulmonary tuberculosis, it cannot provide a conclusive diagnosis of tuberculosis by itself and needs to be evaluated in combination with additional clinical and laboratory results.

Sputum culture: To detect the presence of Mycobacterium tuberculosis, the bacterium that causes tuberculosis, a sample of sputum—mucus coughed up from the lungs—must be collected and cultured in a lab.

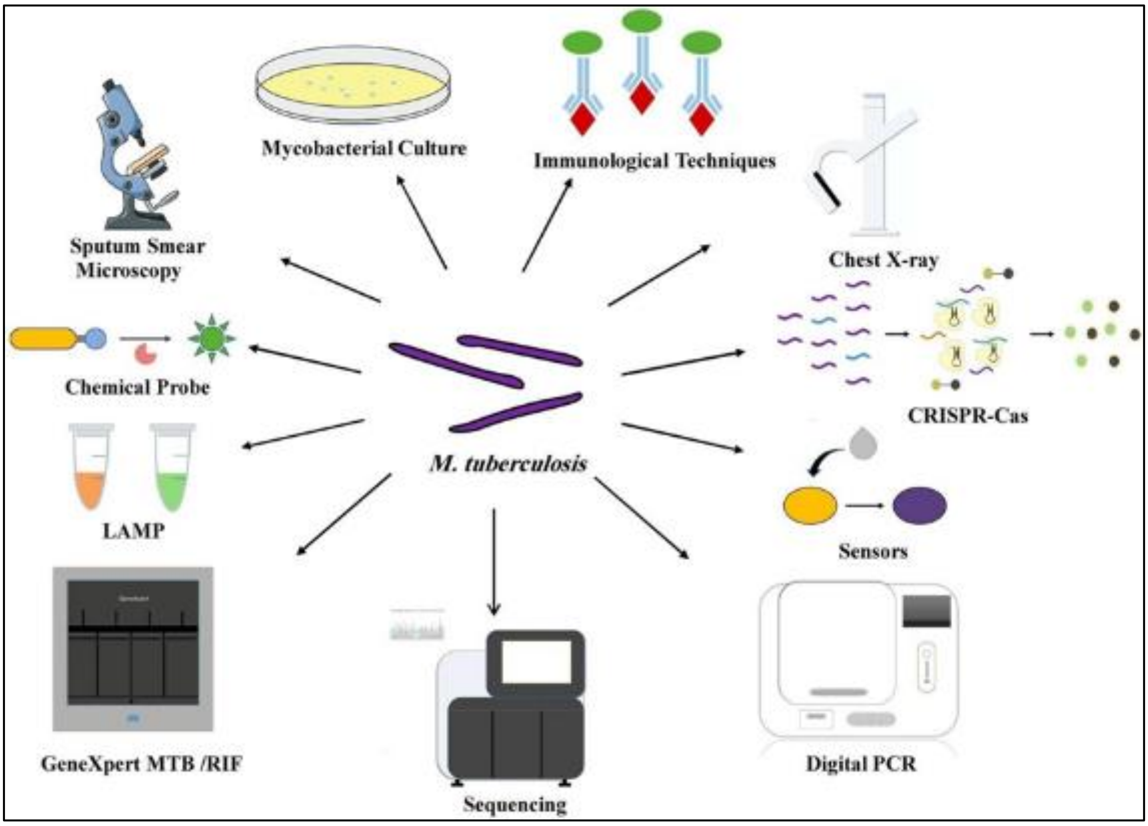

Figure 1 Diagnosis methods for TB

Sputum cultures are regarded as the gold standard for diagnosing tuberculosis (TB) since they offer clear proof of a current TB infection and allow antibiotic susceptibility testing to inform treatment choices.

Sputum culture findings, however, can take several weeks to comeback, which would postpone diagnosis and treatment planning.

To confirm the diagnosis of tuberculosis or evaluate extra pulmonary involvement, further procedures such as bronchoscopy with broncho alveolar lavage (BAL), nucleic acid amplification tests (NAATs), and biopsy of affected tissues may be carried out in certain situations in addition to these diagnostic tests.

A timely and precise diagnosis of tuberculosis is essential for starting treatment and stopping the illness from spreading to other people. For TB cases to be managed effectively, a thorough diagnostic approach that takes into account clinical symptoms, risk factors, imaging findings and laboratory test results is necessary.

Antibiotic Therapy: The main stay of treatment for tuberculosis is a regimen of antibiotics, usually given for a set length of time to guarantee the germs are well eradicated. TB patients most frequently take the following first-line medications:

Isoniazid (INH): Isoniazid is a strong antibiotic that prevents the production of mycolic acids, which are vital elements of the cell wall of mycobacteria. It plays a crucial role in tuberculosis treatment regimens and is very efficient against susceptible strains of Mycobacterium tuberculosis.

Rifampin (RIF): Another crucial first-line antibiotic used in the treatment of tuberculosis is rifampin (RIF).It works by preventing the creation of bacterial RNA, which prevents bacteria from replicating. In addition to being extremely efficient at stopping Mycobacterium tuberculosis from actively replicating, rifampin is also essential in halting the development of drug resistance.

Ethambutol (EMB): Ethambutol is an antibiotic that stops mycobacteria from synthesizing certain parts of their cell walls, especially arabinogalactan. It is frequently used in combination therapy to increase therapeutic efficacy and stop the emergence of medication resistance.

The bactericidal antibiotic pyrazinamide (PZA): It targets Mycobacterium tuberculosis, which is a microorganism that is aggressively proliferating. It works especially well against dormant or intracellular bacilli, upsetting their metabolism. During the first stage of treatment, pyrazinamide is usually administered to quickly lower the bacterial load.

Treatment Regimens : There are a number of elements that influence treatment regimens for tuberculosis, such as the patient's overall health status, drug susceptibility test findings, drug resistance, and the kind of tuberculosis infection (pulmonary or extra pulmonary). Conventional regimens for treating tuberculosis usually involve an intensive period at first, followed by a continuation phase.

The continuation phase seeks to eradicate any leftover germs and stop recurrence, while the intense phase uses a variety of antibiotics to quickly lower the bacterial load .Depending on the individual regimen and the patient's response, the course of treatment may last anywhere from six to nine months or longer.

Prevention: Taking preventive action is essential to halting the spread of tuberculosis. Among the mare: Influenza Vaccination:

1.3. BCG vaccination

The only vaccination approved for the prevention of tuberculosis is the Bacillus Calmette-Guérin (BCG) vaccine. It is mostly given to babies in nations where tuberculosis is highly prevalent in order to shield them against severe cases of the illness, like disseminated TB and TB meningitis. In prevention of pulmonary TB, the BCG vaccine is not much effective in adults which are more common suspects but it is potentially used in children to treat this type of TB. As such, in nations with low rates of tuberculosis incidence, adults are not usually advised to receive the BCG vaccine.

1.4. Controlling Infections

Good respiratory hygiene can help stop the spread of tuberculosis bacteria through respiratory droplets. Example this hygiene includes covering the mouth and nose when coughing or sneezing with a tissue or elbow.

1.5. Ventilation

Having enough ventilation in doors can help lower the danger of tuberculosis spreading through the air. This is especially important in crowded or communal environments like hospitals, prisons, and homeless shelters.

1.6. Separation and Care

In order to stop the disease from spreading further, people with active tuberculosis must be quickly identified, isolated, and treated. Infection control procedures should be put in place at healthcare facilities to reduce the possibility of tuberculosis spreading to patients, staff, and outside guests.

1.7. Testing &Screening

Routine tuberculosis screening: It can help identify cases early and prevent transmission. High-risk populations include those who are close to someone who has active tuberculosis, healthcare workers, and immigrants from countries with high tuberculosis rates, and people living with HIV/AIDS.

1.8. Diagnostic Testing

Early detection and diagnosis of tuberculosis can be facilitated by the use of sensitive and specific diagnostic tests, such as interferon-gamma release assays (IGRAs) and nucleic acid amplification tests (NAATs). This allows for the prompt initiation of treatment and infection control measures.

2. Immunization

2.1. BCG vaccination

The Bacillus Calmette-Guérin (BCG) vaccine is an effective means of preventing tuberculosis, especially in young individuals. The bacteria Mycobacterium tuberculosis, which causes tuberculosis, is a major global health concern, especially in areas where the disease is highly prevalent.Typically, the BCG immunizations given to infants or young children in nations where tuberculosis is common.

For developing immunization against tuberculosis BCG vaccine is administrated. While it might not offer total immunity against all types of tuberculosis, it considerably lowers the chance of severe forms, particularly in youngsters, such as meningitis and disseminated tuberculosis. If exposure occurs, the vaccine can lessen the severity of tuberculosis by boosting the immune system.

2.2. Infection Control Measures

Tuberculosis is highly contagious disease so strictly enforcement require to control from spreading. These precautions are essential, particularly in hospital sand areas where tuberculosis transmission is common. Important tactics consist of:

2.3. Respiratory Hygiene

Promoting proper respiratory hygiene, such as covering one's mouth and nose when coughing or sneezing, can helps top the spread of infectious droplets that carry the tuberculosis bacteria in people who are experiencing symptoms of the disease, such as coughing.

2.4. Sufficient Ventilation

Lowering the concentration of airborne pathogens, such as Mycobacterium tuberculosis, requires adequate in door ventilation. Effective ventilation systems reduce the danger of transmission by removing and diluting infectious particles from enclosed environments.

2.5. Early Detection and Isolation

Two of the most important strategies for stopping the disease's transmission are the timely identification of people who have active tuberculosis and the fast isolation of contagious people. Early detection enables early treatment and isolation measures to be implemented. Diagnostic procedures that support this early detection include sputum smear microscopy, nucleic acid amplification assays, and chest X-rays.

Communities and healthcare facilities can lessen the likelihood of tuberculosis transmission and, as a result, lower the disease's burden by putting certain infection control techniques into effect.

2.6. Latent tuberculosis infection treatment (LTBI)

Although they do not show signs of an active illness, people with latent tuberculosis infection (LTBI) carry the tuberculosis germs in their bodies. They could, however, eventually become ill with active TB, especially if their immune system deteriorates. In order to avoid the spread of LTB It others and stop the disease from becoming active, it is imperative to manage it. Important elements of LTBI care include of:

Preventive Therapy: Antibiotics like isoniazid (INH) or rifampin are commonly used in LTBI treatment plans to kill latent tuberculosis bacteria. These drugs work well to eradicate latent bacteria, lowering the possibility that the illness would reactivate in the future.

Monitoring and Support: Patients receiving treatment for LTBI need to be regularly monitored to evaluate their compliance with the regimen and any possible drug adverse effects. In order to help patients through the course of therapy, healthcare personnel are essential in addressing any worries or difficulties that patients may have.

Public Health Initiatives: Identification and treatment of LTBI patients are given top priority in public health programmes, especially for those who are more likely to develop the illness, such as those who are close to active tuberculosis cases or have immunosuppressive factors. Public health officials seek to break the cycle of tuberculosis transmission and lessen the overall disease burden in communities by focusing treatment efforts on LTBI.

3. Epidemology of tuberoculosis

3.1. Global Burden of Disease

With an expected 10 million new cases and 1.4 million fatalities recorded in 2019 alone, tuberculosis (TB) continues to pose a serious threat to world health. The bulk of TB infections occur in low- and middle-income nations, especially in sub-Saharan Africa, Southeast Asia, and the Western Pacific region. The disease's burden is not fairly spread. The incidence of tuberculosis (TB) can differ significantly throughout nations depending on variables like socioeconomic position, population density, and healthcare accessibility.

3.2. New Drug Protocols: Pretomanid, Delamanid, and Bedaquiline

Drug-resistant tuberculosis (TB) may be treated with novel anti-TB medications including bedaquiline, delamanid, and pretomanid, which present encouraging alternatives. MDR-TB patients are approved to receive bedaquiline, a diarylquinoline drug that inhibits mycobacterial ATP synthase. Nitroimidazole derivative examined targets the formation of mycobacterial cell walls and is recommended for the treatment of multidrug-resistant tuberculosis. When used in conjunction with bed aquiline and linezolid, the nitroimidazole prodrug protomanidh as shown effective in treating drug-resistant tuberculosis (TB), providing a more manageable and shortened treatment plan for patients with limited therapy alternatives.

- Bedaquiline: Bedaquiline is a breakthrough medication for the treatment of multidrug-resistant tuberculosis (MDR-TB).It belongs to a class of drugs called diarylquinolines and works by inhibiting mycobacterial ATP synthase, an enzyme essential for the generation of energy in Mycobacterium tuberculosis, the bacterium that causes tuberculosis.
- Mechanism of Action: By disrupting ATP synthesis, bedaquiline effectively impairs the energy metabolism of tuberculosis bacteria, ultimately leading to their death.
- Clinical Use: Bedaquiline is indicated for use in patients with MDR-TB who have limited treatment options due to resistance to conventional tuberculosis medications. It is typically administered as part of a multi drug regimen under close medical supervision.
- Efficacy: Clinical trials have demonstrated the efficacy of bedaquiline in improving treatment out comes for MDR-TB patients, leading to higher rates of sputum culture conversion and reduced mortality compared to standard treatment regimens.
- Delamanid: Delamanid is another promising medication for the treatment of multidrug-resistant tuberculosis. It belongs to the nitroimidazole class of drugs and exerts its anti mycobacterial effects by targeting the synthesis of mycobacterial cell walls.
- Mechanism of Action: Delamanid inhibits the synthesis of mycolic acids, essential components of the mycobacterial cell wall, leading to cell wall disruption and bacterial death.
- Clinical Use: Delamanid is recommended as part of a comprehensive treatment regimen for MDR-TB patients, particularly those with limited therapeutic options. It is typically administered orally and may be used in combination with other tuberculosis medications.
- Efficacy: Clinical studies have demonstrated the efficacy of delamanid in improving treatment outcomes for MDR-TB patients, including higher rates of sputum culture conversion and reduced risk of treatment failure.
- Pretomanid: Pretomanid is a newer addition to the arsenal of drugs available for treating drug-resistant tuberculosis. It is a nitroimidazole prodrug that has shown promise, particularly when used in combination with bedaquiline and other medications.
- Mechanism of Action: Pretomanid is activated within tuberculosis bacteria, where it exerts its antimicrobial effects by disrupting bacterial DNA synthesis and other vital cellular processes.
- Clinical Use: Pretomanid is used in combination with bedaquiline and linezolid as part of a regimen known as the BPaL regimen. This combination therapy has demonstrated efficacy in treating highly drug-resistant forms of tuberculosis, including extensively drug-resistant tuberculosis (XDR-TB).
- Efficacy: Clinical trials have shown that the BPaL regimen, incorporating pretomanid, bedaquiline ,and linezolid is highly effective in achieving rapid sputum culture conversion and improving treatment outcomes in patients with difficult-to-treat forms of drug-resistant tuberculosis.

These new drug protocols represent significant advancements in tuberculosis treatment, offering hope for patients with drug-resistant forms of the disease who previously had limited therapeutic options.

By targeting different aspects of tuberculosis bacteria's biology and metabolism, these medications provide more effective and manageable treatment regimens, ultimately improving outcomes for patients and contributing to global efforts to combat tuberculosis.

3.3. New Prospects for Vaccines:

- M72/AS01E: This vaccine is effective against TB disease in adults because it specificallytargets M. tuberculosis antigens. Phase II b trials have yielded encouraging results.
- VPM1002: Developed to enhance vaccination safety and effectiveness, VPM1002 is an attenuated strain of M. tuberculosis. Its potential as a TB vaccine candidate is being assessed in ongoing trials.
- MTBVAC: A live attenuated vaccine made from Mycobacterium tuberculosis. Based on preclinical research, it is being developed as a better BCG substitute, providing more protection against tuberculosis.

These innovative vaccine options are promising developments in the fight against tuberculosis and may provide better protection against the illness, particularly in populations for which the BCG vaccination may not be adequate on its own. To further assess the safety and effectiveness of these vaccinations and get them closer to wider use, more study and clinical trials are necessary.

4. Future directions in tb research

Biomarkers for Treatment Monitoring and TB Diagnosis:

4.1. Research on tuberculosis

It is centered on finding biomarkers, or signs within the body, that can be used to quickly and precisely diagnose tuberculosis and track its progression throughout therapy. These biomarkers may consist of genetic material from tuberculosis bacteria or indicators of the immune system.

4.2. Technologies Omics

Cutting-edge technologies such as transcriptomics, proteomics, metabolomics, and genomes provide novel approaches to identify and validate these biomarkers, yielding important information for tuberculosis research.

4.3. Point-of-Care Testing

Developing rapid, point-of-care tests based on biomarkers can revolutionize TB diagnosis, especially in resource-limited settings where access to sophisticated laboratory facilities is limited.

5. Interventions Guided by the Host (HDTs)

5.1. Boosting TB Treatment

HDTs work to improve TB treatment by altering the immune system's reactions. They specifically target immunological modulation and inflammation, two mechanisms associated with the development of tuberculosis.

5.2. HDT types

Immunomodulatory medications such as cytokine blockers and host-directed antibiotics such as nitric oxide donors are examples of these treatments. To evaluate its usefulness and safety in TB patients, clinical trials are being conducted.

5.3. Creation of Vaccines:

5.3.1. Targeting Latent TB and HIV/TB Co infection

Vaccines against latent TB infection (LTBI) are designed to lower the risk of both active TB and its transmission by preventing TB from reactivating in individuals with latent infections. In order to better control TB, vaccines for TB-HIV co infection aim to strengthen immune responses in HIV-positive people.

5.3.2. Novel Vaccination Options

To meet the needs of these vulnerable populations, research is looking into novel vaccine types, such as those based on protein subunits or viral vectors.

6. Conclusion

In conclusion, efforts must be made in concert to effectively control and eventually eradicate tuberculosis (TB), as it continues to pose a serious threat to world health. TB continues to be a major global source of illness and mortality despite advances in diagnosis, treatment, and prevention techniques. Vulnerable populations are disproportionately affected by tuberculosis (TB), especially those living in low-and middle-income nations where access to healthcare facilities may be limited and socioeconomic factors may accelerate the spread of the disease.

The thorough analysis provided here emphasizes how critical it is to keep funding and fostering innovation in TB research and control initiatives. There are encouraging options for lowering the prevalence of TB and fulfilling the WHO's challenging target of putting an end to the TB epidemic by 2030, from creating innovative treatment regimens and vaccinations to enhancing diagnostics.

Furthermore, addressing the social determinants of tuberculosis (TB), such as poverty, overcrowding, and insufficient access to healthcare, is crucial to addressing the disease's underlying causes and guaranteeing that all people have equitable access to services for diagnosis, treatment, and prevention. To advance TB control and make a significant worldwide impact, multisectoral, collaborative initiatives including governments, healthcare providers, civil society, and impacted communities are essential.

In conclusion, persistent political commitment, resource mobilization, and international solidarity are necessary in the fight against tuberculosis. Together, we can overcome the obstacles presented by tuberculosis (TB) and get closer to a world free of this age-old illness by emphasizing evidence-based interventions. Let's take this chance to quicken our efforts to put an end to the TB pandemic and guarantee everyone's health and well-being.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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