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Mini Review

Tuberculosis: a short glimpse

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Abstract

Mycobacterium tuberculosis is an acid-fast bacterium, that cause the disease of significant burden worldwide i.e. tuberculosis (TB). Because of its airborne transmission, it remains a milestone and a very strong hurdle to limit its spread. More significantly, its targeting area mostly is alveolar macrophages present in the lungs, in which it can reside as a silent killer. This mini review aims to highlight the fundamentals of *Mycobacterium tuberculosis*, its disease-causing pattern, and treatment options that have been developed to tackle the disease. TB has been categorized into re-emerging disease in many parts of the world, so there is a need to look on it. Further prevention and controlling strategies also discussed in last to highlight the importance in which sense the TB prevalence could potentially be reduced.

Keywords: disease, macrophages, *Mycobacterium tuberculosis*

Introduction

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, a serious human pathogen that infects about one-third of the human's population globally [1]. It has emerged as a major health issue worldwide and considered the second most fatal contagious disease [2]. TB is an airborne infectious disease in which lungs are affected, leading to cough, fever, and chest pain [3]. According to estimation by the World Health Organization (WHO), about 650,000 prevalent cases of multidrug-resistant tuberculosis found worldwide in 2010. However, the rate of TB is high in Asia and Africa [2].

The infection of TB can be latent or asymptomatic. The activation of latent infection into disease can be prevented through a cell-mediated immune response. However, uncontrolled infection results in clinical signs and symptoms of TB infection [4]. The mechanism of TB infection follows as the mononuclear cells are phagocytosed by *Mycobacterium tuberculosis* [1].

Commonly young adults, health care workers, immunocompromised patients, or smokers have high susceptibility for this infection of tuberculosis [3]. For the diagnosis of TB, different conventional methods like drug sensitivity can be used. However modern detection methods include polymerase chain reaction, restriction fragment length polymorphism (RFLP), and chemotherapy of drug resistance or even surgery in severe cases [2].

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Epidemiology and Etiology of Tuberculosis

In 1882, Robert Koch was identified that the *Mycobacterium tuberculosis* is a causative agent of TB. It is an infectious disease that can target any body parts and commonly cause the pleural, central nervous system (CNS), lymph nodes, bones and joints, and military tuberculosis [5]. An infection of TB is more prone in those individuals who have a weak immune system, in young adults mostly in males, and health care worker who are more exposed to the disease environment [3].

According to the WHO report, one out of three people of the world's population is affected by bacilli infection. During the period of life, 2-23% of the disease developments occur. In the year 2017, the worldwide distribution of TB cases was very high, it is one of the leading causes of death with co-infections of HIV/AIDS [5,6].

The chances of TB transmission are also interlinked with the intensity of exposure, time duration, pathogenic factors of the disease, living in unhygienic conditions, and some other related factors like sputum smear positivity. It is revealed that TB patients have the potential to produce as many as 10⁵-10⁷ bacterial load per milliliter of sputum with positive and infectious smear. It is a very complex disease that is associated with different factors; includes pathogen factors, host factors, and environmental factors [5].

Pathogen factors include all the bacterial virulence factors such as toxin production, cord factors, and some enzymes like protein kinase G. Host factors are associated with behavioral and social events such as genetic polymorphisms with the involvement of HLA and TLR genes, physiological factors like age and sex along with nutritional factors. Behavioral factors include alcohol abusing and smoking habits. Socioeconomic status and living conditions are under the environmental factors which are more contribute to tuberculosis disease prevalence. Now, it is considered as the major issue for the poor community [5].

It was globally estimated that 10.0 million people developed TB disease in 2017 in which 5.8 million men, 3.2 million women, and 1.0 million children were present. This was a condition in all countries and in all age groups, but most adults are suffered from TB (90%) who have an age of ≥15 years and 9% were HIV patients.

Pathogenesis of Tuberculosis

About 5% to 10% of infected people develop clinical disease and 90% infection is asymptomatic. The untreated disease progresses slowly, the majority of TB cases contain latent TB infections in lungs with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculosis disease. In those with HIV, the risk of developing active tuberculosis is high. If effective treatment is not given, the death rate for active TB cases is up to 66%.

Tuberculosis can be divided into three categories:

1. Primary tuberculosis
2. Secondary tuberculosis
3. Extra-pulmonary tuberculosis

Primary tuberculosis: Infectious dose is 10 cells. *Mycobacterium tuberculosis* is phagocytosed by alveolar macrophages and multiplies intracellularly. After 3-4 weeks' immune system attacks, forming tubercles and granulomas consisting of a central core containing bacilli surrounded by white blood cells (WBCs - tubercle). If the center of tubercle breaks down into necrotic caseous lesions, they gradually heal by calcification.

Secondary tuberculosis: If the patient does not recover from primary tuberculosis, reactivation of bacilli can occur. Tubercles expand and drain into the bronchial tubes and upper respiratory tract. Gradually the patients experience more severe symptoms. Violent coughing, greenish or bloody sputum, fever, anorexia, weight loss, fatigue. Untreated patients will have a 60% mortality rate.

Extra-pulmonary tuberculosis: During secondary TB, bacilli disseminate to regional lymph nodes, kidneys, long bones, genital tract, brain, and meninges. These complications involved many organs damage.

Treatment

Main objectives of treatment for TB disease are:

- Cure the individual patient
- Reduce the risk of death and disability
- Reduce the transmission of bacteria

TB disease must be treated for at least six months and in some cases even longer. Four-drug therapy is a standard treatment for initiating the treatment of TB disease. A single drug treatment leads to bacterial population resistance.

Anti-TB drug classes

First-line drugs

The core of initial treatment regimen formed by isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), ethambutol (EMB). Rifabutin* (RBT) can be used as a substitute for RIF in the treatment of all types of TB caused by organisms that are known to be susceptible to this agent. During the continuation phase of treatment, rifapentine (RPT) may be used once weekly with INH. Those patients are HIV-negative with noncavitary, drug-susceptible pulmonary TB, and who have negative sputum smears at the completion of the initial phase of treatment.

Second-line drugs

Streptomycin (SM) considered to be the first-line drug and in some instances, is still used in the initial treatment. Cycloserine, capreomycin, p-aminosalicylic acid, levofloxacin*, moxifloxacin*, gatifloxacin*, amikacin/kanamycin*, and ethionamide. These drugs are reserved for special situations such as drug intolerance or resistance.

In new treatment models, novel medication is used. It replaces the drug resistance illness. The regular six-month regimen is replaced with two months' rigorous stage employing ethambutol instead of gatifloxacin followed by a two-month stage of maintaining gatifloxacin, rifampicin, and isoniazid.

Linezolid is a drug of choice for TB, caused by multi-drug resistant (MDR) and extensively drug resistant strains. All the treatment regimens for drug-susceptible TB disease can be given in specific durations if they are directly observed.

Table 1. Outcomes of treatment [7]

Outcomes measures	Results
Cure	A patient with negative sputum smear and culture in the last month of treatment
Treatment completed	Completed the treatment with no evidence of failure but tests were not done
Treatment failure	Patient who remains sputum smear and culture positive in 5 months or later treatment duration
Died	Patient dies during treatment
Treatment success	Who has both completed treatment and is cured

*Not approved by the U.S. Food and Drug Administration.

Prevention and Control

Close contacts, infection control, and vaccines are the preliminary approaches to reduce the morbidity and mortality rate, also early diagnosis of TB is the best way to control it [8]. The testing of immunocompromised patients and new cases by seeking health care services, including directly observed therapy (DOT) is needed [9]. Moreover, when the infection is at the initial stage, a heavy dose of antibiotics can eliminate the cells that are persistently affected by *Mycobacterium tuberculosis* and hence the rest of them will be eliminated by the immune system of the host that has been experimentally observed in mice [10].

The individuals who have been previously treated for tuberculosis has a much more frequency rate to spread the disease in comparison with the native cases of patients, so targeted interventions can help in controlling and avoiding recurrence of the disease in new patients [11].

Conclusion

TB is a disease with mild to severe kind of complications, involving different kinds of organs like skin, lungs, etc. The immunocompromised patients are more prone to it such as HIV patients and patients having organ transplanted. So, it is important to know about its transmission, illness, and symptoms. Moreover, significant attention should be drawn towards prevention and controlling strategies. Otherwise, the swords of outbreaks are always hanging in different parts of the world, especially the countries of tropical origin.

Conflict of interest

All authors declare that they have no conflict of interest.

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