



Overview of the Complexities in Diagnosing Treating and Preventing Tuberculosis along with the Most Effective Dosage Plans

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Abstract

Mycobacterium tuberculosis is the name of the bacterium that causes tuberculosis (TB), which typically affects the lungs. Lifetime exposure to TB bacteria increases the risk of developing TB by 5–10%. A person's likelihood of getting sick rises if they lead an unhealthy lifestyle or have a compromised immune system. A person may take several months before showing symptoms of active TB disease. As a result, getting medical help may take longer, and the virus may spread to more people. Rifampicin, isoniazid, pyrazinamide, and ethambutol are given as part of the traditional treatment for pulmonary TB during the first two months, and then rifampicin and isoniazid are given for the following four months. For the treatment of multidrug-resistant TB, levofloxacin, moxifloxacin, and bedaquiline are suggested.

Keywords: *Tuberculosis*; Dosage Plans; Bacteria

Abbreviations: TB: Tuberculosis; TST: Tuberculin Skin Test; BCG: Bacille Calmette Guérin; MDR-TB: Multidrug-Resistant Tuberculosis.

Introduction

One of the oldest diseases known to man, tuberculosis (TB) co-evolved with humans for at least several million years before. The oldest known DNA evidence of tuberculosis was found in a 9000-year-old human bone [1]. The pulmonary form of TB was linked to "tubercles" by Dr. Richard Morton as early as 1689 and it was given the name "tuberculosis" by Martini, et al. [2]. A group of bacterial species that cause tuberculosis is known as the *Mycobacterium tuberculosis* complex. Currently, *Mycobacterium tuberculosis* is the principal culprit behind TB in humans. While *M. bovis* is

the primary agent of TB in other animal species and has a greater host range. Meat from infected animals, milk, and milk derivatives can all spread *M. bovis* to humans [3].

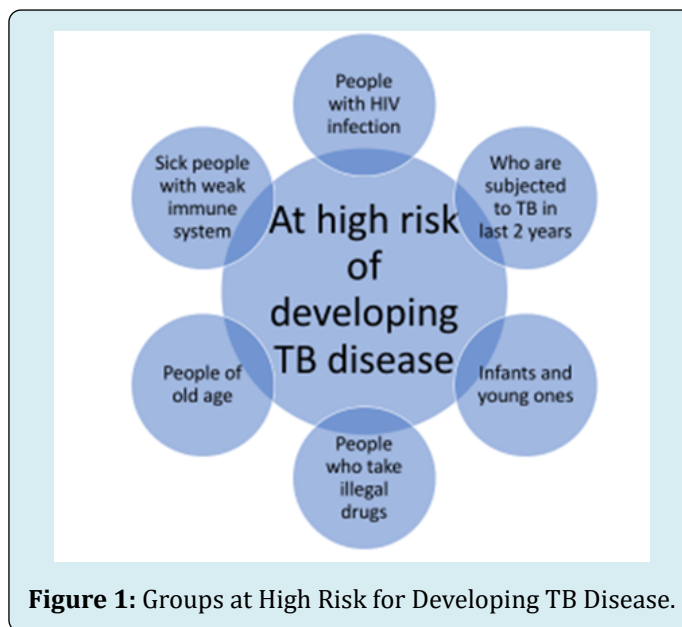
Since the TB bacteria typically affect the lungs, airborne transmission of TB between individuals is widespread. When TB patients cough, sneeze, or spit, the TB germs are released into the air, and only a few number of these microorganisms need to enter a person's lungs for them to become unwell. A quarter of the world's population has TB infection, meaning they have the germs in their bodies but are not ill and are unable to spread the disease. A lifetime exposure to the TB bacteria increases the risk of developing TB by 5–10%. A person may take several months before showing symptoms of active TB disease. As a result, getting medical help may take longer, and the virus may spread to more people. Through

intimate contact, people with active TB can infect 5–15 more people over the course of a year [4].

Risk Factors for TB

The majority of TB patients are in the prime of their careers. But there is risk for people of all ages. More than 80% of illnesses and fatalities occur in low and middle-income

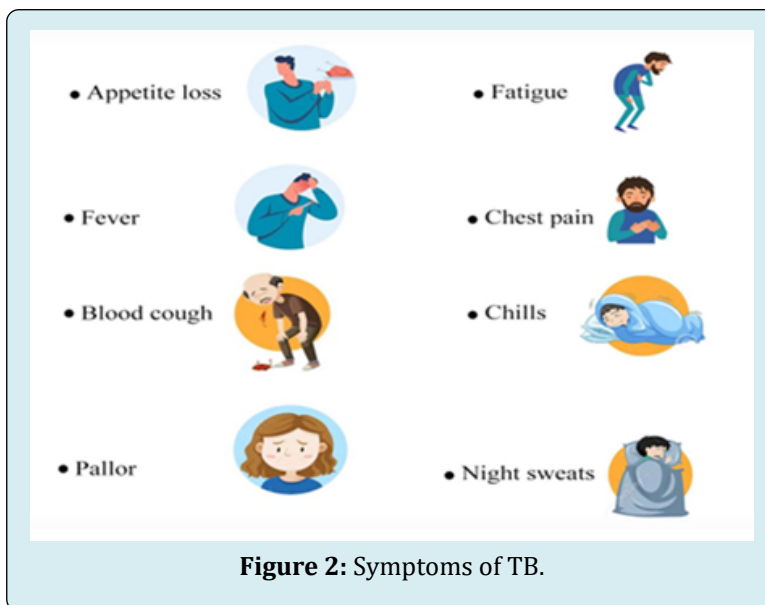
countries. HIV-positive individuals have an 18 times higher risk of developing active TB. In addition, those who suffer from other immune-system-damaging conditions are more likely to have active TB. People who are undernourished are three times more vulnerable [5]. Smoking, excessive alcohol consumption and malnutrition all increase the risk of TB [6] (Figure 1).



Signs and Symptoms of TB

Chest pains, fatigue, weight loss, fever, night sweats, and

coughs that occasionally produce sputum and blood are all common symptoms of active lung TB [7] (Figure 2).



Diagnosis

In order to detect the TB bacteria in the body, two types of tests are used.

TB Skin Test

The Mantoux tuberculin skin test (TST), sometimes referred to as the TB skin test, is performed by injecting a tiny amount of tuberculin fluid into the patient's skin. Based on the hard or swollen part of the arm, the outcome will be determined. If the skin test is successful, it indicates that the individual has TB germs in their body. For children under the age of five, TB skin tests are preferred [8].

TB Blood Test

In blood tests for TB, also called interferon-gamma release assays or IGRAs, patient's blood is taken and sent to the laboratory for inspection. A positive result means the person has been diagnosed with TB bacteria. Individuals who have already been injected with the TB vaccine Bacille Calmette-Guérin (BCG) are preferred to get blood tests [9]. Diagnosis of active TB is done with the help of the patient's medical history, physical examination, chest x-ray, and other tests.

Treatment of TB

Vaccination

BCG vaccine has 50% efficiency against TB [10]. One dose is recommended in healthy babies after birth. Dose

includes infants less than one year of 0.05ml intradermal and children over one year with 0.1ml intradermal.

Latent Tuberculosis Treatment

In this type, a person is infected with TB but does not have any symptoms yet. Its treatment includes the course of ATT, Rifampicin, and isoniazid (3 months course) OR Rifinah (Rifampicin and isoniazid together in tablet) or Isoniazid only (6 months course) [11]. Latent TB should be cured properly because one in ten people with latent TB develops active TB later on, removing the bacteria from your body is the only treatment.

Active Tuberculosis Treatment

In this type, the bacterium is in the body and multiplies. It is of two types i) Pulmonary TB (damaging lungs) ii) Extra Pulmonary TB (affects organs or bones outside lungs). Treatment for pulmonary TB involves a 6-month course of rifinah and an initial 2-month treatment of ATTs (ethambutol and pyrazinamide). The same ATT combination that is used to treat pulmonary TB can also be utilised to treat extra pulmonary TB [12]. For a few weeks, corticosteroids may be recommended together with your ATTs if you have TB in the surrounding sacs of your heart or brain. Multidrug-Resistant Tuberculosis (MDR-TB) Treatment. The TB germs in MDR-TB are resistant to the drugs isoniazid and rifampin (the drug most potent for TB). Levofloxacin and moxifloxacin have been approved by the WHO for the treatment of MDR-TB. Bedaquiline was given FDA approval as a medication to treat MDR-TB [13] (Table 1).

ATTs	Dose	Preparation
1. Isoniazid	Children:	<ul style="list-style-type: none"> Tablets (50mg, 100mg, 300mg) Syrup (50mg/5ml) Aqueous solution (100mg/ml) for IM or IV injections
	<ul style="list-style-type: none"> 10-15 mg/kg (300mg) daily 20-30mg/kg (900mg) twice weekly 	
	Adult:	
	<ul style="list-style-type: none"> 5mg/kg (300mg) daily 15mg/kg (900mg) once, twice, or thrice a week 	
2. Rifampicin	Children:	<ul style="list-style-type: none"> Capsules (150mg,300mg)
	<ul style="list-style-type: none"> 10-20mg/kg (600mg) once daily or twice weekly 	
	Adult:	
	<ul style="list-style-type: none"> 10mg/kg (600mg) once daily twice weekly or three times weekly 	

3. Rifabutin	Children:	• Capsule (150 mg)
	• Unknown appropriate dosing	
	Adult:	
	• 5mg/kg (300mg) daily twice or thrice time weekly (if used with efavirenz dose of rifabutin increased to 450-600mg)	
4. Rifapentine	Children:	• Tablet (150mg, film-coated)
	• Not approved for children's use	
	Adult:	
• 10mg/kg(600mg) once weekly		
5. Pyrazinamide	Children:	• Tablet (500mg)
	• 15-30mg/kg(2.0g) daily	
	• 50mg/kg (2.0g) twice weekly	
	Adult:	
• 20-25mg/kg per day		
6. Ethambutol	Children:	• Tablets (100mg,400mg)
	• 15-20mg/kg (2.5g) per day	
	• 50mg/kg (2.5g) twice weekly	
	Adult:	
• 15-20mg/kg per day		

Table 1: First-Line Treatment for TB [14].

To prevent neuropathies Vitamin B6 is given with Isoniazid (Table 2).

Second-line ATTs:	I. Injectable aminoglycosides:
	• Amikacin
	• Kanamycin
	• Streptomycin
	II. Injectable Fluoroquinolones:
	• Levofloxacin
	• Moxifloxacin
	• Ofloxacin
	• Gatifloxacin
	III. Injectable polypeptides:
	• Capreomycin
	• Viomycin
	<i>Pretomanid is a new 2nd line drug.</i>

Table 2: Second-Line Treatment for TB [15].

They do not have any proven efficiency right now, used as a last resort for TB drugs (Table 3).

Antibiotic	Dose	Preparation
1. Clarithromycin	500mg orally every 12 hours	· 500 mg tablets · 125mg/5ml suspension
2. Linezolid	Adult: · 600mg daily or twice a day	· Tablets 600mg · Syrup 100mg/5mL
	Children: · 15mg/kg once daily	
3. Clofazimine	Adults: · 100 mg to 200mg once daily	· 100 mg capsules (unlicensed medicine)
	Children: · 2-5mg/kg once daily	
4. Amoxicilli/clavulanate	500mg/125mg three times daily	
5. Imipenem/ cilastatin	Adult >50kg: · 1g twice a day (intravenous)	· 500/500mg 250mg powder for solution for infusion
	Adult <50kg: · 15mg twice a day (intravenous)	
	Children: · Not used in patients less than 15 years	

Table 3: Third-Line Treatment for TB [16].

Adverse Effects of TB Medicines

Rifinah may disturb the menstrual cycle, sickness, flu-type symptoms, hormonal changes, redness, itching, rashes, hypersensitivity, and red-orange urine color. The use of isoniazid could cause sickness, diarrhea, numbness, and rashes, while retrobulbar neuritis could be triggered by ethambutol. Pyrazinamide usage may result in acute gouty arthritis, rash, nausea, and hepatotoxicity. Optic neuropathy, lactic acidosis, nausea, and diarrhea may be brought on by taking Linezolid.

Preventions of TB

M. Tuberculosis is present in airborne particles called the droplet nuclei and spreads when patients with TB cough, speak and sneeze. They are very small, and they remain suspended in the air. In order to prevent the formation of droplet nuclei and reduce the likelihood of bacterium transfer, patients with active TB should receive the appropriate care and testing at healthcare facilities. Additionally, local exhaust ventilation should be offered because the bacterium persists in the air without ventilation for a long period of time. The patients must be kept in healthcare facilities with enough sunshine to kill the microorganisms that are killed by germicidal UV lights. Needles, catheters, and surgical tools used in patient care that come into touch with blood directly

must be cleansed and sterilized [17]. Give respiratory programme training in educational institutions so that students learn how to protect themselves from the sickness (Figure 3).

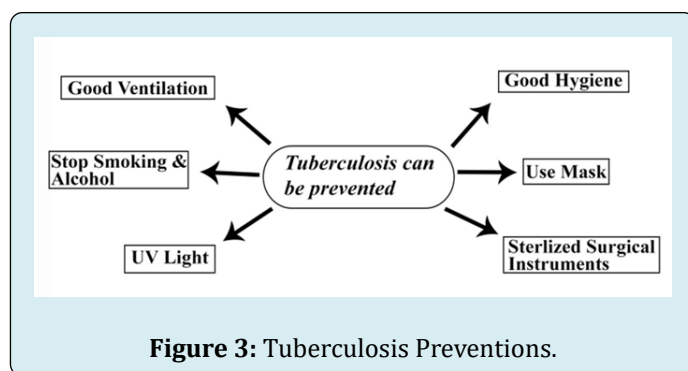


Figure 3: Tuberculosis Preventions.

Future Strategies and Recommendations

Considering the size of Pakistan, we need proper implementation of a TB program. The current National Tuberculosis Program has suffered a lot because of the negligence of the government.

The actions listed below must be followed to lower TB.

- All public or private hospitals should be properly equipped to carry out the tests and proper guidelines should be given to the workers.

- The message regarding the severity of the disease must be passed to the public so that they must protect themselves.
- Proper attention must be given to laboratories and the government should be informed about any of the needed drugs.
- The personnel in charge of tehsils and districts must keep a record of the total number of patients suffering from the disease.

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