Sputum smear examination of adult tuberculosis patients admitted in National Institute of Diseases of the Chest and Hospital (NIDCH)

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This research paper is dedicated to my beloved parents

Certificate

Declaration by the Research Instructor and Department Chairperson

10 July, 2012

It is pleasure to certify that the research paper entitled "Sputum smear examination of adult tuberculosis patients admitted in National Institute of Diseases of the Chest and Hospital (NIDCH)" is prepared by Sanjida Halim Topa, a student of the Department of Pharmacy, East West University, Dhaka. She prepared the paper under my supervision. This is her original work.

Dr. Sufia Islam

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Signature of the candidate

Sanjida Halim Topa

Abstract

Objective:

The objective of this study was to assess the improvement of the adult tuberculosis patients admitted in National Institute of Diseases of the Chest and Hospital (NIDCH) using AFB microscopic examination.

Materials and methods:

The study had been conducted among adult TB patients admitted in NIDCH, Dhaka. There were 21 adult patients in this study. The study had been started with preparing a questionnaire to assemble all the necessary information related to TB disease. All of the patients in this study were suffering from pulmonary TB. The existence of this fatal disease among these patients had been confirmed after performing AFB microscopic test. Before performing the AFB microscopic test, a verbal consent from all of the patients was collected. After confirmation of the pulmonary TB, they had been started to take anti-TB drugs. Among these 21 patients, only 7 patients had been included in the 2nd AFB microscopic examination due to some limitations. The outcomes of these two tests were examined to assess the rate of progression of the patients. The hematological report of all the patients were also assessed during the study period to observe other associated risks as well as their health condition due to the presence of TB disease among the patients.

Results:

In the 2nd AFB microscopic examination of this study, there were only 3 patients among 7 follow up patients showing all negative results. This indicates the success of the treatment among these 3 patients (43%). AFB microscopic results of remaining 4 patients (57%) were still positive showing the presence of *Mycobacterium tuberculosis* in the sputum. AFB microscopic results of rest of the patients were not negative as they were improving in a slow rate. Therefore, they were responsing slowly towards anti-TB drugs. Another important finding of this study was, there were only 7 patients (33%) present in the 2nd AFB microscopic examination, but in TB disease routine checkup is very crucial to observe the improvement rate. This low percentage indicates the carelessness among the patients.

Conclusion:

The result demonstrates that proper management of tuberculosis is indeed to rule out this deadly disease from the country. This study can proceed further to have more comprehensible results.

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AFB	Acid Fast Bacillus
AIDS	Acquired Immunodeficiency Syndrome
CBC	Complete Blood Count
DOTS	Directly Observed Treatment Short Course
E	Ethambutol
ESR	Erythrocyte Sedimentation Rate
FDC	Fixed-Dose Combinations
H	Isoniazid
HIV	Human Immunodeficiency Virus
PTB	Pulmonary Tuberculosis
R	Rifampicin
S	Streptomycin
SS+	Sputum Smear Positive
SS-	Sputum Smear Negative
TB	Tuberculosis
WHO	World Health Organization
Z	Pyrazinamide

Chapter 1

1. Introduction

1.1 Tuberculosis

According to World Health Organization (WHO), “Tuberculosis, or TB, is an infectious bacterial disease caused by *Mycobacterium tuberculosis*, which most commonly affects the lungs. It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease.” Another definition in reference to Medilexicon`s medical dictionary, tuberculosis is “A specific disease caused by infection with *Mycobacterium tuberculosis*, the tubercle bacillus, which can affect almost any tissue or organ of the body, the most common site of the disease being the lungs.” Therefore, TB primarily affects the lungs, but it can also affect other organs, like, central nervous system, lymphatic system and circulatory system among others. The disease was called "consumption" in the past because of the way it would consume from within anyone who became infected (Crosta P, 2009).

Tuberculosis (TB) is one of the most prevalent infections of human beings and contributes considerably to illness and death around the world. It is estimated by the World Health Organization (WHO) that one third of the global population is infected with TB and that seven to eight million new cases of TB occur each year. It is also estimated by WHO that between 2000 and 2020 nearly one billion people will be newly infected, 200 million will get sick, and 35 million will die from TB if global control is not further strengthened (NSW health, 2005).

When a person becomes infected with tuberculosis, the bacteria in the lungs multiply and cause pneumonia along with chest pain, coughing up blood, and a prolonged cough. Additionally, lymph nodes near the heart and lungs become enlarged. As the TB tries to spread to other parts of the body, the body's immune system often interrupts with it. The immune system forms scar tissue around the TB bacteria and this helps to fight the infection and prevents the disease from spreading throughout the body. If the body's immune system is unable to fight TB or if the bacteria break through the scar tissue, the disease returns to an active state with pneumonia and causes damage to kidneys, bones, and the meninges that line the spinal cord and brain. TB is spread through the air from one person to another. When a person with TB disease of the lungs or throat coughs or sneezes, the bacteria are spread into the air. When people nearby breathe in these bacteria, get infected with tuberculosis. People who are infected with TB do not feel sick, do not have any symptoms, and cannot spread TB. But in the future at any time they may develop TB disease. People with TB disease can be treated easily and cured if they seek medical help at right time (Crosta P, 2009).

1.2. Causative agent

Mycobacterium tuberculosis is the etiologic agent of tuberculosis in humans. According to Peclzar, *Mycobacterium tuberculosis* is responsible for over 90% of all cases of tuberculosis (Peclzar. M. J., 2009). This is an acid fast bacterium, which can form acid-stable complexes when certain arylmethane dyes are added. All species of mycobacterium have ropelike structures of peptidoglycan that are arranged in such a way to give them properties of acid fast bacteria. Mycobacteria are abundant in soil and water, but humans are the only reservoir for *Mycobacterium tuberculosis* (Todar K, 2012). Since as many as 32% of the human population is affected by Tuberculosis (TB), an airborne disease caused by infection of *M. tuberculosis* in one way or another, and about 10% of them becomes ill per year, it is not hard to imagine the significance in understanding the genome of this pathogen to develop and improve strategies for treatment by developing specific drugs that target the gene products of *M. tuberculosis* (Harries A.D. and Dye C, 2006).

Figure 1.1: *Mycobacterium tuberculosis*

1.3. Cell structure of *M. tuberculosis*

M. tuberculosis has a tough cell wall that prevents passage of nutrients into and excreted from the cell, therefore giving it the characteristic of slow growth rate. The cell wall of the pathogen looks like a Gram-positive cell wall. The cell envelope contains a polypeptide layer, a peptidoglycan layer, and free lipids. In addition, there is also a complex structure of fatty acids such as mycolic acids that appear glossy (Velayat A. *et al*., 2008). The *M. tuberculosis* cell wall contains three classes of mycolic acids: alpha-, keto- and methoxymycolates. The cell wall also contains lipid complexes including acyl glcolipids and other complex such as free lipids and sulfolipids. There are porins in the membrane to facilitate transport. Beneath

the cell wall, there are layers of arabinogalactan and peptidoglycan that lie just above the plasma membrane (Riley, L.W, 2006).

1.4. Transmission of *Mycobacterium tuberculosis*

Tuberculosis is spread from person to person through the air by droplet nuclei. These are airborne particles of 1 to 5 µm in diameter that contain *M. tuberculosis* complex. When persons with pulmonary or laryngeal tuberculosis cough, sneeze, speak, or sing, droplet nuclei are produced. They also can be produced during medical procedures, such as respiratory therapy, aerosol treatments, sputum induction, aerosolization during bronchoscopy, or processing of tissues or secretions in the hospital or laboratory. Air currents normally present in any indoor space can keep droplet nuclei airborne for long periods of time because droplet nuclei that contain two to three *M. tuberculosis* organisms are so small. Droplet nuclei are small enough to reach the alveoli within the lungs and the organisms start replication. Although patients having tuberculosis generate larger particles containing numerous bacilli, these particles cannot act as effective vehicles in transmitting infection as they do not remain airborne. If these particles are inhaled, they fail to reach alveoli (CDC, 2005). When these organisms are deposited on intact mucosa or skin, they do not invade tissue. Once large particles are inhaled, they impact on the wall of the upper airways. Then they are trapped in the mucous blanket and carried to the orpharynx. Hereafter they are swallowed or expectorated (American Thorasic Society, 2000).

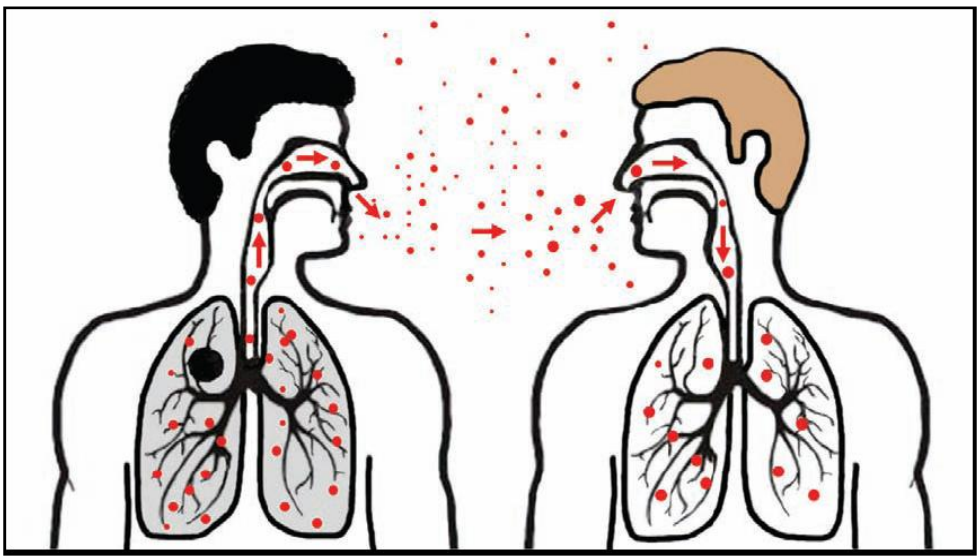


Figure 1.2: Transmission of *Mycobacterium tuberculosis*

There are five closely related mycobacteria present in the *M. tuberculosis* complex. These are:

- *M. tuberculosis*

- *M. bovis*
- *M. africanum*
- *M. microti* and
- *M. canetti.*

Mycobacterium tuberculosis is carried through the airborne route. There are no known animal reservoirs for this organism. Due to ingestion of milk containing large numbers of *Mycobacterium bovis*, it can penetrate the gastrointestinal mucosa or invade the lymphatic tissue of the oropharynx, the incidence of human infection with *M. bovis* has decreased significantly in developed countries due the pasteurization of milk and as well as effective tuberculosis control programs for cattle. *M. bovis* and *M. africanum* can also be transmitted through airborne route. A live-attenuated strain of *M. bovis* is *Mycobacterium bovis* BCG. It is extensively used as a vaccine for tuberculosis (CDC, 2005).

HIV-infected persons and persons with impaired cell mediated immunity are generally considered to be more likely to become infected with *M. tuberculosis* after exposure than persons with normal immunity. HIV-infected persons and others with impaired cell-mediated immunity are much more likely to develop disease in faster way if they are infected (American Thorasic Society, 2000).

Table 1.1: Factors that determine the probability of *M. tuberculosis* transmission (CDC, 2005)

Factors	Description
Susceptibility	Susceptibility (immune status) of the person who is exposed.
Infectiousness	Infectiousness of the person having TB disease is directly related to the number of tubercle bacilli that he or she expels into the air. Persons whom are expelling more tubercle bacilli are more infectious than persons expelling little or no tubercle bacilli.
Environmental	Environmental factors that affects the concentration of *M. tuberculosis* organisms will be discussed in Table 1.2
Exposure	Proximity, frequency and the length of time. Table 1.3

Table 1.2: Environmental factors enhancing the probability of *M. tuberculosis* to be transmitted (CDC, 2005)

Factors	Description
Concentration of infectious droplet nuclei	With the increasing number of droplet nuclei in the air, the probability of *M. tuberculosis* to be transmitted will be increased.
Space	Exposure in small and enclosed spaces will increase the transmission.
Ventilation	Inadequate local or general ventilation which may result in insufficient dilution or removal of infectious droplet nuclei will boost the transmission rate.
Air circulation	Recirculation of air containing infectious droplet nuclei will have positive impact on transmission rate.
Specimen handling	Improper specimen handling procedures can generate infectious droplet nuclei which may consequence in increased transmission rate.
Air Pressure	Positive air pressure in infectious patient's room causes *M. tuberculosis* organisms to flow to other areas, therefore, resulting in increased transmission rate.

Table 1.3: Proximity, frequency and the length of time that enhance the probability that *M. tuberculosis* will be transmitted (CDC, 2005)

Factors	Description
Duration of exposure to a person with infectious TB	The longer the duration of exposure, the higher the risk for transmission.
Frequency of exposure to infectious person	The more frequent the exposure, the higher the risk for transmission.
Physical proximity to infectious person	The closer the proximity, the higher the risk for transmission.

1.5. Pathogenesis of TB

The droplet nucleus is carried down the bronchial tree after inhalation. It implants in a respiratory bronchiole or alveolus. The bacterial virulence and the inherent microbicidal ability of the alveolar macrophage will determine whether or not an inhaled tubercle bacillus

establishes an infection in the lung (CDC, 2005). When tubercle bacilli are ingested by these alveolar macrophages, the majority of these bacilli are destroyed or inhibited. If the bacillus is able to survive these initial defenses, it will able to multiply within the alveolar macrophage. The tubercle bacillus grows slowly. It divides approximately every 25 to 32 hours within the macrophage. The organisms grow for 2 to 12 weeks, until they reach 10^3 to 10^4 in number. If these bacilli alive, they may spread by way of lymphatic channels or through the bloodstream to more distant tissues and organs (American Thorasic Society, 2000). The areas of the body in which TB disease is most likely to develop include, regional lymph nodes, apex of the lung, kidneys, brain, and bone. This process of dissemination will elicit the immune system for a systemic response. Therefore, pathogenesis of latent tuberculosis infection (LTBI) and TB disease can be described in the following steps with the Figure 1.3**:**

Step 01: Droplet nuclei which contain tubercle bacilli are inhaled. After entering the lungs, they will travel to the alveoli.

Step 02: Tubercle bacilli will multiply in the alveoli.

Step 03: A small number of tubercle bacilli will enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body.

Step 04: Macrophages which are special immune cells ingest and surround the tubercle bacilli. The cells will form a barrier shell which is known as granuloma. Granuloma will keep the bacilli under control which is termed as “Latent tuberculosis infection”, in short LTBI.

Step 05: If the immune system fails to keep the tubercle bacilli under control, the bacilli begin to multiply rapidly which will be termed as TB disease (CDC, 2005).

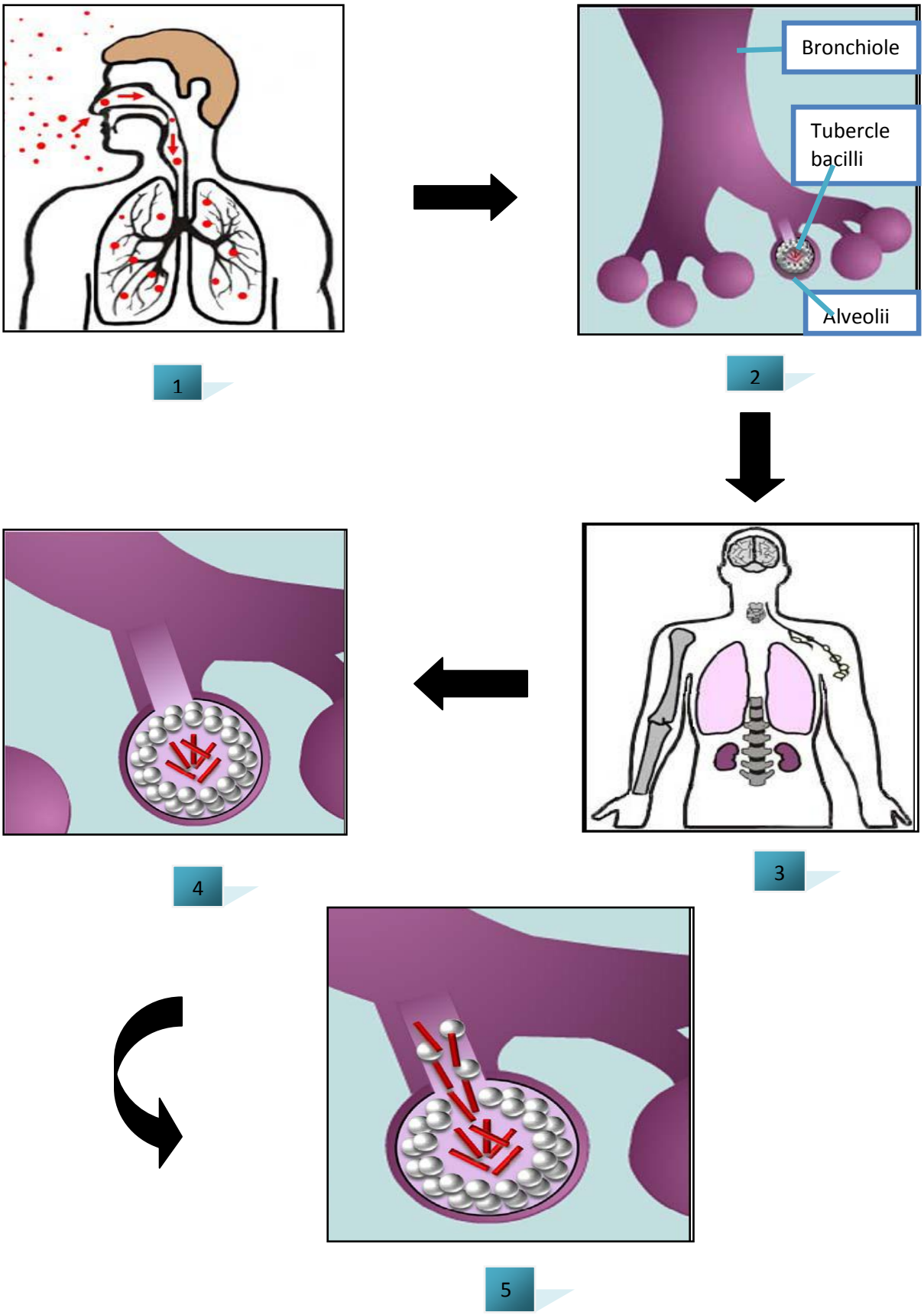


Figure 1.3: Pathogenesis of LTBI and TB disease (CDC, 2005)

1.6. Classification of TB

1.6.1. WHO (World Health Organization) classification of TB

The current clinical classification system for tuberculosis (TB) is based on the pathogenesis of the disease. Classifications of tuberculosis according to exposure history, infection and whether the disease is latent or active are given below:

1.6.1.1. Class 0

Classification 0 is "No TB exposure," with no infection and has a negative tuberculin skin test which is known as Mantoux test. This test concludes whether a person is already been infected with *M. tuberculosis*. This test measures how sensitive a person's immune system is to proteins, called tuberculins, from the tuberculosis mycobacteria cultures (Lingohr-Smith M, 2011).

1.6.1.2. Class 1

Classification 1 means that there has been TB exposure to an infected individual but a negative reaction to a tuberculin skin test indicates no evidence of current infection. In this case, treatment for latent tuberculosis infection must be initiated if the person is immune compromised and especially if the person is HIV positive (Liles V, 2010).

1.6.1.3. Class 2

Classification 2 states that there is a TB infection as there is a positive tuberculin skin test. But there is no current definite active disease state exists. This classification shows a documented positive reaction to a tuberculin skin test but a negative bacteriologic study. There will be no clinical, bacteriologic or radiographic evidence of tuberculosis. Some persons in this class may possibly be treated for latent tuberculosis infection (Lingohr-Smith M, 2011).

1.6.1.4. Class 3

Clinically active TB infection is present in this class. *M. tuberculosis* is apparent and there is significant clinical, bacteriologic or radiographic evidence of a current disease. Patients with active tuberculosis may have some abnormalities in the upper lung lobes which can be distinguished using a chest radiograph. Patients who have a past active tuberculosis may possess nodules and fibrotic scars in the upper lung lobes (Liles V, 2010).

1.6.1.5. Class 4

This class states that patients in this class have active TB in the past, but is no longer clinically active. There may be an abnormal but stable radiographic finding. Unlike the third classification, this classification can result in a positive reaction to the tuberculin skin test, or

a negative bacteriologic study and no existing clinical or radiographic indication of active TB (Lingohr-Smith M, 2011).

1.6.1.6. Class 5

An individual is considered to be in this class having active TB but the diagnosis is pending. The disease should be treated within three months based on clinical, bacteriologic or radiographic evidence. After doing a tuberculin skin test, mycobacterial culture and chest x-ray the person should be classified in one of the other former classes (Liles V, 2010).

1.6.2. Clinical classification of tuberculosis

Tuberculosis is divided into 2 clinically important categories:

1.6.2.1. Inactive tuberculosis or, Latent Tuberculosis Infection (LTBI)

Persons with LTBI have *M. tuberculosis* in their bodies, but do not have TB disease and cannot spread the infection to other people. A person with LTBI is not regarded as having a case of TB. The process of LTBI begins when extracellular bacilli are ingested by macrophages and presented to other white blood cells. This triggers the immune response in which white blood cells kill or encapsulate most of the bacilli, leading to the formation of a granuloma (McHargue R, 2012). At this point, LTBI has been established. LTBI may be detected by using the tuberculin skin test (TST) or an interferon-gamma release assay (IGRA). It can take 2 to 8 weeks after the initial TB infection for the body's immune system to be able to react to tuberculin and for the infection to be detected by the TST or IGRA. Within 6 weeks after infection, the immune system is usually able to halt the multiplication of the tubercle bacilli, preventing further progression (CDC, 2005).

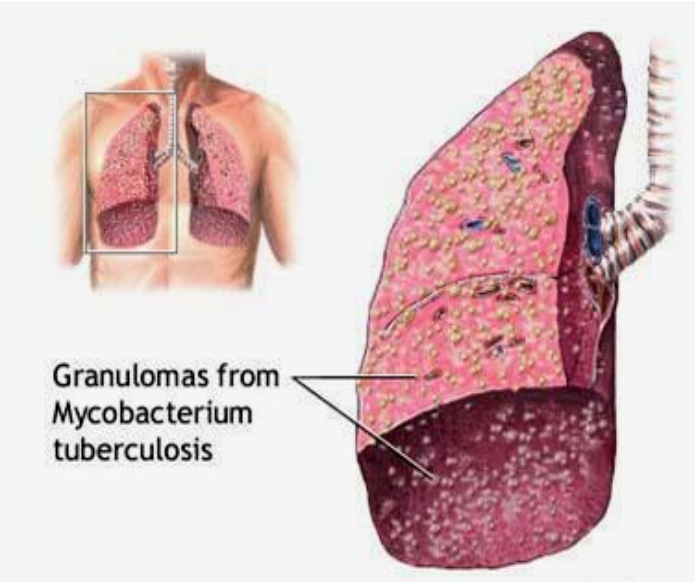


Figure 1.4: Latent Tuberculosis Infection (LTBI)

1.6.2.2. Active tuberculosis

In active tuberculosis the host is infected with the bacterium that causes TB. In people with active TB, the body's immune system is unable in eliminating or corralling the pathogens. In this type of TB, TB bacterium rapidly multiplies and invades different organs of the body. A person with active TB disease may spread TB to others by airborne transmission of infectious particles when they are coughed sneezed or spited into the air (Iseman D. *et al*., 2009).

1.6.3. Classification according to anatomical site of disease

1.6.3.1. Pulmonary tuberculosis (PTB)

PTB refers to a case of TB involving the lung parenchyma. Because the bacterium that causes TB needs oxygen to survive, the oxygen-rich air sacs of the lungs are an ideal breeding ground. Symptoms of an infection in the lungs by TB include a chronic cough, coughing up blood, along with chest pain or pain associated with breathing or coughing. Early in the course of the illness cough may be nonproductive, but subsequently, as inflammation and tissue necrosis ensue, sputum is usually produced and is key to most of our diagnostic methods. Pulmonary TB causes severe pneumonia, and if untreated, can very easily result in death. As an active form of TB, it is highly contagious (Chandler S, 2010).

1.6.3.1.1. Classification of PTB by anatomical site

There are five different types of pulmonary tuberculosis; primary pneumonia, laryngeal, cavitary, miliary and pleurisy.

1.6.3.1.1.1. Primary Tuberculosis Pneumonia

An individual who has never been exposed to the tuberculosis bacteria before can be affected by primary tuberculosis pneumonia. This form of tuberculosis is very uncommon. It occurs most commonly in the very young, the very old or those with immune-compromised systems, such as someone infected with HIV (human immunodeficiency virus) (Franco V, 2010). Individuals having corticosteroid therapy are also at a higher risk of developing such type of illness. Primary tuberculosis pneumonia is a very contagious type, presents as pneumonia. It involves inflammation of the lungs. Symptoms include a high fever accompanied by a productive cough (Swierzewski S.J, 2000).

1.6.3.1.1.2. Tuberculosis Pleurisy

This usually develops soon after initial infection. A granuloma located at the edge of the lung ruptures into the pleural space, the space between the lungs and the chest wall. A pleural effusion, also known as pleurisy, is inflammation and the build-up of fluid that occurs between the membranes that surround the lungs (Swierzewski S.J, 2000). Usually, a couple

of tablespoons of fluid can be found in the pleural space. Once the bacteria invade the space, the amount of fluid increases dramatically and compress the lung. A chest x-ray shows significant amounts of fluid. Tuberculosis pleurisy generally resolves without treatment; however, two-thirds of patients with tuberculosis pleurisy develop active pulmonary TB within 5 years (Chandler S, 2010).

1.6.3.1.1.3. Laryngeal tuberculosis

Laryngeal tuberculosis is very uncommon, representing only 1 percent of tuberculosis cases, according to the study conducted by Dr. Tesic-Vidovic and published in "The Internet Journal of Otorhinolaryngology." Laryngeal tuberculosis is a rare disease and it is often misdiagnosed. It is mostly common in adults without BCG vaccination or in cases of the acquired immune deficiency syndrome. An inflammed lesion of the left vocal cord and the ventricular strip is found in such type of disease. Regular thickening of the left vocal cord associated with irregular thickening of the posterior laryngeal wall are common in this type of disease. It may lead to ulceration of the vocal cords and laryngeal mucosa (Kettani N. *et al*., 2010).

1.6.3.1.1.4. Cavitary Tuberculosis

Cavitary tuberculosis occurs as a final stage of the disease. It affects the upper lobes of the lung because they are highly oxygenated. This is an environment in which *M. tuberculosis* thrives. In such type of TB, bacteria cause progressive lung destruction by forming cavities, or enlarged air spaces. This is the main type of pulmonary tuberculosis that is transmitted from person to person, according to the Centers for Tuberculosis Research at Johns Hopkins University School of Medicine (Chandler S, 2010). Patients with cavitary TB are highly contagious. Occasionally, disease spreads into the pleural space and causes TB empyema which means pus in the pleural fluid (Swierzewski S.J, 2000).

1.6.3.1.1.5 Miliary Tuberculosis

Miliary tuberculosis is when the pulmonary tuberculosis becomes chronic (long-lasting) and spreads through either the bloodstream or the lymph system to infect other organs in the body. Miliary TB is also known as disseminated TB. "Miliary" describes the appearance on chest x-ray of very small nodules throughout the lungs that look like millet seeds. Miliary TB can occur shortly after primary infection. If the infection reaches bone marrow, it can cause anaemia. The infection in the blood causes uncontrolled multiplication of white blood cells, thereby leading to leukaemia-like conditions (Bhowmik D. *et al.,* 2009). This type of TB can be rapidly fatal. It can be difficult to diagnose because the initial chest x-ray may be normal.

Patients who are immunosuppressed and children who have been exposed to the bacteria are at high risk for developing miliary TB (Swierzewski S.J, 2000).

1.6.3.1.2. Classification of PTB by bacteriological status

1.6.3.1.2.1. Pulmonary smear-positive TB (PTB+)

- A patient with at least two sputum specimens positive for AFB
- A patient with only one sputum specimen positive for AFB and chest radiological X-ray abnormalities consistent with active TB and diagnosis made by a graduate physician
- A patient with only one sputum specimen positive for AFB and a culture positive for *M .tuberculosis*

1.6.3.1.2.2. Pulmonary smear-negative (PTB-)

- A patient with symptoms suggestive of TB with three sputum specimens negative for AFB
- Persisting symptoms after a course of antibiotics
- Again three negative sputum specimens for AFB during repeat sputum examination
- Chest X-ray abnormalities consistent with active TB (WHO, 2008).

1.6.3.2. Extrapulmonary tuberculosis (EPTB)

The term EPTB has been used to describe isolated occurrence of tuberculosis at body sites other than the lung. The organs include lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. However, when an extrapulmonary focus is evident in a patient with pulmonary tuberculosis, such patients have been categorized under pulmonary tuberculosis as per the guidelines of the World Health Organization (WHO). Extrapulmonary tuberculosis usually presents more of a diagnostic problem than pulmonary tuberculosis. In part this relates to its being less common and, therefore, less familiar to most clinicians. In addition, extrapulmonary tuberculosis involves relatively inaccessible sites and, because of the nature of the sites involved, fewer bacilli can cause much greater damage. The combination of small numbers of bacilli and inaccessible sites causes bacteriologic confirmation of a diagnosis to be more difficult, and invasive procedures are frequently required to establish a diagnosis (Sharma S. *et al*., 2004).

1.6.3.2.1. Lymphatic TB

When the TB bacterium impacts the lymph nodes and causes them to become enlarged, lymph node disease is diagnosed. This extrapulmonary TB can even cause the lymph nodes to become so large they rupture through the skin if not diagnosed in time. It is most

commonly found in the cervical or supraclavicular regions and predominates in women of Asian background from TB-widespread areas (Franko V, 2010).

1.6.3.2.2. Osteal TB

This type of TB results from haematogenous spread and the most common sites of involvement are the vertebral column, especially the lower thoracic and lumbar regions, hip, and knee. TB involving the spine is also known as Pott's disease (WHO, 2008).

1.6.3.2.3. Abdominal tuberculosis (Hepatobiliary, pancreatic and splenic tuberculosis)

Abdominal tuberculosis is the term used to encompass TB of the gastrointestinal tract, peritoneum, omentum, mesentery and its nodes and other solid intra-abdominal organs such as liver, spleen and pancreas (Sharma S. *et al*., 2004). Peritoneal TB arises from reactivation of *M. tuberculosis* foci established in the peritoneum from haematogenous spread or may occur in disseminated TB. Risk factors include cirrhosis, peritoneal dialysis, and diabetes mellitus (BMJ, 2011). Tuberculosis peritonitis tends to infect the intestine's outer lining, causing abdominal pain. The inner abdominal wall can also become infected which can cause fluid in this area similar to what occurs with TB pleurisy (Tuberculosis's Facebook Notes 2011)**.** Hepatobiliary and pancreatic TB are rare and are often associated with miliary tuberculosis, and occur more often in immune-compromised patients. The clinical manifestations are non-specific and depend on the site and extent of disease (Sharma S. *et al*., 2004).

1.6.3.2.4. Ocular tuberculosis

Ocular involvement has described in 2 to 30 per cent of patients with tuberculosis and usually develops as a result of haematogenous dissemination. While tuberculosis can affect all the part of the eye, choroid is the most commonly affected structure. Tuberculosis affects the eyelids infrequently (Sharma S. *et al*., 2004).

1.6.3.2.5. Tuberculosis of the breast (Tuberculosis mastitis)

Tuberculosis mastitis is extremely rare and is thought to occur due to direct immunization of the breast by *M. tuberculosis* through skin abrasions or duct openings in the nipple. The organisms may reach the breast through lymphatic route or haematogenous routes, or by contiguous spread from the ribs, pleural space (Sharma S. *et al*., 2004).

1.6.3.2.6. Cutaneous Tuberculosis

Cutaneous tuberculosis accounts for 0.11 to 2.5 per cent of all patients with skin diseases. Cutaneous tuberculosis is TB of the skin or mucous membrane from an external source of

mycobacteria. There are several types of cutaneous tuberculosis: Lupus vulgaris, tuberculosis verrucosa cutis and milary tuberculosis.

- Lupus vulgaris is a persistent type of cutaneous TB. The symptoms are small reddish brown lesions that are found on the face, eyelids, around the nose, cheeks, and ears.
- Tuberculosis verrucosa cutis is only contracted through direct skin inoculation when an individual had been previously exposed to mycobacteria. This type of cutaneous TB can last for years. The symptoms are reddish brown wart-like growths on the body, skin lesions on hands, feet, buttocks, elbows and knees. Sometimes pus will leak through the cracks present in the lesions.
- Milary tuberculosis of the skin is a cutaneous TB that starts off as a pulmonary TB infection which then travels through the bloodstream. The symptoms are small red spots on the skin which are sometimes concentrated to the trunk of the body, necrosis of infected areas, and the development of ulcers or abscesses on the skin (Sharma S. *et al*., 2004).

1.6.3.2.7. Genitourinary TB (GUTB)

Genitourinary tuberculosis is TB that initially begins as a pulmonary TB infection which then travels through the bloodstream to the genitourinary tract. The genitourinary tract includes the urinary tract and the reproductive system (Tuberculosis's Facebook Notes 2011). Initially metastatic lesions which are known as tubercles are formed in the kidneys. Usually, these lesions heal spontaneously or as a result of treatment. Active GUTB usually develops 5 to 25 years after the primary pulmonary infection and is usually encountered between the second and fourth decades of life (Sharma S. *et al*., 2004).

1.6.3.2.8. Neurological tuberculosis

Neurological tuberculosis may be classified into three clinico-pathological categories. These are: tuberculosis meningitis (TBM), tuberculoma, and arachnoiditis (Sharma S. *et al*., 2004).
Tuberculosis meningitis: The critical event in the development of meningitis is the rupture of a subependymally located tubercle resulting in the release of infectious material into the subarachnoid space. This potentially fatal form of extrapulmonary tuberculosis infects the brain (Sharma S. *et al.*, 2004).
Tuberculoma: It is a mass of granulation tissue made up of a accumulation of microscopic small tubercles. The size of cerebral tuberculomas is highly variable. In most cases their diameters range from a few millimetres (mm) to three to four centimeters (cm) (Sharma S. *et al.*, 2004).

1.6.3.2.9. Pericardial tuberculosis

Tuberculosis pericarditis occurs when excess fluid builds around the heart. When TB affects this area the ability of the heart to fill with blood and beat properly can be hampered. TB pericarditis occurs most commonly in the third to fifth decade of life (Sharma S. *et al.*, 2004).

1.6.3.2.10. Adrenal Tuberculosis

Adrenal TB is an extrapulmonary form of TB that affects the adrenal gland and the production of adrenal hormone. Patients with this form of TB often feel weak or faint due to insufficient adrenal gland production (Franko V, 2010).

1.7. Persons at increased risk for progression of LTBI to TB disease

- Persons infected with HIV.
- Children younger than 5 years of age.
- Persons who have recently infected with *M. tuberculosis* (within the past 2 years).
- Persons with a history of untreated or inadequately treated TB disease.
- Persons with fibrotic changes on chest radiograph consistent with prior TB disease.
- Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists.
- Person with systemic corticosteroids equivalent to/greater than 15 mg of prednisone per day, or immunosuppressive drug therapy following organ transplantation.
- Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, or cancer of the head, neck, or lung.
- Persons who have had a gastrectomy or jejunoileal bypass.
- Persons with weigh less than 90% of their ideal body weight.
- Cigarette smokers
- Persons who abuse drugs and/or alcohol.
- Populations defined locally as having an increased incidence of disease due to *M. tuberculosis*, including medically underserved, low-income populations (CDC, 2005).

1.8. Clinical features of TB

Tuberculosis (TB) will not cause any symptoms until the infection has reached the lungs. As the bacteria are very slow moving, the condition develops very slowly. Symptoms might not begin until many years after initially exposed to the bacteria.

1.8.1. Pulmonary tuberculosis

Symptoms of pulmonary TB include:

- Persistent cough that brings up thick phlegm, which may be bloody

- Breathlessness, which is usually mild to begin with and gradually gets worse
- Weight loss
- Lack of appetite
- High temperature of 38C (100.4F) or above
- Extreme tiredness
- A sense of feeling unwell (NHS choices, 2011)

1.8.2. Extrapulmonary tuberculosis (TB)

TB can spread any part apart from pulmonary which has been discussed in 1.6.3.2. section of this paper. The main parts of extrapulmonary region of the body where TB can easily spread include lymph node, skeletal, gastrointestinal tract, genitourinary tract, central nervous system. Symptoms of these extra pulmonaty TB are described below.

1.8.3. Lymph node TB

Lymph nodes are small, oval glands that are part of the immune system. They remove unwanted bacteria and particles from the body. Symptoms of lymph node TB include:

- Persistent, painless swelling of the lymph nodes, which usually affects nodes in the neck, but swelling can occur in nodes throughout the body
- Over time, the swollen nodes can begin to release a discharge of fluid through the skin

1.8.4. Skeletal TB

Symptoms of skeletal TB include:

- Bone pain
- Curving of the affected bone or joint
- Loss of movement or feeling in the affected bone or joint
- Weakened bone that may fracture easily

1.8.5. Gastrointestinal TB

Symptoms of gastrointestinal TB include:

- Abdominal pain
- Diarrhoea
- Bleeding from anus

1.8.6. Genitourinary TB

Symptoms of genitourinary TB include:

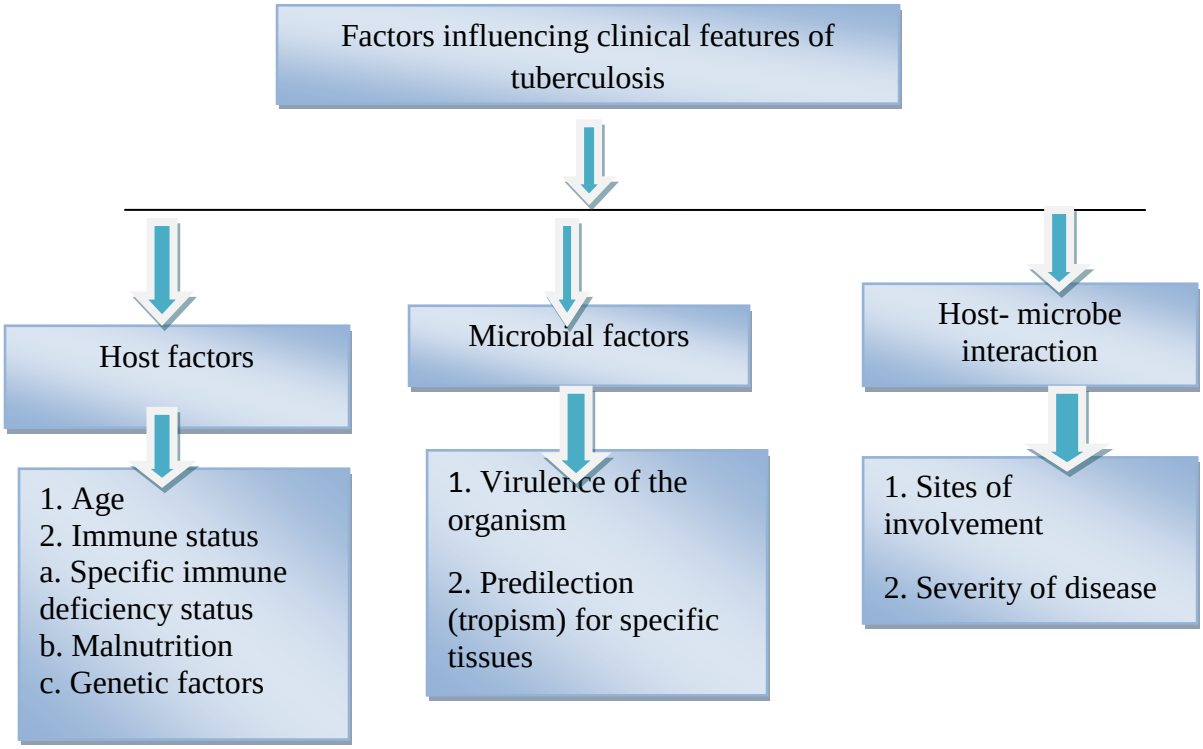
- A burning sensation when one urinates
- Blood in urine
- A frequent urge to pass urine during the night
- Groin pain

1.8.7. Central nervous system TB

Symptoms of central nervous system TB include:

- Headaches
- Being sick
- Stiff neck
- Changes in mental state, such as confusion
- Blurred vision
- Fits (NHS choices, 2011)

1.9. Factors influencing clinical features of TB (American Thorasic Society, 2000).



1.10. Diagnosis of TB

The contribution of the microbiology laboratory to the diagnosis and management of tuberculosis involves the detection and isolation of mycobacteria, the identification of the mycobacterial species or complex isolated, and the determination of susceptibilities of the organisms to anti mycobacterial drugs. Only laboratories having a sufficient volume of work and assured competence should provide clinical mycobacteriology services. Such procedures are time-consuming and employ reagents and special techniques not used routinely in the study of bacteria in other genera (American Thorasic Society, 2000).

Mycobacterial disease may occur in almost any site in the body, a variety of clinical materials may be submitted to the laboratory for examination. In addition to the common specimens,

such as sputum (natural or induced) and gastric aspirate, others include urine, cerebrospinal fluid, pleural fluid, bronchial washings, material from abscesses, endometrial scrapings, bone marrow, and other biopsy specimens or resected tissue (American Thorasic Society, 2000).

1.10.1. Tools for diagnosis of TB will be discussed below

1.10.1.1. Sputum smear examination (AFB microscopic examination)

Mycobacterium tuberculosis is an acid fast bacillus (AFB). The highest priority for tuberculosis (TB) control is the identification and cure of infectious cases, such as, patients with sputum smears positive pulmonary TB. The highest priority in the diagnosis of TB is thus given to sputum microscopy (WHO, 2006). It is the easiest and quickest procedure that can be performed, and it provides the physician with a preliminary confirmation of the diagnosis. Also, because it gives a quantitative estimation of the number of bacilli being excreted, the smear is of vital clinical and epidemiologic importance in assessing the patient's infectiousness (American Thorasic Society, 2000).

Smears may be prepared directly from clinical specimens or from concentrated preparations. The acid-fast staining procedure depends on the ability of mycobacteria to retain dye when treated with mineral acid or an acid–alcohol solution. Two procedures are commonly used for acid–fast staining:

- Carbolfuchsin methods:
  - ❖ Ziehl–Neelsen method
  - ❖ Kinyoun method
- Fluorochrome procedure using auramine- O or auramine–rhodamine dye (American Thorasic Society, 2000).

Several quantitative studies have shown that there must be 5,000 to 10,000 bacilli per milliliter of specimen to allow the detection of bacteria in stained smears. In contrast, 10 to 100 organisms are needed for a positive culture. Concentration procedures in which a liquefied specimen is centrifuged and the sediment is used for staining increases the sensitivity of the test. Smears of concentrated material are preferred. Negative smears, however, do not preclude tuberculosis disease. Factors influencing the sensitivity of smears are:

- ❖ Staining technique,
- ❖ Centrifugation speed,
- ❖ Reader experience, and

- Prevalence of tuberculosis disease in the population being tested (American Thorasic Society, 2000).

The most cost effective tool for screening pulmonary TB suspects is microscopy examination of their sputum by the Ziehl–Neelsen method.

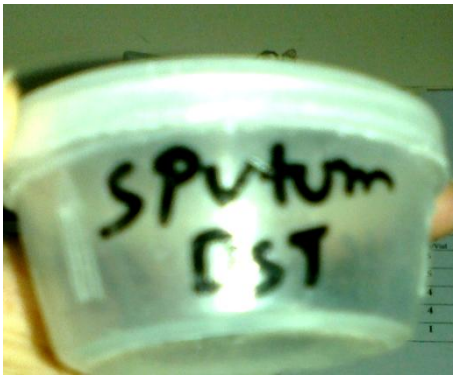


Figure 1.5: Sputum container

Diagnosis of pulmonary TB by sputum microscopy is simple, easy, inexpensive, rapid, technically not very demanding and more reliable than X-rays. The purposes of the sputum microscopy are:

- Diagnosis of the patients with infectious tuberculosis
- Monitoring the progress (WHO, 2006).

Microscopy should be performed on 3 sputum examinations. These are:

- On the spot specimen: The first specimen is collected on the spot when a patients is identified as a pulmonary TB suspect. (Spot-1 specimen)
- Early morning specimen: the patient is given a sputum container to collect the second at home on the following morning.
- Second on the spot specimen: The third specimen is collected when the patients return to the health facility with the early morning specimen (Spot II specimen) (WHO, 2008).

1.10.1.1.1. Collection of sputum sample

- A good wide-mouthed sputum container need to be selected, which is disposable, made of clear thin plastic, unbreakable and leak proof material.
- A sputum container with the laboratory serial number written on it is given to the patient. The patient must be instructed how to open and close the container and the importance of not rubbing off the number written on the side of the container is to be explained.
- The patient has to be instructed to inhale deeply 2-3 times, cough up deeply from the chest and spit in the sputum container by bringing it closer to mouth.

- The sputum sample should be of good quality. A good sputum sample is thick, purulent and sufficient in amount (2-3 ml).
- For taking early morning sample, the patient should be informed to rinse his/her mouth with plain water before bringing up the sputum (WHO, 2006).

1.10.1.1.2. Storage and transportation of specimens

The specimen should be transported to the laboratory within 3-4 days of collection. The specimen should be collected in the containers meant for the purpose, lid tightly secured, properly labelled and kept away from the sun and heat. These can be placed in a special box which can withstand leakage of contents, shocks and other conditions incident to ordinary handling practices. These boxes should be kept in the cooler conditions and then transported to the laboratory (WHO, 2006).

1.10.1.1.3. Preparation of smear

At first a new unscratched slide need to be selected. The slide must be labeled with laboratory serial number. From yellow purulent portion of the sputum, smear will be made using a bamboo stick. A good smear is spread evenly, 2 cm x 3 cm in size and is neither too thick nor too thin. Then the smear will be air dried for 15-30 minutes. After that, the smear is fixed by passing the slide over the flame 3-5 times for 3-4 seconds each time. Then the smear is stained by Ziehl Neelsen method (WHO, 2006).

1.10.1.1.4. Ziehl Neelsen staining (AFB staining)

- **Carbolfuchsin stain:**
  - Basic fuchsin: 0.3 g
  - Ethanol 95%: 10 ml
  - Phenol: 5 ml
  - Distilled water: 95 ml

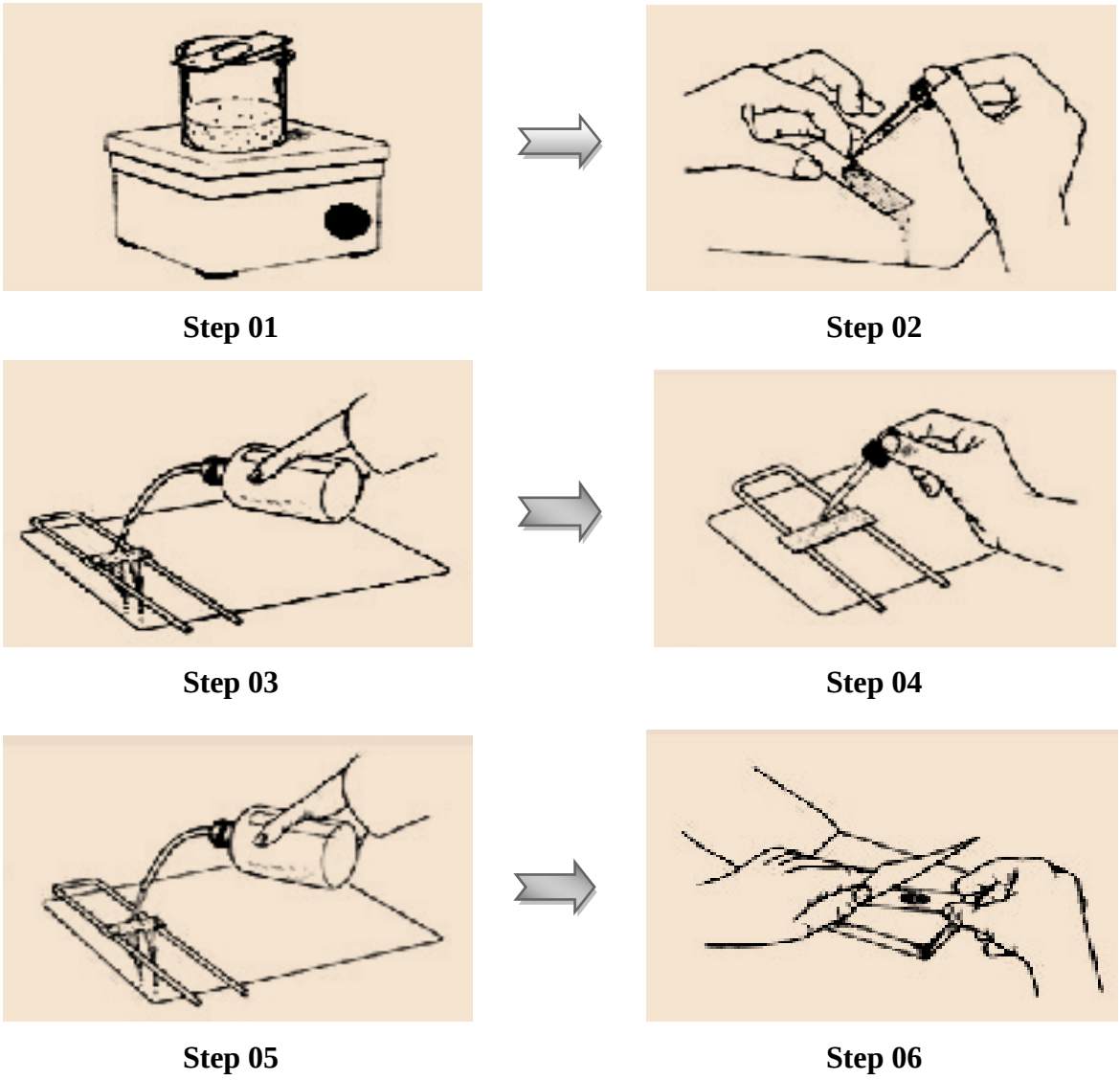
At first the basic fuchsin is dissolved in the ethanol and then the phenol is added which is dissolved in the water. After mixing the mixture is kept for several days. The mixture need to be filtered before use.

- **Decolorizing solvent:**
  - Ethanol: 97 ml
  - Hydrochloric acid (concentrated): 3 ml
- **Counterstain:**
  - Methylene blue chloride: 0.3 g
  - Distilled water: 100 ml (Hussy M. A., Zayaitz A, 2012).

Ziehl Neelsen staining procedure:

Step 01: The entire slide is flooded with carbol fuchsin to ensure enough stain is added. It will help to keep the slides covered throughout the entire staining step. Then the slide is steamed over boiling water for 8 minutes. Additional stains may need to be added if stain boils off.

Step 02: After cooling the slide, decolorizing solvent is applied for 15-20 seconds.



Step 01 **Step 02**

Step 03 **Step 04**

Step 05 **Step 06**

Figure 1.6: Ziehl Neelsen staining procedure (Dempsey S, 2000)

Step 03: Then decolorizing action will be stopped by rinsing briefly with gentle and indirect stream of water. The decolorizing and the washing must be repeated until the stained smear appears faintly pink.

Step 04: Then counter stain will be done using counterstain for 30 seconds.

Step 05: The slide will be rinsed briefly with water to remove the excess methylene blue. Rinsing with water must be done gently and indirectly.

Step 06: Then the slide is gently blot dried with bibulous paper. After that the slide will be examined carefully under oil immersion. Acid-fast bacteria will be appeared red, and non-acid-fast bacteria (and other organisms and cellular materials) will be appeared blue (Dempsey S, 2000).

Grading of microscopy smears

The results will be recorded in laboratory form and laboratory register appropriately as per Table 1.4 given in the next part:

Table 1.4: Grading of microscopy smears

Examination	Result	Grading	No. of fields to be examined
More than 10 AFB per oil immersion fields	Positive	3 +	20
1-10 AFB per oil immersion fields	Positive	2 +	50
10-99 AFB per 100 oil immersion fields	Positive	1 +	100
1-9 AFB per 100 oil immersion fields	Scanty	Record exact number seen	100
No AFB per 100 oil immersion fields	Negative	0	100

All positive and negative slides must be stored till instructed by supervisor to destroy them (WHO, 2006).

1.10.1.2. Cultivation of Mycobacteria

All clinical specimens suspected of containing mycobacteria should be inoculated onto culture media for four reasons:

- Culture is much more sensitive than microscopy. It is able to detect as few as 10 bacteria/ml of material.
- Growth of the organisms is necessary for precise species identification.
- Drug susceptibility testing requires culture of the organisms and
- Genotyping of cultured organisms may be useful to identify epidemiological links between patients or to detect laboratory cross-contamination.

Three different types of traditional culture media are available:

- Egg based

- Agar based and
- Liquid

In the solid media, growth of mycobacteria tends to be slightly better on the egg-based medium but more rapid on the agar medium. Growth in liquid media is faster than growth on solid media.

Liquid systems allow for rapid growth. It allows the detection of mycobacterium growth within 1–3 weeks compared with solid media, where growth takes 3–8 week, whereas agar media provide an opportunity to examine colony morphology and detect mixed cultures. At least one container of solid medium should be inoculated and used in conjunction with broth culture systems. Egg-based media is an important backup for rare *M. tuberculosis* strains that may not grow on the other media. Automated liquid systems should be checked at least every 2–3 days for growth while solid media should be checked once or twice a week. Mycobacterial growth observed on solid culture media should be quantified. Growth in liquid culture systems cannot be similarly quantitated although a qualitative measure of organisms in the inoculum can be made by noting the time required for liquid culture to turn positive. Table 1.5 presents a widely used scale for quantitating growth on agar plates (American Thorasic Society, 2000).

Table 1.5: Quantitation scale for mycobacterial growth on agar plates

Number of colonies seen	**Quantity reported**
No colonies seen	Negative
Fewer than 50 colonies	Report actual number seen
50-100 colonies	1^{+}
100-200 colonies	2+
200-500 colonies	3^{+}
>500 colonies (confluence)	4^{+}

(American Thorasic Society, 2000)

1.10.1.3. Mantoux tuberculin skin test (TST)

The Mantoux tuberculin skin test (TST) is currently the only widely used method for identifying infection with *M. tuberculosis* in persons who do not have tuberculosis disease. The TST is an intradermal injection. The TB antigens used in a tuberculin skin test are called purified protein derivative (PPD). A measured amount (0.1 ml) of PPD in a shot is put under the top layer of skin on forearm (CDC, 2011). The reaction should be measured in millimeters of the induration (palpable, raised, hardened area or swelling). The reader should

not measure erythema (redness). The diameter of the indurated area should be measured across the forearm (perpendicular to the long axis). When placed correctly, if the injection produces a pale elevation of the skin (a wheal) 10 mm or more in diameter, it indicates the test is positive. The skin test reaction should be read between 48 and 72 hours after administration (Healthwise, 2011). The injection should be made with a tuberculin syringe, with the needle bevel facing upward. This is a good test for finding a TB infection. It takes 2-8 weeks after infection for the skin test to become positive after a person is infected (Jackson J. C, 2012).

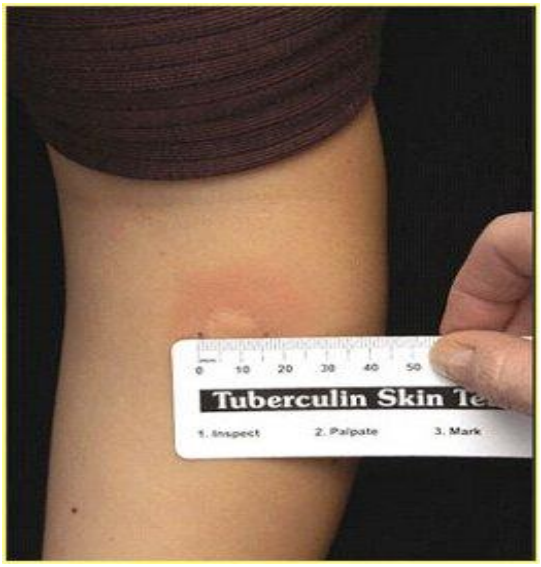


Figure 1.7: Mantoux tuberculin skin test

It is often used when symptoms, screening, or testing, such as a chest X-ray, show that a person may have TB. A tuberculin skin test cannot tell how long one has been infected with TB. It also cannot tell if the infection is latent (inactive) or is active (Healthwise, 2011). The cut-off point for a positive reaction depends on the person's overall risk.

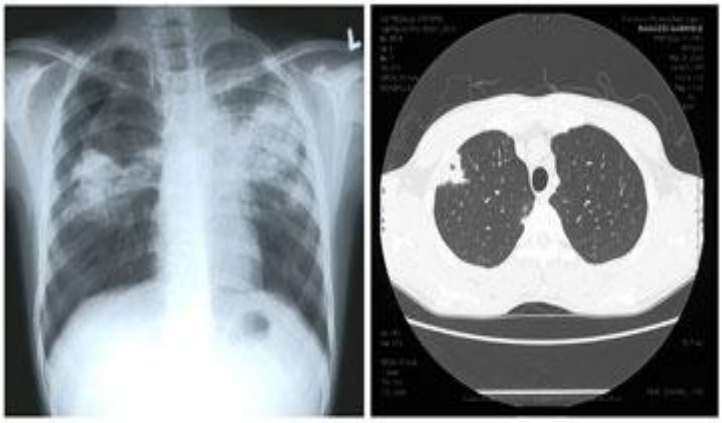
Skin test interpretation depends on two factors:

- Measurement in millimeters of the indurations
- Person’s risk of being infected with TB and of progression to disease if infected. (CDC, 2011)

1.10.1.4. Radiological (X- ray) examination of the lungs

Chest x-ray is used to check for lung abnormalities in people who have symptoms of TB disease. The results of a chest x-ray may be suggestive of TB. The technique is not specific as many other diseases can produce similar features. Therefore the results from a chest x-ray cannot confirm that a person has TB disease. The chest x-ray also has poor sensitivity; in the early stages of disease, the damage to the lungs may not yet have become sufficiently marked

to be detectable so people who have active TB are missed. It is therefore an imperfect ‘rule out' test. Clearly the chest x-ray is completely useless as either a rule in or a rule out test if the TB is not in the lungs. So in the 40% of all cases of active TB where the disease is not found in the lungs (extrapulmonary TB) the chest x-ray is of no use (Oxford Immunotec, 2012). However, if the germ has attacked and caused inflammation in the lungs, an abnormal shadow may be visible on the chest X-rays. The doctor may be able to see spots where immune cells are surrounding the TB bacteria or larger diseased areas indicating active TB disease. An X-ray of the lungs may show signs of pneumonia, cavities (holes in the lung), or scarring, all of which can happen in active TB disease. These people may need further diagnostic tests (sputum tests) and will need treatment (National Jewish Health, 2009).



Chest X- ray CT Scan

Figure 1.8: Chest X- ray and CT Scan

In some hospitals Computerised Tomography (CT Scan) and Magnetic Resonance Imaging (MRI) have proved useful for imaging tuberculosis lesions, particularly those in the brain and spine. CT scans are therefore often used to identify non-pulmonary TB (Oxford Immunotec, 2012).

1.10.1.4. ALS assay

One of the major research areas for tuberculosis (TB) focuses not only on diagnostics but also on biomarkers that can provide prognostic data about the disease course and response to treatment. Young children are at increased risk of progressing to TB after exposure, and may suffer from disseminated forms of the disease. Therefore, an accurate surrogate marker of disease may be crucial to improving the diagnosis of paediatric TB. A novel B-cell assay called the antibodies in lymphocyte supernatant, or ALS, is very well in diagnosing TB disease both in Asia and Africa. In ALS assay, ALS is used as a biomarker in children with culture-confirmed TB.

The ALS assay is based on a principle similar to that of the enzyme-linked immunosorbent spot assay, measuring antibody-secreting cells in cultures of peripheral blood mononuclear cells (PBMCs). The ALS assay detects antibody secretion from in vivo activated plasma B cells that migrate throughout the peripheral circulation in response to TB antigens that are present during active disease but not latent TB infection. ALS assay will be discussed briefly in the following:

- Phlebotomy of 3.5 ml of blood is required in order to isolate 5 million PBMCs.
- These cells are incubated in tissue culture plates without stimulation for 48–72 hours.
- The supernatant is collected, placed into BCG-coated microtitre plates and IgG responses to BCG are measured by ELISA.

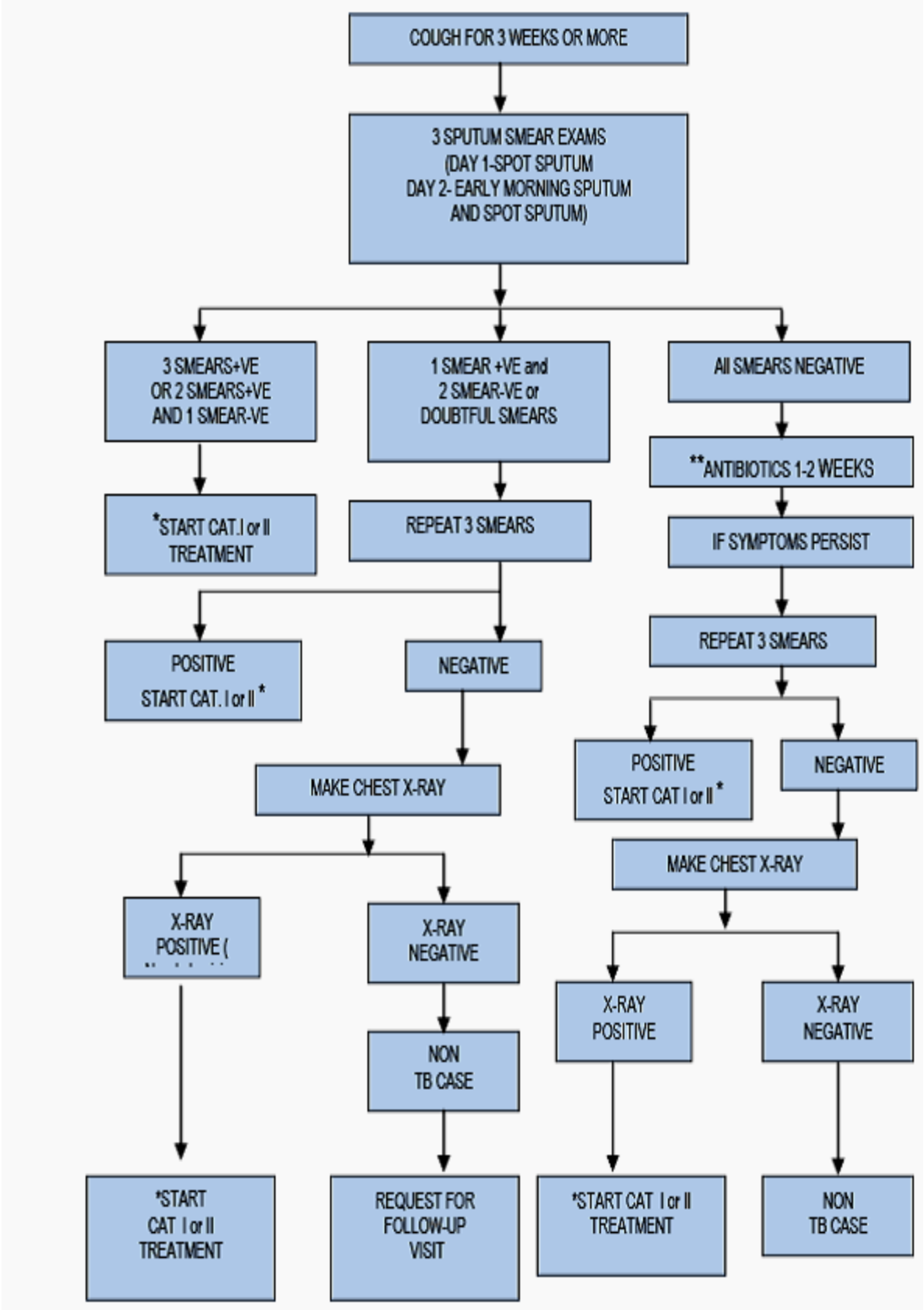
The ALS assay is different from traditional serological tests that quantify TB-specific IgM, IgG or IgA levels in serum. Since the serum containing pre-existing antibodies in vivo is removed on isolation of PBMCs, the ALS assay focuses on assessing active antibody secretion from TB-specific plasma cells circulating during TB disease. The ALS assay is a novel method that is feasible and has high accuracy in detecting TB disease in children and adults. (Raqib R. *et al.*, 2011)

1.10.1.5. FNAC

The use of fine needle aspiration cytology (FNAC) is an accurate tool in the diagnosis of tuberculous lesions. It has become an acceptable and widely practised minimally invasive technique, which is safe, simple, rapid and relatively pain-free (Koo V. *et al.*, 2006). It has been used for the diagnosis of tuberculous lesions presenting as superficial lumps and bumps, ulcers, and sinuses, and for deep-seated, space-occupying lesions under imaging guidance. It is also ideal for sample collection for ancillary studies such as Ziehl-Neelsen (Z-N) stain for acidfast bacilli (AFB), as well as culture, radiometric, and molecular biologic studies of Mycobacterium tuberculosis. FNAC is highly cost effective and accurate as a first line investigative technique with differential diagnoses including reactive hyperplasia/inflammatory conditions, granulomatous disorders and malignancy, stratifying cases requiring further investigations, surgical intervention or clinical follow-up (Das D. K, 2000).

Chapter 1

Flow chart for diagnosis and follow up of pulmonary TB:



(WHO, 2008)

1.11. Treatment of TB

Medications are the cornerstone of tuberculosis treatment. But treating TB takes much longer than treating other types of bacterial infections. With tuberculosis, patient must take antibiotics for at least six to nine months. The exact drugs and length of treatment depend on patient's age, overall health, possible drug resistance, the form of TB (latent or active) and its location in the body. The aims of treating TB are:

- To cure the patient of TB
- To prevent death from active TB or its late effects
- To prevent relapse of TB
- To decrease transmission of TB to others
- To prevent the development of acquired drug resistance (WHO, 2008)

1.11.1. Treatment phases:

Treatment of TB can be categorized into two phases. These are:

- The initial or intensive phase: in this phase drugs are administered daily for two months in new cases and three months in re-treatment cases. The aim of this phase is to rapidly reduce and eliminate the multiplying bacilli without allowing the development of acquired resistance to the prescribed drugs. During the intensive phase, the tubercle bacilli are killed rapidly. The infectious patients quickly become non-infectious (within approximately two weeks).
- The continuation phase: This phase is essential to eliminate the remaining bacterial population. Drugs administered daily for the rest of the treatment duration according to category. (WHO, 2008)

There are 10 drugs currently approved by the U.S. Food and Drug Administration (FDA) for treating TB. Of the approved drugs, the first-line anti-TB agents that form the core of treatment regimens include:

- Isoniazid (H)
- Rifampin (R)
- Pyrazinamide (Z)
- Ethambutol (E)
- Streptomycin (s) (WHO, 2008)

1.11.2. Standardized treatment regimen for each diagnostic category (Adults)

Table 1.6: Standardized treatment regimen for each diagnostic category (Adults)

TB Diagnostic Category	Patient category	Treatment regimen: Intensive Phase (Daily)	Treatment regimen: Continuation Phase (daily)
1	✓ New smear-positive patients ✓ New smear-negative PTB ✓ Extra-pulmonary TB ✓ Concomitant/associated HIV/AIDS	2(HZRE)	4(HR)
2	✓ Sputum smear-positive PTB with history of treatment of more than one month ✓ Relapse ✓ Treatment failure after category ✓ others	2((HRZE)S/1(HRZE)	4(HR)

(WHO, 2008)

Here, digit before the brackets ( ) indicates for how long (month) the patient should take the drugs. For example, 2(HRZE) indicates the patient has to take HRZE for 2 months on daily basis. H for isoniazid 300 mg, R for rifampin 150 mg, Z for pyrazinamide 500 mg, and E for ethambutol 400 mg. (WHO, 2008)

1.11.3. Dosages of FDC tablets:

FDC tablets are composed as follows:

- 4-FDC: rifampicin 150 mg + isoniazid 75 mg + pyrazinamide 400 mg + ethambutol 275 mg
- 2-FDC: rifampicin 150 mg + isoniazid 75 mg

1.11.3.1. Category I:

Table 1.7: Category 1

Pre-treatment Weight(KG)	Intensive Phase Daily (first 2 months) Number of 4FDC tablets	Continuation Phase Daily (Next 4 months) Number of 2 FDC tablets
30-37	2	2
38-54	3	3
55-70	4	4
>70	5	5

(WHO, 2008)

1.11.3.2. Category II:

Table 1.8: Category II

Pre-treatment Weight(kg)	Intensive Phase		Continuation phase	
	Daily (first 3 month) Number of 4-FDC tablets	Daily (first 2 month) Injection Streptomycin	Daily (next 5 months) Number of 2-FDC tablets	Ethambutol 400mg (Number of tablets)
30-37	2	500mg	2	2
38-54	3	750mg	3	3
55-70	4	1gm*	4	3
>70	5	1gm*	5	4

(WHO, 2008)

*The dose of streptomycin should not exceed 750 mg daily after the age of 50 years

1.11.3. Second line anti-tuberculosis drugrs:

- Aminoglycosides: Amikacin, Kanamycin
- Polypeptides: Caprcomycin
- Quinolones: Ciprofioxacin, Ofioxacin
- Thioamides: Ethionamide & Prothionamide

- Paraminosalicyclic acid (PAS)
- Cycloserine

1.11.4. Completing treatment is essential

After a few weeks, the patient will not be contagious and may start to feel better. It might be tempting to stop taking TB drugs. But it is crucial to finish the full course of therapy and take the medications exactly as prescribed by the doctor. Stopping treatment too soon or skipping doses can allow the bacteria that are still alive to become resistant to those drugs, leading to TB that is much more dangerous and difficult to treat.

To help people stick with their treatment, a program called directly observed therapy (DOT) is sometimes recommended. In this approach, the patients will be administered medications by a health care worker so that patient does not have to remember to take it on his or her own (Mayo Clinic, 2011).

1.12. Worldwide epidemiology of tuberculosis

TB occurs in every part of the world. About one-third of the world's population has latent TB, which means people have been infected by TB bacteria but are not yet transferred to TB disease and cannot transmit the disease. People infected with TB can infect up to 10-15 other people through close contact over the course of a year. Without proper treatment up to two thirds of people ill with TB will die. In 2010, the largest number of new TB cases occurred in Asia, accounting for 60% of new cases globally. However, Sub-Saharan Africa carried the greatest proportion of new cases per population with over 270 cases per 100 000 population in 2010. In 2010, about 80% of reported TB cases occurred in 22 countries. These 22 countries are considered “high-burden countries (HBCs),” accounting for approximately 80% of new TB cases each year; most HBCs are in Africa and Asia. India, China, South Africa, Nigeria, and Indonesia have the highest number of new TB cases in the world (U.S. Global Health Policy, 2010).

Some countries are experiencing a major decline in cases, while cases are dropping very slowly in others. Brazil and China for example, are among the 22 countries that showed a sustained decline in TB cases over the past 20 years. China, in particular, has made dramatic progress in TB control. Between 1990 and 2010, the TB death rate in the country fell by almost 80% and the total number of people ill with TB dropped by half (WHO, 2012).

Since 1995, over 46 million people have been successfully treated and an estimated 7 million lives saved through use of DOTS and the Stop TB Strategy recommended by WHO. In 2010, 8.8 million individuals became ill with TB and 1.4 million died. Both these statistics reflect a

decline compared with prior years. The number of individuals infected with TB peaked in 2005, when 9 million individuals became ill. The death peaked at 1.8 million in 2003.

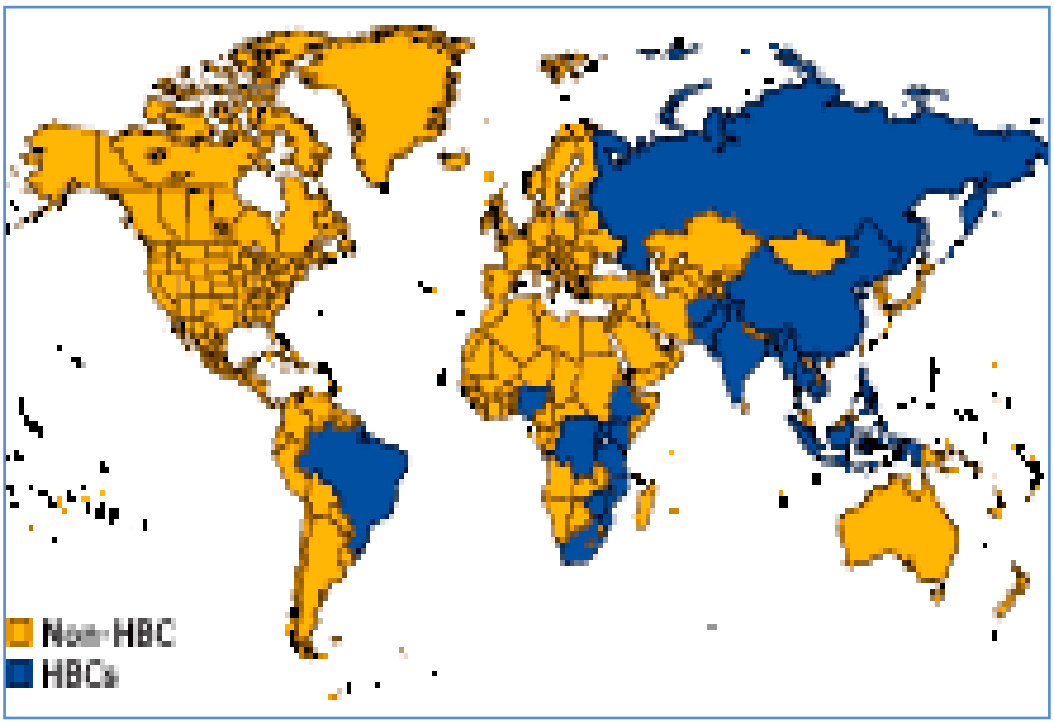


Figure 1.9: TB prevalence around the world

Table 1.9: Worldwide data of tuberculosis by WHO, 2010

WHO Region	Number of cases (thousands)	Rate per 100,000
Africa	2300	276
The Americas	270	29
Eastern Mediterranean	650	109
Europe	420	47
South-East Asia	3500	193
Western Pacific	1700	93

The estimated prevalence and incidence rates of all forms of tuberculosis were respectively 387 and 223 per 100 000 population, in 2007 (WHO, 2009) It has achieved a case-detection rate of over 71% and cure rate of over 91% at the national level (NTP Annual Report, 2008). Tuber culosis is an ancient disease, which is still a major public health challenge in Bangladesh. Case detection rate of TB from 1993 to 2005 and treatment success rate in TB from 1993 to 2004 will be included in the next part of this paper.

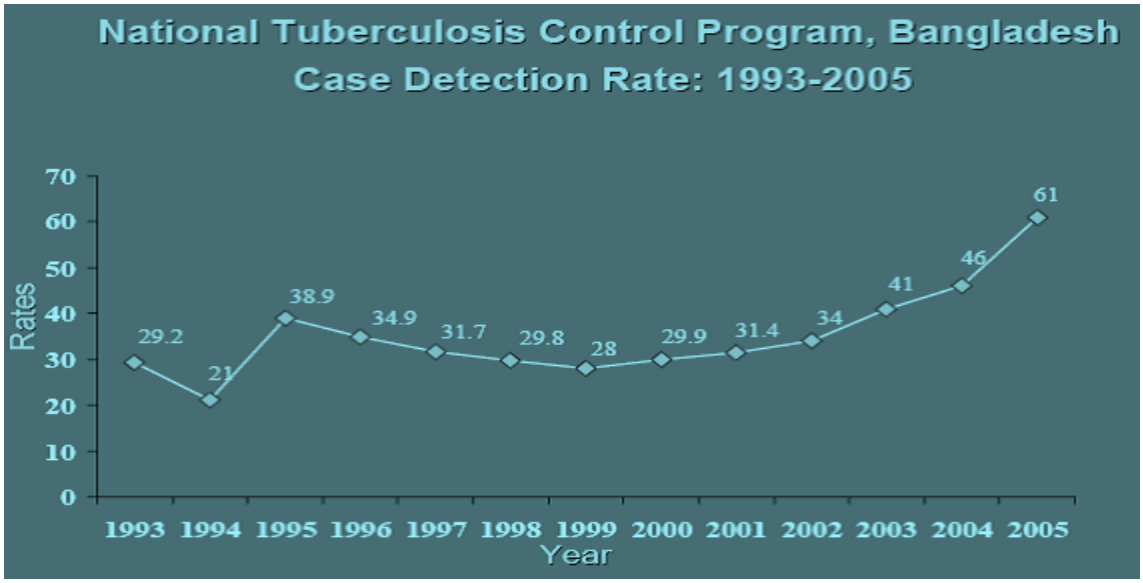


Figure 1.10: Case detection rate in TB in Bangladesh

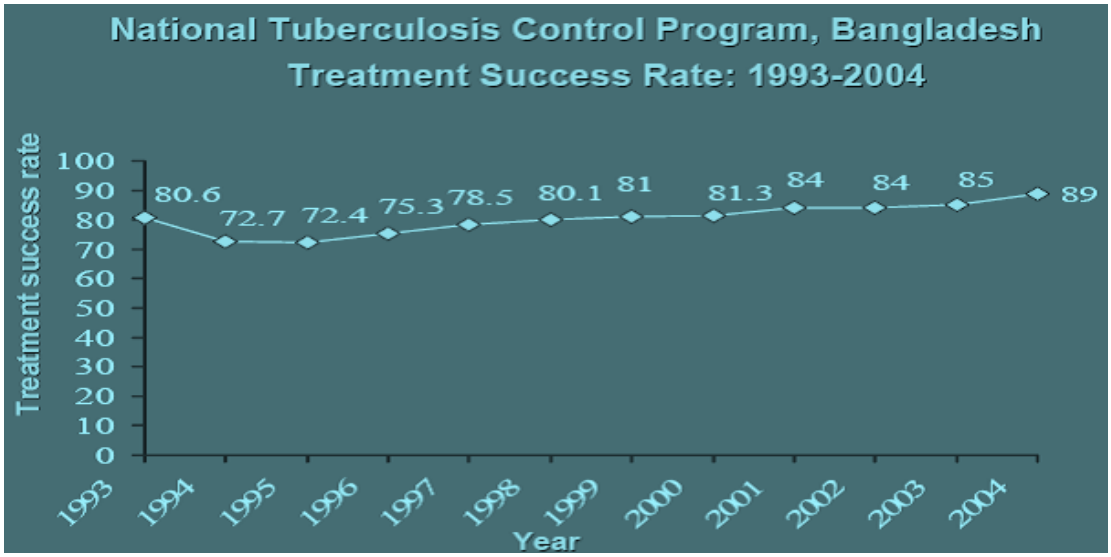


Figure 1.11: Treatment success rate in TB in Bangladesh

1.13. Significance of study with TB in Bangladesh:

Tuberculosis (TB) continues to be an important contributor to overall disease burden and preventable death in nearly all developing countries, killing around 70,000 people per year in Bangladesh, and around two million worldwide. With a population of 150 million, Bangladesh ranks sixth among countries with a high TB burden (NTP Annual Report, 2008) People ill with TB can infect up to 10-15 other people through close contact over the course of a year. Without proper treatment up to two thirds of people ill with TB will die. TB in Bangladesh is growing out of control, but there is a strong desire from the people and Parliament in Bangladesh to move firmly beyond the confines of the short-term vision of a

‘control’ programme, to a long-term commitment to eliminate TB. TB control measures are of extreme importance for the epidemic of TB in Bangladesh to be halted. The most cost effective public health measure for the control of tuberculosis is effective identification and cure of infectious patients. Currently, the National TB Control Programme is emphasizing the diagnosis and treatment of pulmonary smear positive, extra-pulmonary TB and childhood tuberculosis. Due to the huge epidemic of tuberculosis in our country, the study has been focused on adult patients suffering from tuberculosis.

Chapter 2

2. Methodology:

The study has been carried out by taking adult tuberculosis patients from National Institute of Diseases of the Chest and Hospital (NIDCH) after getting permission from the director of NIDCH, Dhaka, Bangladesh. At the beginning of the study a questionnaire has been prepared to get adequate information regarding socio demographic history, awareness about the disease, smoking history, associated risk factors and diagnosis history of the adult TB patients. All the information regarding patients' health care has been collected from the management and as well as from the patients. The main focus of this study was on AFB microscopic examination of adult patients suffering from tuberculosis. This test is relatively a quick way to determine whether the patient is suffering from tuberculosis or not.

The first AFB microscopic examination has been performed in all the patients of the study. There is a form in NIDCH which needs to be filled up before doing the sputum smear examination of the tuberculosis patients. An idea about the present disease status of the all the adult patients in this study has been provided by the first AFB microscopic examination. Tuberculosis disease of the patients has been confirmed after getting the result of first AFB microscopic examination. The study has been followed up by performing another AFB microscopic examination of these patients after one month. The aim of this study is to reveal that whether the adult patients suffering from tuberculosis are being cured after taking treatment from NIDCH or they need more awareness regarding their health from the management as well as from themselves.

2.1. Study place:

The study will be conducted at National Institute of Diseases of the Chest and Hospital (NIDCH). National Institute of Diseases of the Chest and Hospital (NIDCH) is a state supported research institute and hospital in Bangladesh. It was established in 1955 as TB Hospital. In 1962 it was upgraded as National Chest Diseases Institute.

2.2. Inclusion criteria:

The study has been performed considering some criteria among the patients. These specific criteria are:

- Adult (18-49 years) TB patients
- Patients with pulmonary TB
- Patients having their hematological report

2.3. Exclusion criteria:

- ✓ TB patients with age range below 18 years or above 49 years

- ✓ Multi-drug resistant TB patients
- ✓ Extra pulmonary TB patients
- ✓ Adult TB patients along with following disease:
  - Cancer
  - AIDS
- ✓ Pregnant adult female TB patients

2.4. Study type: This was a prospective study to observe the improvements of adult TB patients after having treatment from NIDCH.

2.5. Study period: This study has been conducted for about one year. This one year starts from the very beginning of the study design and ends up with taking 2nd AFB microscopic examination from the adult TB patients admitted in NIDCH, Dhaka.

2.6. Sample size: There were 21 adult TB patients in this study. Among them there were 15 male patients and 6 female patients. In this study 20 patients were suffering from smear positive pulmonary TB and remaining one was suffering from smear negative pulmonary TB.

2.7. Sampling technique: Adult TB patients have been included in the study randomly from NIDCH, Dhaka.

2.8. Study population: All the adult TB patients admitted in NIDCH during this study were considered as possible sample in this study.

2.9. Data analysis: All the data in this study has been compiled using Microsoft Office Excel 2007. The data is analyzed by using bar diagram and pi-chart. These statistical analysis will provide an apparent idea the effectiveness of the treatment getting from NIDCH and as well as it will also reveal the reasons behind the failure of the treatment.

Chapter 3

Results and Discussion

3.1. Socio-demographic history

3.1.1. Distribution of patients according to their gender

Table 3.1: Distribution of patients according to their gender

Topic	Number of patients
Male	15
Female	6

The table provides the information about the adult TB patients in NIDCH. There were 15 male and 6 female patients out of 21 patients. This indicates the occurrence of TB among male patients in higher rate due to several factors of transmission of TB, such as, environmental factors (Table 1.3 in Chapter 1). Another study done by Zaman K. clearly stated the incidence of TB among adult male TB patients is high due to their smoking habit.

3.1.2. Distribution of the patients according to different age ranges

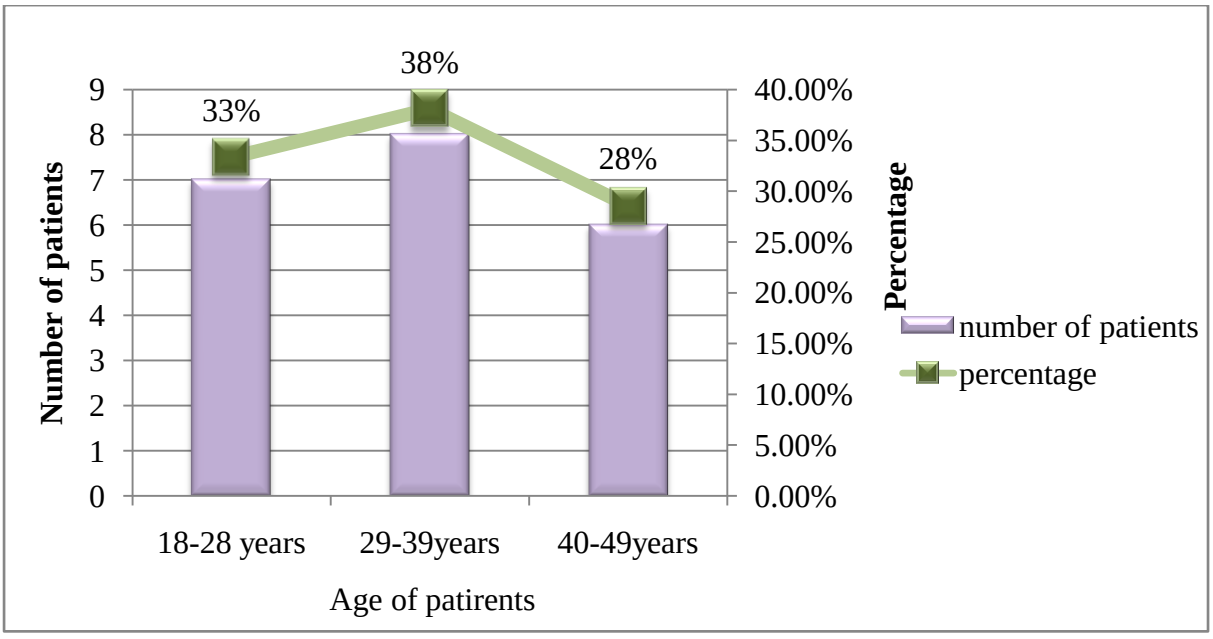


Figure 3.1: The number of patient with different age ranges

This table is showing the number of patient according to different age ranges. There were 7 patients (33%) within the range of 18-28 years. There were 8 patients (38%) within the range of 29-39 years and there were 6 patients (28%) within the range of 40-49years. This table indicates the probability of occurring TB in different age ranges among adults. All the patients within 29-39 years were earning persons and as TB disease is a contagious disease, they may be affected somehow from their co-workers suffering from TB disease.

3.1.3. Distribution of the patients according to different weight ranges

Table 3.2: Distribution of the patients according to different weight ranges

Weight range	Number of patients
26-35 kg	2
36-45 kg	12
46-55 kg	7

The table is showing the number of patients with different weight ranges. There were 2 patients of 26-35 kg. There were 12 patients of 36-45 kg and there were 7 patients of 46-55 kg. In this study there were 15 patients with age ranges from 18-39years for whom the weight should be in between 45-50 kg. The data is showing that there were 14 patients with weight ranges from 26-45kg which is below the standard. Therefore, it is clear that weigh loss is a very common feature among the TB patients.

3.1.4. Distribution of the patients according to their education level

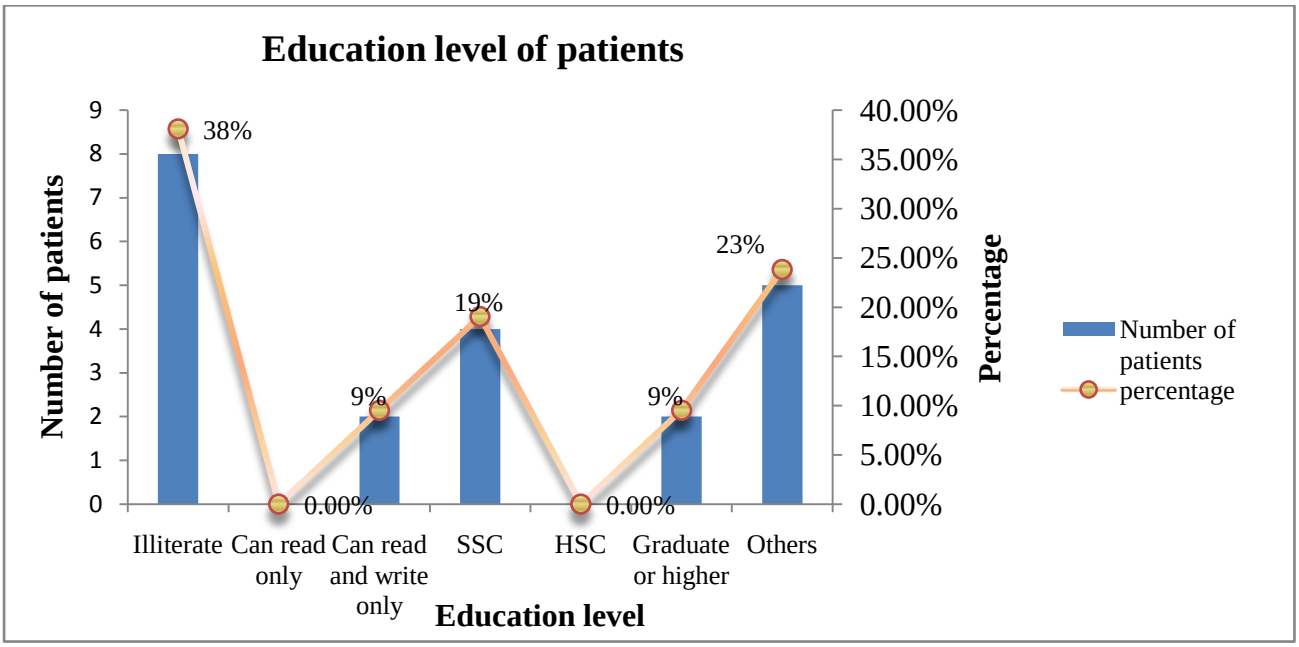


Figure 3.2: The education level of patients

The bar chart is showing the distribution of the patients according to the educational level of patients. There were 8 patients (38%) who were illiterate, there were 2 patients (9%) who can read and write only, there were 4 patients (19%) who had passed SSC, there were 2 patients (9%) who were graduates. In this study there were 8 patients (38%) among 21 whom were illiterate. Therefore they were less aware about the management of this disease from the

others. But after getting admitted in NIDCH, they were very much conscious about the management of the disease.

3.1.5. Area of residence of the patients

Table 3.3: Area of residence of the patients

Place of residence	Number of patients
Rural	16
Urban	2
Semi- Urban	3
Slum	0

The table is showing the area of residence of patients. There were 16 patients who live in rural area. There were 2 patients who live in urban area. There were 3 patients who live in semi urban area. There were no patients who live in slum. The table indicates the incidence of TB mostly among the rural people due to lack of awareness. In the rural area most of the people were suffering from malnutrition as well as they were living in an unhygienic condition. All these might cause TB disease to them.

3.1.6. Distribution of patients according to their living status

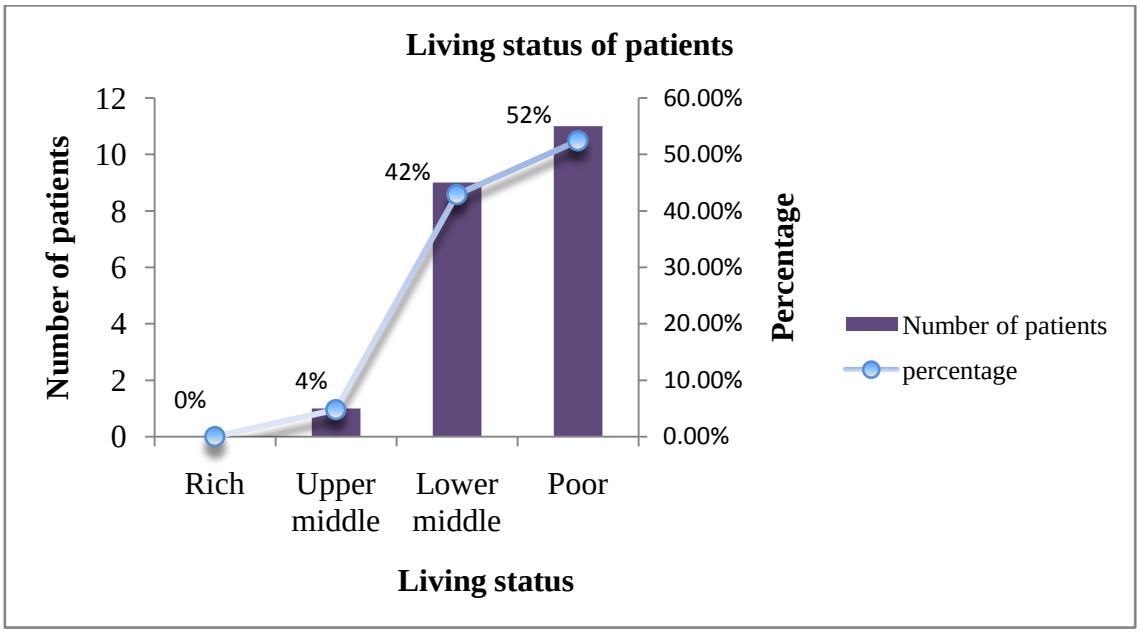


Figure 3.3: Distribution of patients according to their living status

The bar chart is showing the number of patients with their living status. There were no rich patients. There was only 1 upper middle class patient (4%). There were 9 lower middle class patients (42%) and there were 11 poor patients (52%). It is clearly understandable that TB disease mostly occurs among the poor people due to unhygienic condition of the area of their

residence. Apart from this, the poor patients were very much unconscious about their health condition earlier. At the very initial stage of their disease they were not aware about their proper management of this fatal disease.

3.1.7. Awareness about contagiousness

Table 3.4: Patients' awareness about the disease

Patients' awareness about contagiousness	Number of patients
Yes	21
No	0

Tuberculosis is the most contagious disease of the globe. If a person who has tuberculosis does not treat himself, he or she can infect in a year about other people. All of the patients were aware about this matter after admitting in NIDCH. All of them were using masks to protect others from this highly contagious disease. They were very worried about their health conditions and were taking their medicines properly to get rid from this deadly disease as early as possible.

3.1.8. Vaccination status among the patients

Table 3.5: Vaccination status among the patients

Vaccination status	Number of patients
Vaccinated	9
Not- vaccinated	12

The table is showing that 12 patients were taken vaccine and 9 patients were not vaccinated. A person previously vaccinated may have a positive reaction to a TB skin test, potentially causing confusion for health care providers attempting to determine if that person has TB. In this research work the maximum patients were not vaccinated. That means they were not aware about TB disease earlier. Vaccination can prevent or reduce the risk of development of tuberculosis.

3.2. Patients' smoking history

Table 3.6: Patients' smoking history

Smoking history	Number of patients	
	Yes	No
Habit of smoking before diagnosis for TB	7	8
Quit smoking after diagnosis	7	0

Smoking does not cause tuberculosis, but those who smoke are at higher risk to get infected by tuberculosis. Smoking appears to increase the risk of becoming infected with tuberculosis and the risk for the development of active disease upon infection. Therefore, smokers are more prone to developing TB. In this study there are 7 patients who have habit of smoking before diagnosis for TB and 8 patients were non-smoker and & people quit smoking after diagnosis. All the 7 patients who had smoking habit quit their habit after diagnosed with tuberculosis.

3.3. Risk factors among the patients

Table 3.7: Risk factors among the patients

Risk factors	Number of patients
Unhygienic	18
Smoking habit	7
Advanced age	6

The most common cause of tuberculosis is low body immunity. Habits of life, poverty, personal choices are situations that support to develop tuberculosis. As maximum patients were poor so they have a very high rate of incidents of tuberculosis because they were suffering from malnutrition. As well as, maximum patients in this study were leading their life in unhygienic condition which has increased risk for developing tuberculosis. The table is showing that 18 patients were leading an unhygienic life, 17 patients were suffering from malnutrition, 6 patients were in advanced age and 7 patients had smoking habit which has been discussed in Table 3.6.

3.4. Diagnosis results

3.4.1. Microscopy results

3.4.1.1. 1st specimen of 1st test in adult male patients

Table 3.8: 1st specimen of 1st test in adult male patients

Result	Number of patients
Negative	6
Scanty (1-29)	1
1^+	5
2^+	2
3^+	1

The table is indicating the condition of the male patients in the 1st specimen of 1st test in this study. The result is showing the presence of *M. tuberculosis* among 9 adult male patients. But in the study all of these patients were suffering from TB which had been confirmed observing

all three microscopic results of male patients in the study. All of them were smear positive pulmonary TB patients except one.

3.4.1.2. 1st specimen of 1st test in adult female patients

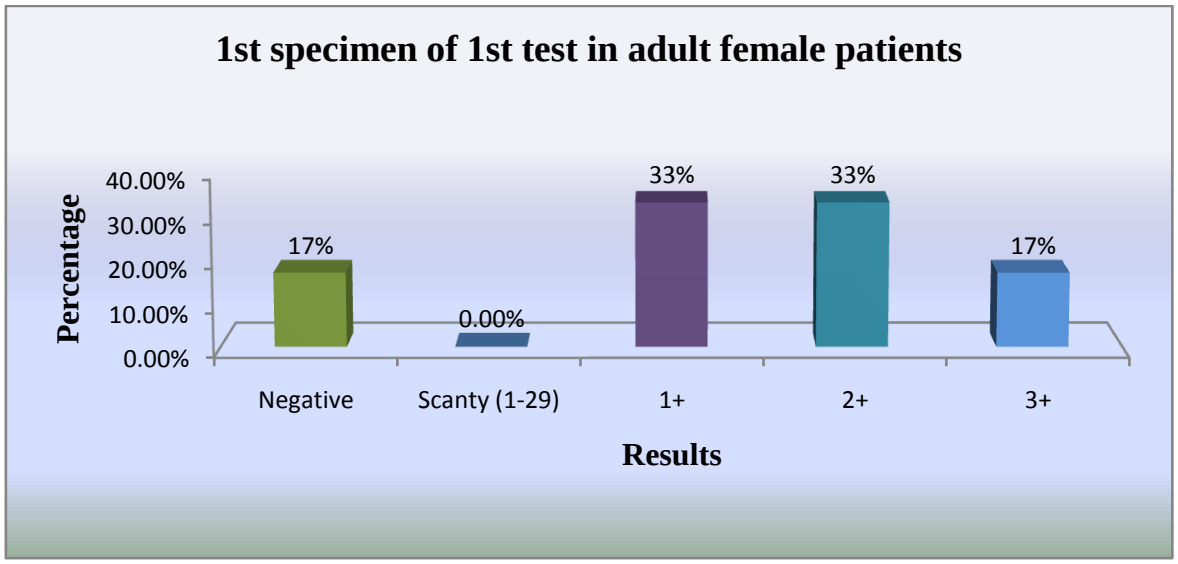


Figure 3.4: 1st specimen of 1st test in adult female patients

The table is showing the severity of TB disease among the female patients. Although the chart is representing 1 (17%) smear negative TB patient, but the presence of *M. tuberculosis* in all the patients had been confirmed by sputum smear examination. In this study all the female patients were suffering from smear positive pulmonary TB. In the 1st specimen of 1st test there was only 1 female patient (17%) who had high number of AFB in the specimen showing 3+ in the result.

3.4.1.3. 2nd specimen of 1st test in adult male patients

Table 3.9: 2nd specimen of 1st test in adult male patients

Result	Number of patients
Negative	3
Scanty (1-29)	2
1^+	6
2^+	2
3^+	2

The table is indicating the condition of the male patients in the 2nd specimen of 1st test in this study. The result is showing the presence of *M. tuberculosis* among 12 adult male patients. But in the study all of these patients were suffering from TB which had been confirmed observing all three microscopic results of male patients in the study. All of them were smear positive pulmonary TB patients except one.

3.4.1.4. 2nd specimen of 1st test in adult female patients

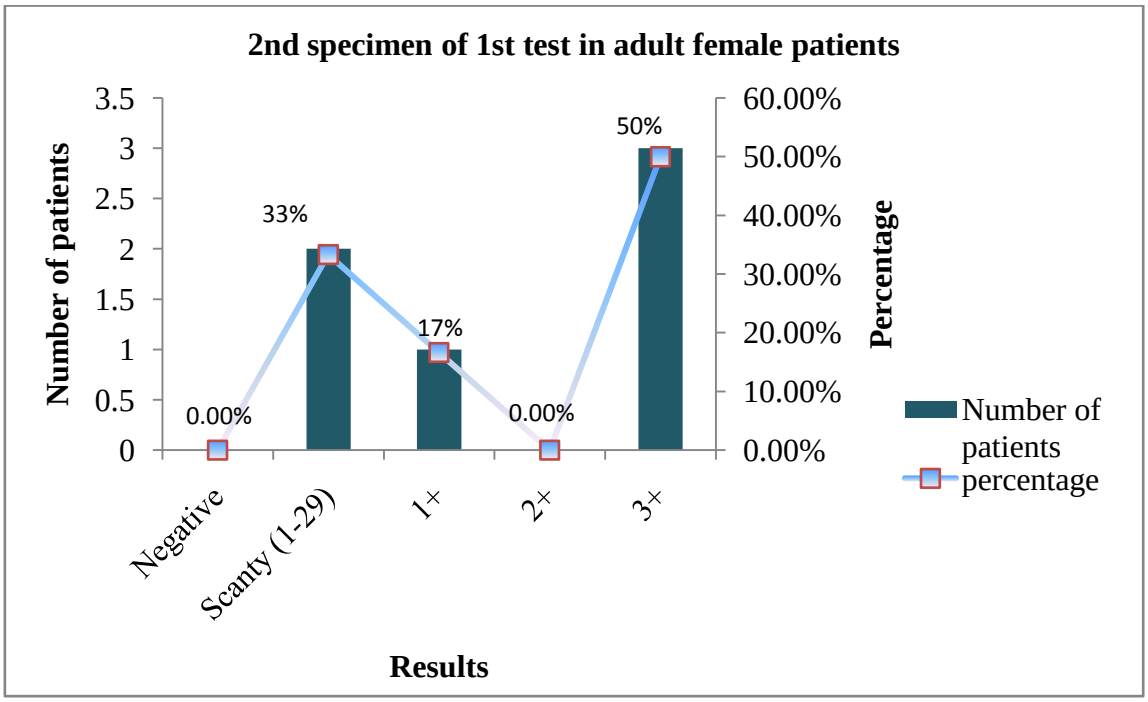


Figure 3.5: 2nd specimen of 1st test in adult female patients

The graph is showing the severity of TB disease among the female patients. The chart is representing 3 patients (50%) having more than 10 AFB per oil immersion fields which indicates the severity of the disease among these patients. In this study all the female patients were suffering from smear positive pulmonary TB.

3.4.1.5. 3rd specimen of 1st test in adult male patients

Table 3.10: 3rd specimen of 1st test in adult male patients

Result	Number of patients
Negative	2
Scanty (1-29)	3
1^+	6
2^+	1
3^+	3

The table is indicating the condition of the male patients of this study. It indicates the presence of *M. tuberculosis* among 13 adult male patients and negative result in sputum smear test in 2 patients. But in the study all of these patients were suffering from TB which had been confirmed observing all three microscopic results of male patients in the study. All of them were smear positive pulmonary TB patients except one. The table is representing three patients having more than 10 AFB per oil immersion fields which indicates the severity of the disease among these patients.

3.4.1.6. 3rd specimen of 1st test in adult female patients

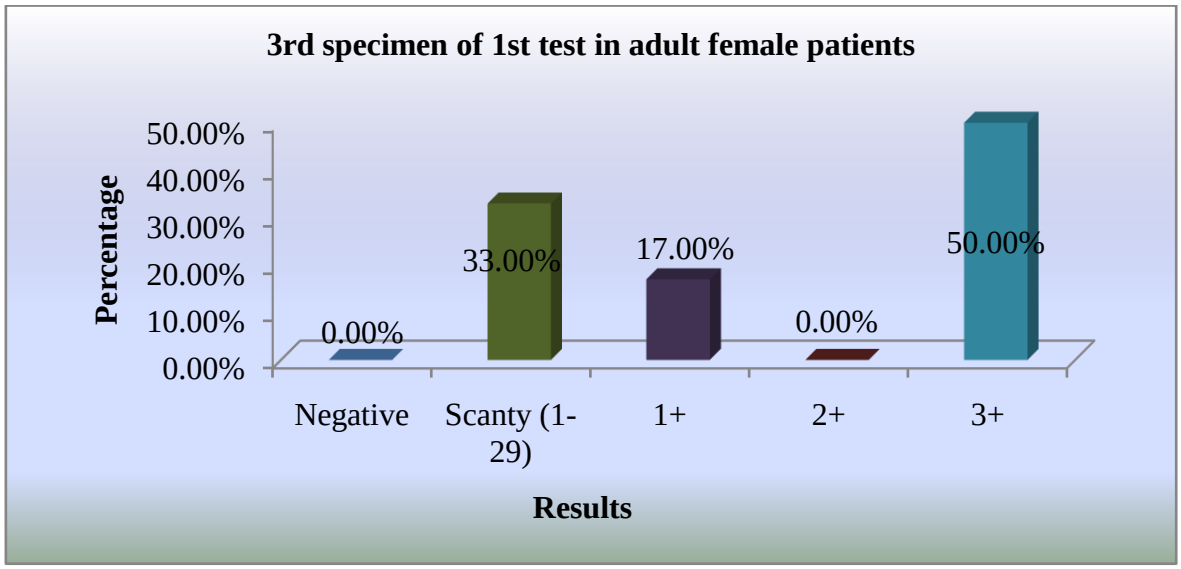


Figure 3.6: 3rd specimen of 1st test in adult female patients

The table is showing the severity of TB disease among the female patients. The table is representing 3 patients (50%) having more than 10 AFB per oil immersion fields which indicates the severity of the disease among these patients. In this study all the female patients were suffering from smear positive pulmonary TB. In the 3rd specimen there were no female patients showing negative results in microscopic examination. In this specimen there were 2 patients (33%) showing very doubtful result as they had AFB in very small amount.

3.4.2. Results of follow-up patients

3.4.2.1. AFB microscopic results of patient number 1

Patient number 1 was 34 years old. The first AFB microscopic test was carried out on April 30, 2012. The presence *M. tuberculosis* was clear in 3 specimen of 1st test. Patient number 1 had all positive results in the entire 3 specimen. Then the patient was under close observation in NIDCH for 1 month. After getting proper treatment from NIDCH there was a speedy improvement in the microscopic results showing all negative in the 2nd follow up test done on June 04, 2012.

Table 3.11: 1st AFB microscopic results of patient number 1

Date	**Specimen**	**Result**				
		Negative	Scanty	1+	2+	3+
30.04.2012	1.				✓	
	2.			✓		
	3.			✓		

The 2nd follow up result clearly indicating that patient number 1 had a very remarkable improvement after taking anti-TB drugs. Although after 1 month patient 1 had all negative results in 2nd AFB microscopic test, but still the patient must need to continue anti- TB drugs for complete recovery.

Table 3.12: 2nd follow up AFB microscopic results of patient number 1

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
04.06.2012	1.	✓				
	2.	✓				
	3.	✓				

3.4.2.2. AFB microscopic result of patient number 2

Table 3.13: 1st AFB microscopic result of patient number 2

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
24.04.2012	1.			✓		
	2.				✓	
	3					✓

Table 3.14: 2nd follow up AFB microscopic results of patient number 2

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
19.05.2012	1.			✓		
	2.	✓				
	3.	✓				

Table 3.13 and 3.14 are showing the smear sputum examination results of the second follow up patient in this study. Patient number 2 was chain smoker before diagnosed with TB disease. The 1st AFB test was carried out on April 24, 2012. In the first report, the presence *M. tuberculosis* was clear. All the specimens of the 1st test were positive. There was a comparatively slow improvement in the microscopic results showing two negative results in the 2nd test on May 19, 2012. There was only 1 positive result in the 2nd AFB microscopic examination. From the table 3.14 it is clearly understandable that the severity of the disease was decreased in a higher rate in this patient but required more close observation. The response of this patient towards anti- TB drug is quite good.

3.4.2.3. AFB microscopic result of patient number 3

Table 3.15: 1st AFB microscopic result of patient number 3

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
03.04.2012	1.	✓				
	2.			✓		
	3			✓		

The table is showing the smear sputum examination results of the third follow up patient in this study. In the first report, the presence *M. tuberculosis* was clear as there were two positive results among the three sputum test. Although in the 1st specimen the result was negative, but 2 positive results were indicating that the patient was infected with TB disease. There was a comparatively slow improvement in the microscopic results showing only one negative result in the 2nd test. From the table 3.16 it is clearly understandable that the severity of the disease is decreasing in a slower rate in this patient.

Table 3.16: 2nd AFB microscopic result of patient number 3

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
13.05.2012	1.	✓				
	2.			✓		
	3.		✓			

3.4.2.4. AFB microscopic result of patient number 4

Table 3.17: 1st AFB microscopic result of patient number 4

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
05.05.2012	1.			✓		
	2.			✓		
	3			✓		

The table is showing the smear sputum examination results of the forth follow up patient in this study. The first AFB microscopic examination of this patient was carried out on 5 May, 2012. In the first report, the presence *M. tuberculosis* was clear. All of the specimens in the 1st test were positive. There was a relatively fast improvement in the microscopic results showing all negative results in the 2nd test. From the table 3.18 it is clearly understandable that the severity of the disease was decreased in a higher rate in this patient. Although all the

specimens were smear negative, but still the patient must need to continue anti-TB drugs. Completion of the anti-TB course is very crucial in TB disease.

Table 3.18: 2nd AFB microscopic result of patient number 4

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
30.05.2012	1.	✓				
	2.	✓				
	3.	✓				

3.4.2.5. AFB microscopic result of patient number 5

The table is showing the smear sputum examination results of the fifth follow up patient in this study. In the first report, the presence *M. tuberculosis* was doubtful showing only one positive result. There was a relatively fast improvement in the microscopic results showing all negative results in the 2nd test. From the table it is clearly understandable that the severity of the disease was decreased in a higher rate in this patient after getting proper treatment.

Table 3.19: 1st AFB microscopic result of patient number 5

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
24.04.2012	1.	✓				
	2.		✓			
	3			✓		

Table 3.20: 2nd AFB microscopic result of patient number 5

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
02.06.2012	1.	✓				
	2.	✓				
	3.	✓				

3.4.2.6. AFB microscopic result of patient number 6

The table is showing the smear sputum examination results of the sixth follow up patient in this study. In the first report, the presence *M. tuberculosis* was clear as there were all positive results among the entire three sputum tests. There was a comparatively slow improvement in the microscopic results showing only one negative result in the 2nd test.

Table 3.21: 1st AFB microscopic result of patient number 6

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
02.04.2012	1.					✓
	2.			✓		
	3			✓		

From the table 3.22 it is clearly understandable that the severity of the disease is decreasing in a slower rate in this patient. More awareness regarding the management of TB is required here for this patient.

Table 3.22: 2nd AFB microscopic result of patient number 6

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
12.05.2012	1.	✓				
	2.			✓		
	3.			✓		

3.4.2.7. AFB microscopic result of patient number 7

Table 3.23: 1st AFB microscopic result of patient number 7

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
10.05.2012	1.			✓		
	2.			✓		
	3			✓		

Table 3.24: 2nd AFB microscopic result of patient number 7

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
13.06.2012	1.	✓				
	2.	✓				
	3.	✓				

Table 3.23 and 3.24 is showing the smear sputum examination results of the seventh follow up patient in this study. In the first report, the presence *M. tuberculosis* was apparent. There was a relatively fast improvement in the microscopic results showing all negative results in

the 2nd test. From the table it is evidently understandable that the severity of the disease was reduced in a higher rate in this patient

3.4.3. Hematological report

3.4.3.1. Hematological report of male patients

Table 3.25: Hematological report of male patients

Specimen	**Number of patients**	
	Within normal range	**Without normal range**
Hemoglobin level	7	8
Total count of WBC	10	5
Erythrocyte sedimentation rate	2	13
Platelet count (PC)	5	10
Packed cell volume (PCV)	5	10
Neutrophils	9	6
Lymphocytes	11	4
Monocytes	15	0

The hemoglobin level is expressed as the amount of hemoglobin in grams (gm) per deciliter (dL) of whole blood, a deciliter being 100 milliliters. The hemoglobin levels of 15 male patients were considered among them 7 patients had hemoglobin level within normal range, 12.5-17.5 gm/dl and 8 patients had hemoglobin level without normal range.

White blood cell (WBC) count was performed on 15 male patients among whose 10 had normal range of WBC which is 3,900- 10,000/cmm and 5 had WBC count without normal range. A high number of WBCs is called leukocytosis.

Erythrocyte sedimentation rate (ESR) is a test that indirectly measures how much inflammation is in the body. The test was carried out on 15 male patients. Among them 2 had normal range of ESR which is 12mm or less in 1st hour and the remaining 13 patients had ESR without the normal range. Determination of ESR value can be another parameter in TB disease, although it will not ensure the presence of *M. tuberculosis*.

A platelet count is a test to measure how many platelets one has in his or her blood. The test was performed on 15 male patients among whose 5 had normal range of WBC, which is 140,000- 390,000/cmm and 10 had without normal range.

Packed Cell Volume (PCV) describes the volume that is occupied by a cell pellet after centrifugation. The test was carried out on 15 male patients. Among them 5 had normal range of packed cell volume, which is 40-52% and the rest 10 had PCV level without normal range. Most of the male patients in this study had been showed abnormal PCV value which pointing on the significance of PCV value in TB disease.

Neutrophils are the most common type of white blood cell. The amount of neutrophils on blood work tests is known as the ANC (absolute neutrophil count). The test was carried out on 15 male patients. Among them 9 had normal range of neutrophil, 40-75% and the rest 6 had without normal range.

Approximately 20% to 47% of white blood cells are lymphocytes. The count of lymphocytes on WBC was carried out on 15 male patients. The test result showed that 11 patients had normal range of lymphocytes, 20-47% and 4 had without normal range.

Monocyte count test measures the amount of monocytes in blood. The test was carried on 15 male patients and the test result showed normal range (2-10%) of monocyte count for all the patients. Therefore TB has no significant effect on monocytes level.

3.4.3.2. Hematological report of female patients

Table 3.26: Hematological report of female patients

Specimen	**Number of patients**	
	Within normal range	**Without normal range**
Hemoglobin level	2	4
Total count of WBC	2	4
Erythrocyte sedimentation rate	0	6
Platelet count (PC)	0	6
Packed cell volume (PCV)	3	3
Neutrophils	3	3
Lymphocytes	2	4
Monocytes	5	1

As there were 6 female patients in this study, hemoglobin level of all these patients were measured. Among them hemoglobin level of 2 patients were within normal range, but the hemoglobin level of remaining 4 female patients were without the normal range which was 11.5- 16.5gm/dl. This may be due to the existence of TB or some other associated risk factors.

The normal range of the total count of WBC is 3,900- 10,000/cmm. Most of the female patients had their total count of WBC without the normal range. The study found that there were only 2 female patients out of 6 female patients whom had their total count of WBC within the normal range.

Erythrocyte sedimentation rate can be another parameter in diagnosis of TB disease as all of the female patients in this study had their ESR level without the normal range which is 15 mm or less in 1st hour.

Similar to ESR level, platelet count (PC) of all the female patients in this study were having their PC level without the normal range which is140, 000- 390, 000/cmm.

Packed cell volume (PCV) level of 3 female patients were within the normal range, 35-47%. Remaining 3 female patients had their PCV level without the normal range. It can be concluded that it is not obvious that PCV level will be affected in TB disease.

Like PCV level, neutrophils level of 3 female patients was within the normal range, 40-75%. Another 3 female patients were having their neutrophils level without the normal range.

Among the 6 female patients there were only 2 female patients whom had their lymphocytes level within the normal range which is 20-47%. The result indicates the impact of TB disease in lymphocytes level among the patients.

The normal range of monocytes level is 2-10%. In this study there was only 1 female patient who had her monocytes level without the normal range.

3.5. Discussion:

This was a preliminary study to assess the progression of adult TB patients admitted in NIDCH using AFB microscopic examination. The aim of the study was to monitor the rate of improvement among the adult TB patients after getting treatment from NIDCH. This study included socio demographic history, awareness about the disease, smoking history, associated risk factors and most importantly diagnosis history of the adult TB patients.

According to Oxfordshire Tuberculosis (TB) Nursing Services, "After the first two weeks of antibiotic treatment, someone who has TB of the lung or throat generally stops being infectious." In this study there were only 3 patients among 7 patients of follow up study (43%) whose microscopic results were negative after 1 month of starting the antibiotic treatment. Remaining 4 patients did not respond properly to anti-TB drugs. This may be either due to failure of the treatment or lack of consciousness about proper management of the disease.

A 15 year study of 280,000 subjects in south India found that the risk of progression from infection to disease for pulmonary TB was 8.6% among men and 3.1% among women.(Gender and health 2002) This study also supports this statement because during conducting this study, there were 15 male adult patients, whereas, there were only 6 male patients.

Another recent study of ICDDR,B showed that the prevalence of tuberculosis is higher among the males and rural population compared to urban areas. This study also supports this study as there were 16 patients (76%) whom were living in rural area and they were affected by the deadly disease TB.

A study named, "Socioeconomic inequalities of tuberculosis in India" done by Muniyandi M and Ramachandran R. clearly stated, "Among the marginalized people, TB was 1.5 times more prevalent. TB was disproportionately high among the poor." This study also concludes the same. In this study there were 52% people whom were living below the poverty line and they were affected by TB disease.

Smoking has been linked to increased individual risk of tuberculosis infection and mortality. Recent reviews show weak infrastructure to regulate tobacco use and increasing smoking in the areas with endemic tuberculosis. (WHO, 2008) This study reveals that many of the adult male patients were chain smoker before diagnosed with TB. The good news is that all of them were highly concerned about their treatment and management of TB after diagnosed with TB and all of them quit smoking.

Chapter 3

In this study there were some limitations. There were total 21 adult TB patients in the study, but during performing the 2nd AFB microscopic examination, there were only 7 patients were included (33%). It was not possible to include all the patients of this study in 2nd microscopic examination as their residence were far away from NIDCH, Dhaka. If the study would get required funding, then it would be possible to convince all the patients to perform this test along with arrangement of their accommodation and close monitoring of these patients during the study period.

Nevertheless, the study will be further conducted to examine the AFB microscopic results of the remaining patients.

Chapter 4

Conclusion

Tuberculosis (TB) is a major public health problem in Bangladesh since long. The problem is aggravated by the increasing population density, rapid urbanization, poverty and illiteracy. TB control program is emphasizing in the diagnosis and treatment of this disease. Among all the other forms of TB, smear positive TB can be easily diagnosed and it is easy to get well soon after taking proper treatment. Course completion is very crucial in TB disease. All the patients must be very careful about the proper management of the disease and completion of anti-TB therapy even when the AFB microscopic result will be negative.

Annex I

Case Report Form (CRF) for patients

Study Name: Follow up study of the diagnosis outcomes based on AFB microscopy in the geriatric tuberculosis patients admitted in National Institute of Diseases of the Chest and Hospital (NIDCH).

By- Sanjida Halim Topa

ID# 2008-3-70-030

Patients' Identification:

1. Patient's name: ……
2. Age: …….
3. Registration number: ……..…

Socio-demographic history:

1. Gender:
   a. Male b. Female
2. Education level:
   - Illiterate
   - Can read only
   - Can read and wrote
   - SSC
   - HSC
   - Graduate or higher
   - others
3. Body weight: …….
4. Place of residence:
   a. Rural
   b. Urban
   c. Semi-Urban
   d. Slum
5. Living status:
   a. Rich
   b. Upper middle
   c. Lower middle
   d. Poor

Patients' awareness about the disease:

1. Do you know it is contagious?
   a. Yes b. No
2. Is there anyone in your family ever infected with tuberculosis?
   a. Yes b. No
3. Are you aware of the proper management of the tuberculosis treatment?
   a. Yes b. No
4. Did you take vaccine (BCG)?
   a. Yes b. No

Patients' occupation

1. What is your occupation? …….
2. Do you have any working disabilities?
   a. Yes b. No
   If yes, then what?.....

Patients' smoking history:

1. Did you have smoking habit before diagnosing for tuberculosis identification?
   a. Yes b. No
2. Did you quit smoking after being confirmed to have TB?
   a. Yes b. No

Risk factors:

- Unhygienic
- Smoking habit
- Advanced age

Diagnosis:

AFB microscopy:

Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
	1.					
	2.					
	3					
Follow up						
Date	Specimen	Result				
		Negative	Scanty	1+	2+	3+
	1.					
	2.					
	3.					

Hematological Report

Hb: _____

Total count of WBC: _____

ESR: _____

Platelet count (PC): _____

PCV: _____

Differential count of WBC:

Neutrophils:

Lymphocytes:

Monocytes:

Eosinophils:

Basophils:

Annex II

জ্ঞাতলিখিত সম্মতিপত্র

গবেষক ঃ রাবিতা ইসরাত

গবেষণার উদ্দেশ্যঃ

TB একটি নিরাময় অযোগ্য ফুসফুসের রোগ যা প্রকাশ পায় দীর্ঘমেয়াদী শ্লেষ্মাযুক্ত কাশি এবং শ্বাসকষ্ট বৃদ্ধির মাধ্যমে। এটি উন্নয়নশীল দেশসমূহে প্রাপ্তবয়স্কদের অসুস্থতা এবং মৃত্যুর অন্যতম প্রধানকারণ। সাধারণত: ধূমপান, পরিবেশজনিত তামাকের ধোঁয়া, আভ্যন্তরীন বায়ুদূষণ এবং পেশাগত কারণে ধোঁয়া বা ধোঁয়ার কণা/কণিকার সংস্পর্শে আসা হচ্ছেTBহওয়ার কারণ।

অংশগ্রহণকারীর নিকট থেকে প্রত্যাশা ঃ

আপনি যদি এই গবেষণায় অংশগ্রহণের জন্য সম্মতি দেন, তাহলে আমরা আপনাকে কিছু প্রশ্ন জিজ্ঞেস করবো।

গোপনীয়তা, নামহীনতা এবং নিশ্চয়তা ঃ

আমরা আপনাকে আশ্বস্ত করছি যে, আপনার নিকট থেকে সংগৃহীত তথ্য এবং আপনার স্বাস্থ্যগত অবস্থা সম্পর্কে কাউকে জানতে দেয়া হবেনা। এই গবেষণায় কোন কাগজপত্রে আপনার নাম থাকবে না। আপনার নাম অথবা ব্যক্তিগত তথ্য(যা দ্বারা আপনাকে খুঁজে বের করা যাবে)কোথাও প্রকাশ করা হবে না বা কাউকে দেয়া হবে না।

ভবিষ্যতে ব্যবহার যোগ্য তথ্য ঃ

এই গবেষণায় সংগৃহীত তথ্য ভবিষ্যতে গবেষণার কাজে ব্যবহার করা হতে পারে।

অংশগ্রহণ না করার, প্রত্যাহার করার অধিকার ঃ

এই গবেষণায় আপনার অংশগ্রহণ স্বেচ্ছায়। তার মানে হচ্ছে, আপনি এই গবেষণায় আপনার অংশগ্রহণ বর্জন বা পরিহার করতে পারেন। যে কোন সময় আপনি চাইলে আপনার অংশগ্রহণ প্রত্যাহার করতে পারেন, যদিও আপনি পূর্বে বলেছিলেন যেএইগবেষণায় অংশগ্রহণ করবেন। যে কোন ধরনের অস্বস্তিকর প্রশ্নের উত্তর আপনি এড়িয়ে যেতে পারেন।

আপনার কি কোন প্রশ্ন আছে? হ্যাঁ/না

আপনি কি এই গবেষণায় অংশগ্রহণের জন্য রাজী আছেন? হ্যাঁ/না

এখন আমরা আপনাকে এই গবেষণায় অংশগ্রহণের জন্য আমন্ত্রণ জানাচ্ছি। আপনি যদি রাজী থাকেন,তাহলে অনুগ্রহপূর্বক অংশগ্রহণের সম্মতির নির্দেশনা স্বরূপ নীচে নির্ধারিত স্থানে আপনার নাম অথবা স্বাক্ষর দিন।

_____ _____

অংশগ্রহণকারীর স্বাক্ষর অথবা নাম তারিখ

_____ _____

গবেষকেরস্বাক্ষর তারিখ

Annex III

TB 05

NATIONAL TUBERCULOSIS CONTROL PROGRAMME (NTP)
Directorate General of Health Services, Bangladesh
Request Form for AFB Microscopy Examination

(The completed form with results should be sent promptly by the Laboratory to the referring facility)

Name of Referring Facility[1]/Providers: _____ Date: _____

Name of Patient: _____ Age: _____ Sex: ☐ M ☐ F

Occupation _____ Name of Father / Husband _____

Full Address of Patient: _____

_____ Telephone no. (if any): _____

OPD Reg. No. (if any); (For suspects only): _____

Reason for examination: ☐ Diagnosis ☐ Follow-up If follow-up, No. of month of Treatment: _____

Disease Classification: ☐ Pulmonary ☐ Extra-pulmonary (EP) If EP, Site: _____

Nature of Specimen: ☐ Sputum ☐ Urine ☐ Pus ☐ Other, specify: _____

Specimen identification no: _____ Patient TB Registration No: _____
(For follow-up patients)

Signature of person requesting examination: _____

Name & designation of person requesting examination: ----------

1. Including all public and private health facility/providers

---

RESULTS (To be completed in the Laboratory)

Lab Registration No: _____

Visual appearance of the specimen (if it is sputum): ☐ Muco-purulent ☐ Blood-stained ☐ Saliva

Microscopy results

Date of Collection*	Specimen	Result				
		Negative	Scanty (1-9)	1+	2+	3+
	1					
	2					
	3					

Sputum collected by:

Signature: _____

Name: _____

Examined by:

Signature of Medical Tech (Lab) _____

Name: _____

Date: _____

Name of Lab/Organization: _____

* To be completed by the person collecting the sputum

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