Assessing TB infection control and preventive measures in TB patients in Chattogram metropolitan area

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The thesis submitted is in the partial fulfillment of the requirements for the degree of MPH (One Health)

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September, 2021

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(Farzana Rabiul Leela)

August 2022

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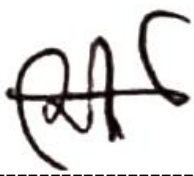

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Chattogram-4225, Bangladesh

August 2022

Acknowledgements

All praises to almighty Allah who gave me the opportunity to be enrolled in the **One Health Institute** for achieving Masters in Public Health. I would like to express my gratitude to honorable supervisor Prof. Shahneaz Ali Khanfor his coherent and articulated instructions. It would not be possible to complete such a laborious task without his scholastic guidelines. It was an exquisite experience for me to work under his supervision. I feel much pleasure to convey my gratitude to honorable co-supervisor Prof. Mohammad Mahmudul Hassan for his valuable suggestions and inspiration. I am grateful to all laboratory personnel at DOTS cornerfor their support and cooperation in relation to data collection during the fieldwork.

I would like to acknowledge the support and encouragement received during MPH programme from other teachers, technical and non-technical staffs of the One Health Institute, CVASU.

I am also grateful to my parents and family members for their support.

Farzana Rabiul Leela

Chattogram, Bangladesh

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List of Abbreviations

Abbreviation	Elaboration
CI	Confidence Interval
TB	Tuberculosis
MTB	*Mycobacterium Tuberculosis*
AFB	Acid Fast Bacillus
DNA	Deoxyribonucleic Acid
PTB	Pulmonary Tuberculosis
EPTB	Extra Pulmonary Tuberculosis
DST	Drug Susceptibility Testing
DR-TB	Drug Resistant Tuberculosis
MDR-TB	Multi Drug Resistant Tuberculosis
XDR-TB	Extensively Drug Resistant Tuberculosis
RR	Rifampicin Resistance
zTB	Zoonotic Tuberculosis
LMIC	Low- and Middle-Income Countries
DOTS	Directly Observed Treatment, Short-Course
FDC	Fixed Dose Combination
HRZE	Isoniazide+ Rifampicin+ Pyrazinamide+ Ethambutol
HRE	Isoniazide+ Rifampicin+ Ethambutol
HR	Isoniazide+ Rifampicin
ICDDRB	The International Centre for Diarrheal Disease Research, Bangladesh
FAST	Find cases Actively, Separate safely and Treat effectively
HCWs	Health Care Workers
NTP	National Tuberculosis Control Programme
SLDs	Second Line Anti-TB Drugs

Abstract

Treatment failure is a serious problem faced by many national tuberculosis control programmes. A total of 534 patients were enrolled in this study after meeting inclusion criteria. After obtaining consent, they were interviewed for history of contact exposure via phone interviews. The outcomes were recorded and analyzed using STATA-13. There were 332 (62.2%) male and 202 (37.8%) females. Majority of the study subjects were adults (95.8%) and belonged to lower socioeconomic class (93.6%). Most of them were married (92.1%) and lived in nuclear families (95.1%). In case of type of dwelling, more than half of the respondents (56.7%) lived in slums. Ten patients (1.87%) were found to have treatment failure with equal proportions in both male and female (50%). In case of type of dwelling, most cases of treatment failure lived in isolated houses (40%) and most cases belonged to nuclear families (90%). All cases of treatment failure were adults and were married (100%). Most of them belonged to lower class (90%). Smoking was the most prevalent risk factor among the study subjects and was present in 243 (45.5%) study subjects. Other common risk factors were previous history of anti-TB treatment (15.7%), comorbidities like diabetes (14.8%), malnourishment (13.3%), immunosuppressive therapy (12.7%), contact with domestic animals (6.7%), consumption of raw milk (5.6%), and history of contact with infected people (4.5%). As for total duration of treatment, 531 (99.4%) patients had taken treatment for 6 months. Only three (0.56%) patients received treatment for a short duration of 2 months due to adverse drug reactions. During treatment, 17 (3.2%) patients skipped medications in between while 517 (96.8%) did not. A significant association was found between shorter duration of treatment ($p<0.001$) and history of skipping medications during treatment ($p=0.037$) against treatment outcome. On observing odds ratio, the odds of getting cured were higher (OR=1.53; 95% CI: 0.28 - 28.36) among patients who were being re-treated for the disease after treatment failure. In order to control the spread of PTB in Bangladesh, interventions such as strengthening diagnosis of pulmonary TB further, implementing targeted communication programs and active case finding to reduce patient level delays, expanding public-private mix to increase access to TB services,

using rapid diagnostics, and providing social protection for vulnerable populations are necessary.

Keywords: *Tuberculosis, treatment compliance, Tuberculosis Control Programme, treatment outcome.*

CHAPTER 1- INTRODUCTION

Tuberculosis is an air born disease caused by the s*Mycobacterium tuberculosis* complex. This communicable and infectious disease is transmitted almost entirely by cough droplets. Pathologically, it is characterized by necrotizing granulomatous inflammation usually located in the lung. However, extra pulmonary infection can be located almost anywhere in the body (Dheda, et al., 2016). There are two types of tuberculosis that is based on the disease's anatomical site, namely, pulmonary and extrapulmonary tuberculosis. Pulmonary tuberculosis involves the lungs and is the active form of TB. Extrapulmonary TB involves parts of the body other than the lungs. These could be lymph nodes, bones or any other organs in the body. There is one other classification of TB based on drug resistance. If tuberculosis bacteria are resistant to just one first line anti-TB drug it is called Mono-drug resistance. However, if TB bacteria is resistant to more than one first line anti-TB drug is called Poly drug resistance. Multi-drug resistance is referred to cases of TB where patient is resistant to both isoniazid and rifampicin. Extensive drug resistance is the type of TB where the infecting TB bacteria is resistant to at least one of three second line anti-TB drug as well as fluroquinolone. Finally, Rifampicin resistance refers to TB cases where the bacteria is resistant to rifampicin with or without resistance to other anti-TB drugs (Park, 2017). Common signs and symptoms of TB includes cough, dyspnea, chest pain, hemoptysis, night sweating and anemia. Patients can also present with tachycardia, lung-auscultation findings, fever, low mid-upper arm circumference and low body mass index (Wejse, et al., 2008).

As reported by the World Health Organization, at least a third of the world's population has already been infected with tuberculosis (World Health Organization, 2021). The German physician and microbiologist, Robert Koch had famously stated that tuberculosis is much more dangerous than the plaque or cholera (Keshavjee & Farmer, 2012; Cruz-Knight & Blake-Gumbs, 2013).This statement holds true even today where about 9 million people were infected with the disease in 2020 and 1.5 million died due to this (World Health Organization, 2021).Exposure is usually from households in high- and low socioeconomic countries, though other congested areas such as hospitals or prisons were also observed to have higher infection rates (Goldman & Schafer, 2011) . The prevalence

of tuberculosis in such surroundings depends on innate immunity, bacterial virulence, and susceptibility of the host. Tuberculosis can occur in any society and from any country. Nevertheless, more than 95% deaths are reported in resource deficit low- and middle-income countries. Among them, majority of deaths are reported from India and China (Goldman & Schafer, 2011).

Tuberculosis is among the top-ten major causes of death globally and is the second most common cause of death from a single source of infection after COVID-19 (World Health Organization, 2021). As part of the Sustainable Developmental Goals (SDG), WHO has launched an End Tuberculosis strategy in the year 2014. The aim of this strategy was to end the global epidemic of tuberculosis by 2035 (WHO, 2015).There are targets to reach in 2030 and 2035 and milestones to touch by2020 and 2025 for the number of TB cases and case fatality rates in order to achieve this goal. In order to achieve the 2025 milestone, it was first necessary to achieve the 2020 milestone. This first milestone was a 20% reduction in the incidence rate of tuberculosis as compared to that in 2015 (WHO, 2015). However, the target was only partially met with 11% reduction in TB cases (WHO, 2021). Similarly, a 35% reduction in deaths due to tuberculosis in the time frame of 2015 to 2020 were targeted. However, achievement of this target was much lower with only 2% reduction in death rates by 2020 (WHO, 2021).

It has been reported that around 26% of the world's population belongs to the South-East Asia (SEA) Region of WHO and the burden of TB incidence in this area is 44%. In fact, 86% of all estimated cases worldwide were from the 30 high TB burden countries. Eight of these countries accounted for two thirds of the total incidences, i.e., India (26%), China (8.5%), Indonesia (8.4%), the Philippines (6.0%), Pakistan (5.8%), Nigeria (4.6%), Bangladesh (3.6%) and South Africa (3.3%). In order to improvement TB treatment, all these regions have sustained a countrywide access to Directly Observed Treatment, Short course. (DOTS) (WHO, 2021).

In 2019, approximately 10 million people got infected and among them, 1.2 million people died from the disease. Around 79% of these cases were from the 30 high-burden countries (WHO, 2021). With an estimated population of 164 million, Bangladesh is listed among the high burden countries for TB and for multi-drug resistant TB (MDR-TB). Around 3.6% of the total cases of tuberculosis is attributed to Bangladesh making it

among the top eight countries that cumulatively make up two-thirds of the Global TB burden. Although it has achieved notable progress in improving a multitude of health indicators over the last decade, including those related to TB diagnosis and treatment, TB remains a public health concern to this day. According to the most current Global TB Report, more than 200,000 cases of tuberculosis has been reported to the National Tuberculosis Control Programme (NTP) in the year 2019 (WHO, 2021). The childhood TB cases reported were nearly 4% of all cases which is still a huge challenge in Bangladesh. The incidence rate for all forms of tuberculosis was 221 per 100,000 population per year. The TB mortality was 24 per 100,000 population per year with over 38,000 deaths annually. Similarly, MDR-TB was 0.7% among new and 11% among retreatment cases with a large absolute number of patients (~3,300 MDR/RR cases) that need to be treated with the second line anti-TB drugs (SLDs). Although TB treatment coverage increased from 27% in 2002 to 81% in 2019, an estimated 68,000 (19%) TB patients remained undetected every year with a static TB incidence - between 225/100,000 and 221/100,000 from 2001 to 2019 (WHO, 2021). Around 80% of all cases of tuberculosis in Bangladesh are pulmonary TB (WHO, 2021).The recent COVID-19 pandemic has reversed years of progress in providing essential TB services and reducing TB disease burden. The most noticeable effect was a large global drop in reporting newly diagnosed cases of TB. This was reduced from 7.1 million in 2019 to 5.8 million in 2020, an 18% decline back to the level of 2012 and far short of the roughly estimated 10 million people who developed TB in 2020. Sixteen countries accounted for 93% of this reduction, with the Philippines, Indonesia and India being the worst affected.

While the burden of tuberculosis in Bangladesh is high, the emergence of resistant strains has further complicated the matter with an increase in demand for better antibiotics to combat the resistant strains. Hence, it is necessary to identify any loopholes or faults in our infection control and prevention methods so as to negotiate and rectify them before the condition worsens. The aim of this study is to assess the infection control and treatment of TB cases among patients in a metropolitan city of Bangladesh.

RATIONALE

According to a recent study by Kak et al (2020), detection of PTB is almost 100% in Bangladesh, as compared to other south Asian countries like Indonesia and the Philippines where detection rates are 30% or less. Despite this, no impact has been observed on the incidence rates of PTB since a large proportion of the undiagnosed cases, and cases of delayed diagnosis continue to supply the transmission process. Moreover, little is known about the reasons for failed treatment among patients who seek care for tuberculosis. Hence, the aim of this study is to identify any gaps in treatment or any predictive factors that can lead to treatment failure among the patients.

OBJECTIVES

General: To find out any gaps in measures of control and prevention of tuberculosis.

Specific:

1. To find out the demographic characteristics of the patients
2. To evaluate risk factors associated with tuberculosis among the patients
3. To identify the causes of treatment failure among the patients

CHAPTER 2- LITERATURE REVIEW

2.1 History and origin of tuberculosis

Tuberculosis (TB) is a transmittable, infectious disease, that is caused by the bacteria *Mycobacterium tuberculosis* (MTB). Owing to its severe social implications, this contagious disease has always been a challenge over the course of human history (Barberis, et al., 2017). The genus Mycobacterium is hypothesized to have originated over 150 million years ago from other, more primitive organisms of the same genus (Adams, 1849). According to many research theories humans were thought to have first acquired tuberculosis in African continent around 5,000 years ago (Zimmer, 2014). Nevertheless, one study shows evidence that the infection happened at least 3,000 years earlier than thought before after discovering TB in human bones from 9,000 years ago (Hershkovitz, et al., 2008). In ancient Greece tuberculosis was recognized under various names such as phthisis, consumption and the White Plague (Adams, 1849). In England and France an illness known as scrofula has infected middle aged people where the disease has affected the cervical lymph nodes. These new clinical features were described to be TB and the disease was called “King’s Evil”. It was believed that only a royal touch could heal the affected person (Murray, et al., 2016).

Then in 1720, an English physician named Benjamin Marten, inferred the infectious origin of Tuberculosis for the very first time and introduced infirmary cure as the first remedy to treat this disease (Barberis, et al., 2017). Following this, many scientists attempted to isolate the tubercle bacilli with the German physician and microbiologist Heinrich Hermann Robert Koch finally succeeding in discovering the cause. In 1882, he was able to isolate the tubercle bacillus using staining by methylene blue using which he identified and cultivated the bacillus in animal serum. This has been a landmark in the battle against TB (Bartolozzi, 2012). In the following decades, the Pirquet’s skin test for TB, the Mantoux tuberculin skin test; the Bacillus Calmette-Guérin(BCG) vaccine, Selman Waksman streptomycin and many other anti-tuberculous drugs were developed (Gradmann, 2001).

2.2 Global epidemiology of tuberculosis

Tuberculosis is a major public health concern around the globe even after having effective treatment. If timely diagnosed and treated using first-line antibiotics continuously for 6 months, most people affected by TB can be cured and can hence limit further transmission of the disease. Specific targets have been defined by The United Nations (UN) Sustainable Development Goals and the World Health Organization's (WHO's) End TB Strategy for 2020–2035. These include a 20% reduction in incidences of TB by 2020 and a 35% reduction in the number of TB deaths as compared to 2015. Since 2000, WHO has been delivering data regarding annual TB estimates for every country (WHO, 2021). In 2011, an estimated 8.7 million incidents of TB were observed globally, ranging between 8.3 million to 9.0 million. This was equivalent to about 125 cases per 100 000 population. Majority of these cases occurred in Asia (59%) and Africa (26%); while only few cases were reported from the Eastern Mediterranean Region (7.7%), the European Region (4.3%) and the Region of the Americas (3%). The rates of infection were relatively constant from 1990 to 2001, and then began to fall by 2% every year. Between 2015 and 2020, a cumulative reduction of 11% was noted. In the year 2017, out of an estimated 10 million incidents, a total of 1.57 million deaths were reported thus demonstrating a 1.8% decline in incidents and a 3.9% decline in deaths respectively from the previous year. In 2018, TB-related deaths further dropped to 1.5 million, however, the disease remained the most infectious killer worldwide, with around 10 million people still falling sick in that year. The burden of the disease varies among different countries, with less than 5 per 100,000 to more than 500 new cases per 100 000 population per year, recording a global average of approximately 130 per 100,000 population per year. Geographically, cases of TB in 2018 were most prevalent in the WHO regions of South-East Asia (44%), Africa (24%) and the Western Pacific (18%), with reduced percentages in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%). Among them, 8 countries made up two thirds of the global total. These were India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). All these countries along with 22 others are recorded as the 30 high TB burden countries in WHO's list and accounted for about 87% of the world's new cases (WHO, 2021). In 2019, an estimated 10 million

people were afflicted with the disease worldwide among which there were 5.6 million men, 3.2 million women and 1.2 million children. Treatment for tuberculosis has increased from around 6 million in 2015, to about 7 million in 2018 and further to 7.1 million in 2019. Along with this, approach to preventive treatment for TB has also increased gradually from 1 million in 2015, to 2.2 million in 2018 and 4.1 million in 2019(WHO, 2020).

Although the TB incidence rate is declining, globally, it could not reach the 2020 milestone of a 20% reduction from 2015 and 2020. The cumulative reduction was 11% during this period and was just over halfway of the target (WHO, 2020). This is due to the setbacks due to the COVID-19 pandemic. People suffering from financial and other resources in many countries have been redistributed from TB to the COVID-19 response. A negative impact was also observed in the data collection and reporting systems. Hence, national TB programs were put under immense pressure leading to an estimated increase in TB deaths in the near future (Buonsenso, et al., 2020).

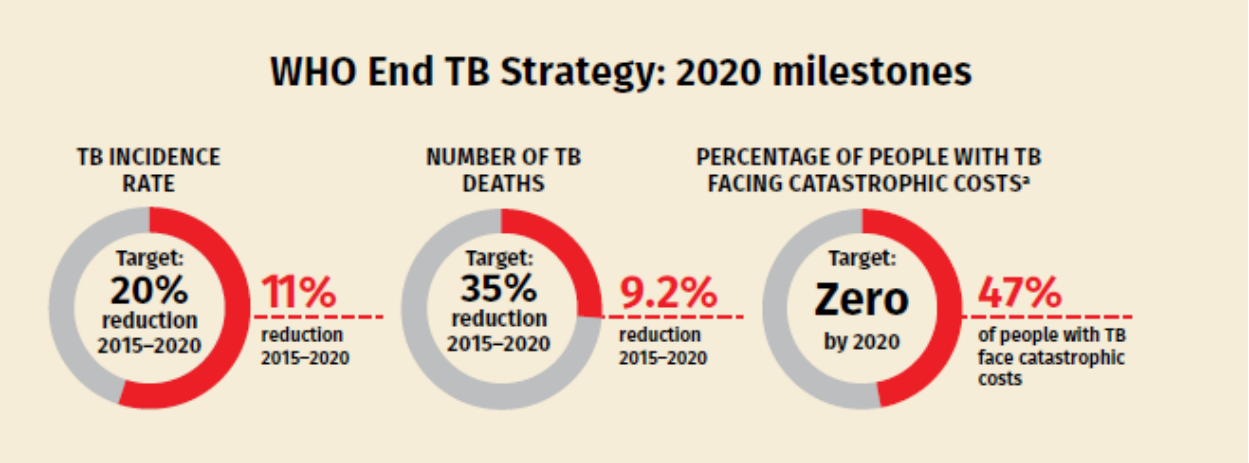


Figure 2.1- Achievements versus the targeted milestones by 2020 (WHO, 2021)

2.3 Out breaks of tuberculosis in Bangladesh

Bangladesh is a highly populated country facing poverty, dense living, overcrowding, poor living and working condition which are factors that cause major spreading of TB. Moreover, maximum population lack of consciousness about TB infection. Most of the metropolitan areas in Bangladesh are heavily populated and about one third of them are

slum dwellers, producing favorable condition for high TB transmission (Banu, et al., 2013). Bangladesh is among the 30 high TB and MDR-TB burden countries. It has one of the highest rates of TB cases in the world. The national MDR-TB prevalence is at an estimated 1.6% for new TB cases and 29% in old, treated TB cases (DGHS & WHO, 2021). Tuberculosis healthcare service started in 1965 under several TB clinic and hospitals and during the 80's the treatment has expanded to 20% areas of the country (in second health and population plan (1980-1986)). In the mid-90's the National tuberculosis control program (NTP) started its field implementation and slowly expanded to cover most part of the country. In 2002, DOTS was extended to Dhaka Metropolitan City and by the year 2003, 99% of the population was given DOTS services (Hossain, et al., 2012). In the year 2006, the 'Stop TB' strategy was adopted by NTP. The country had seen a significant rise in TB cases since 2012 which was mainly due to an increased number of clinically diagnosed pulmonary and extra-pulmonary cases. Following this, the Government of Bangladesh along with collaboration with Non-Government Organizations (NGOs) started implementing TB control programs. In the year 1993, the National Tuberculosis Program (NTP) of Bangladesh adopted the DOTS (Directly Observed Treatment Short course) strategy. The following year, the international developmental organization, BRAC (Building Resources Across Communities) signed an (Memorandum of Understanding) MoU with the government to expand DOTS services nationwide in order to strengthen the health care system (NTP, 2015). BRAC's TB control program now encompasses 298 sub-districts in 42 districts incorporating a population of approximately 93 million including the Hill tracts of Chattogram. Due to the TB Control Programs Bangladesh over the past few years has attained good reporting coverage of case detection and treatment success but still the present findings are not very intense. Hence, TB control actions must be sustained, with an increased focus given to people of an older age and the rural population (CDC, 1997). Bangladesh had adopted a five-year National Strategic Plan for TB control (2015-2020) that has helped reduce the number of TB cases and increased the successful treatment rate to at least 90% for all types of TB. This plan also helped ensure proper treatment of all sorts of MDR-TB and also train all private and public health provider (Van Deun, et al., 2004). Below is a graphical representation of CDR (Case detection rate) which is the number of cases

detected and expressed as a percentage of cases estimated to occur annually (DGHS, 2017).

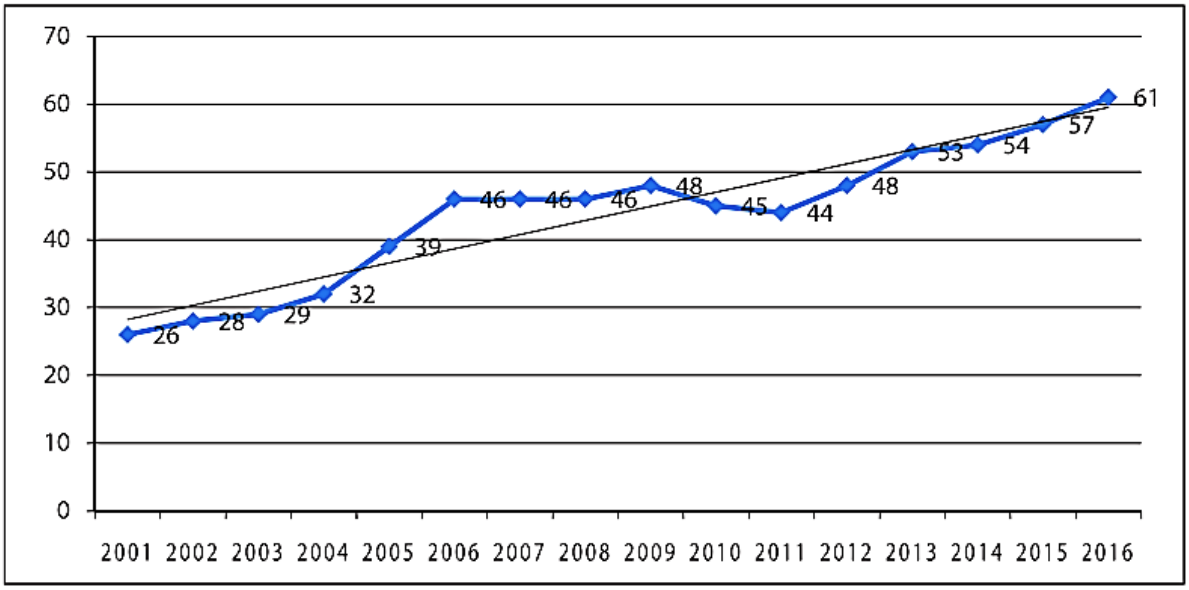


Figure 2.2: TB case detection rate all forms in Bangladesh (2001-2016)

2.4 Pathogenesis and transmission of tuberculosis

Mycobacterium Tuberculosis is an aerobic non spore forming and nonmotile bacillus that has unusual, waxy coating rich in mycolic acid present on its cell surface (Brennan, 2003). It was found to be a complex in 2019 that consists of at least 9 members: *M. tuberculosis sensustricto, M. canetti, M. microti M. caprae, M. mungi, M. pinnipedii, M. orygis, M. bovis and M. africanum*, (van Ingen, et al., 2012).Among these, most of the TB cases are caused by *M. tuberculosis sensu strict*oor or *Mycobacterium africanum*. Few cases occur due to zoonotic members of the M. tuberculosis complex, such as *Mycobacterium bovis*or *Mycobacterium caprae* (Bose, 2014). *M. tuberculosis* organisms are also called tubercle bacilli.

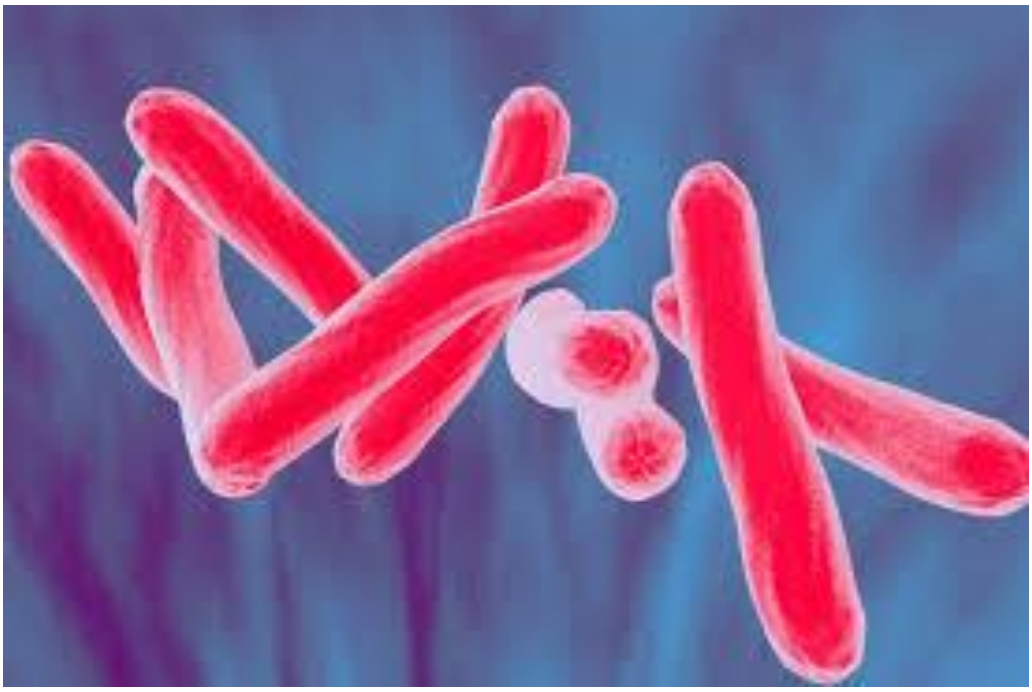


Figure 2.3: *Mycobacterium Tubercolosis* under microscope

M. tuberculosis is carried around in airborne particles of 1– 5 microns in diameter, called droplet nuclei. These droplets are released when the infection is within the pulmonary tract or in the laryngx and patient with TB cough, sneeze, sing or shout. These tiny droplets containing *tubercle bacilli* can stay floating in air for several hours depending on the atmosphere. Air is the only medium for transmitting the disease i.e., when a person breath in these infectious droplet nuclei, it transverse the mouth or nasal passage and goes in to the upper respiratory tract which then reach tiny lung alveoli. Usually after inhalation special immune cells called macrophages engulf and surround the tubercle bacilli within 2 to 8 weeks.

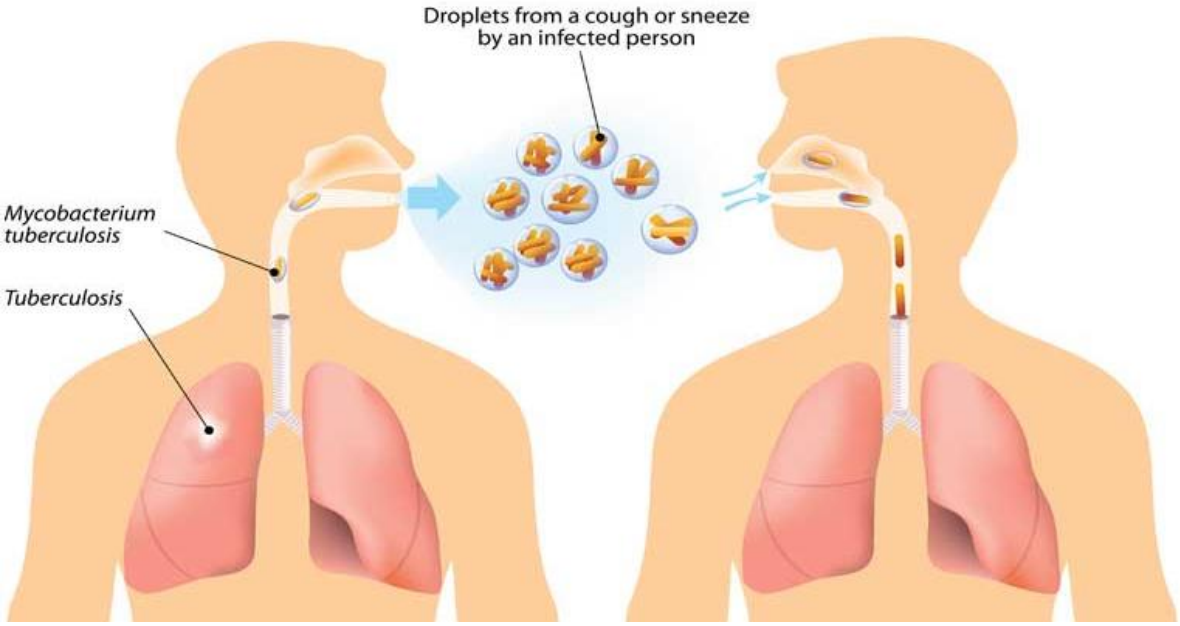


Figure 2.4: TB transmission from one person to another through the air. The dots in the air represent droplet nuclei containing tubercle bacilli.

Once these tubercle bacilli are consumed by alveolar macrophages; most of the bacilli are damaged or inhibited. A few may replicate within the macrophages and be released once it dies. The ingestion of bacilli by the macrophages triggers an immune response where more macrophages, epithelioid cells, B lymphocytes, T lymphocytes, and fibroblasts come together to form granulomas (a barrier shell), and lymphocytes surround the infected macrophages keeping the bacilli under control. This condition is known as latent tuberculosis infection (LTBI). In its early stage, the granuloma usually expands the infection by allowing bacteria to multiply and spread to the new macrophages as displayed in the figure below. But as immunity develop these granulomata restricts bacterial growth. Thus, within a few weeks after infection, if the immune system can stop the multiplication of the tubercle bacilli then further disease progression can be prevented. But in few cases if the immune system cannot control the tubercle bacilli, the infected granuloma macrophages can die and undergo necrosis, forming a necrotic core that maintains bacterial growth and transmission leads to a condition known as TB disease which need immediate medical attention. The active bacilli then may spread via lymphatic system or the bloodstream to more remote tissues and organs such as the apex of the lung, regional lymph nodes, kidneys, brain, and even bones. A person with TB

disease is highly contagious and may propagate the disease to other people. The progression from latent TB to active TB disease can occur at any time, from very soon after infection to many years later.

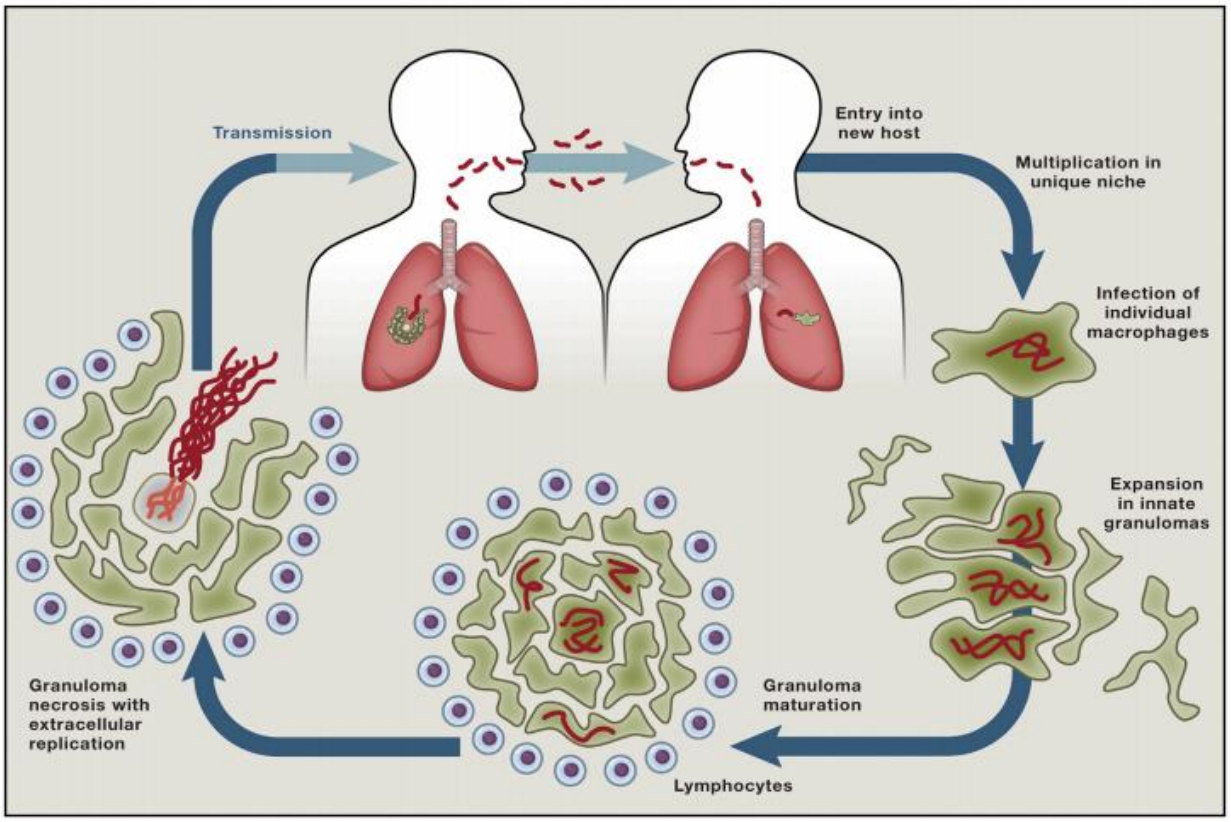


Figure 2.5: Pathogenic Life Cycle of *M. tuberculosis*(Cambier, et al., 2014)

2.5 Classification of TB

TB cases whether they are bacteriologically confirmed or diagnosed clinically, can be classified according to the anatomical site, previous treatment history, resistance to Anti-TB drugs, and HIV status.

2.5.1- Based on the Anatomical site

Based on anatomy, cases can be categorized in to Pulmonary and Extra Pulmonary TB.

Pulmonary TB (PTB)

Pulmonary tuberculosis (PTB) describes any clinically diagnosed or bacteriologically confirmed case of tuberculosis that involves the lung parenchyma or the trachea and

bronchi. Pulmonary tuberculosis also includes miliary TB since lesions are found within the lungs. Intra-thoracic tuberculous lymphadenopathy or pleural effusion due to tuberculosis, without any abnormal radiographic findings in the lungs are considered as extra-pulmonary TB cases. If a patient has both pulmonary and extra- pulmonary TB, they should be classified as a case of PTB.

Extra-pulmonary TB (EP TB)

Any bacteriologically confirmed or clinically diagnosed case of TB that involves organs other than the lungs are known as extra-pulmonary tuberculosis (EPTB). These include the pleura, larynx, meninges, lymph nodes, abdomen, genitourinary tract, bones and joints, skin, spine, etc. The two types of TB are summarized in **Figure 2.6**.

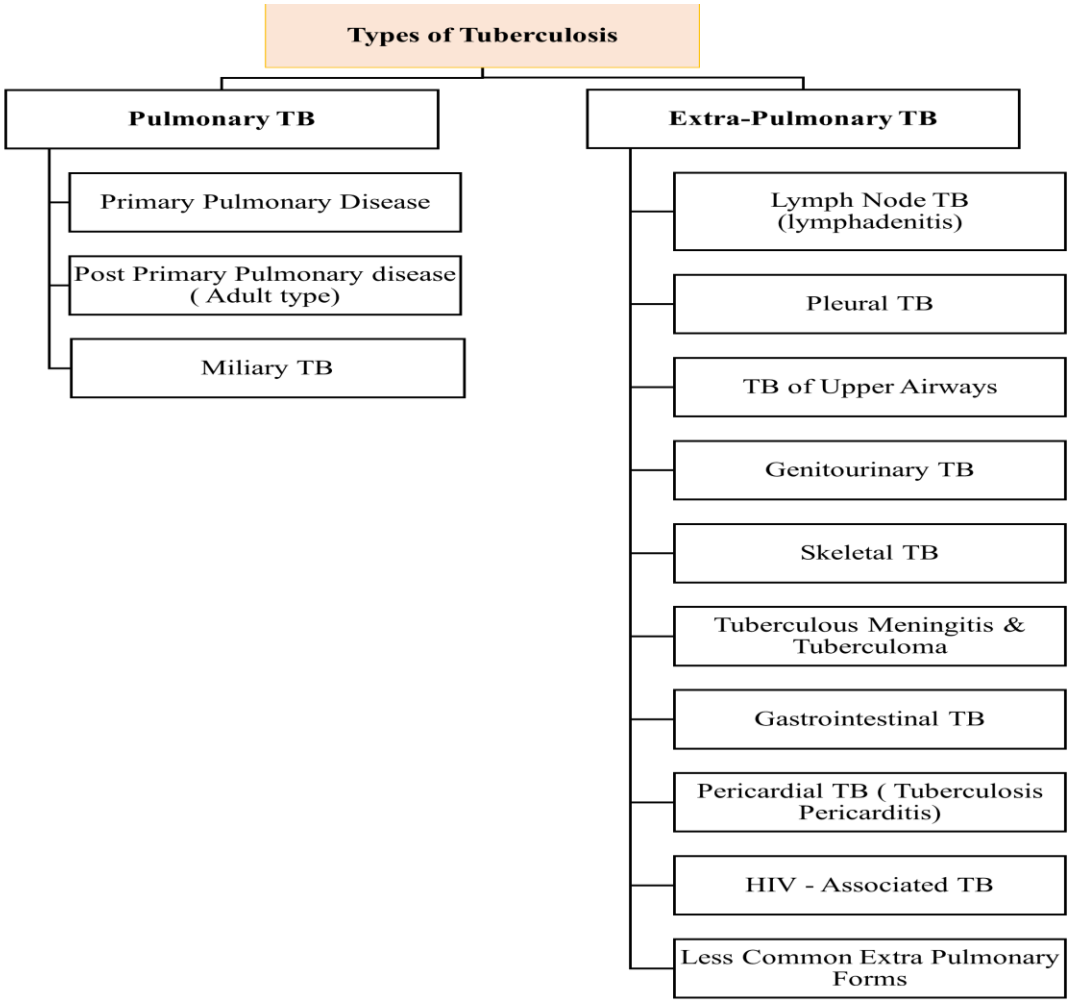


Figure 2.6- Classification of TB based on anatomical site

2.5.2 Based on previous treatment history

New cases: If a patient has never taken treatment for TB or if a patient who has taken treatment for less than one month are defined as new cases. These patients may have positive or negative bacteriology and could contain disease at any site in the body.

Previously Treated: These are patients who has received anti-tuberculosis drugs for treatment for at least one month previously. Based on their most recent course of treatment outcome, they are further sub-classified as treatment after failure, treatment after loss to follow up, relapse cases and previously treated other cases. **Table 2.1** below displays the subclassification of previously treated TB cases.

Table 2.1- Classification of previously treated cases

Relapse	Relapse patients have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).
Treatment after failure	Patients are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.
Treatment after loss to follow up	Patients have previously been treated for TB and were declared lost to follow-up at the end of their most recent course of treatment.
Other previously treated	Other previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

2.5.3 Based on Drug resistance

Mono- resistance- Resistance to only one first-line anti-tuberculosis drug.

Poly- resistance- Resistance to more than one first-line anti TB drug except for isoniazid and rifampicin combination.

Multi-drug resistant TB (MDR-TB)- Resistance to at least isoniazid and rifampicin, with or without resistance to other first line drugs.

Extensively drug resistant TB (XDR-TB)- Refers to MDR-TB with additional resistance to drugs such as levofloxacin or moxifloxacin or and to one of any of the two other group A drugs (Bedaquiline, Linzolid)

Rifampicin Resistance- This is detected using phenotypic or genotypic methods where the TB is resistant to rifampicin alone.

2.5.4 Based on HIV status

People infected with human immunodeficiency virus (HIV) are more likely to become severely ill with tuberculosis. Here both HIV and TB work together thus reducing host lifespan and quality of living.

An **HIV- positive TB patient** is a clinically diagnosed or bacteriologically confirmed TB patient who also has a positive HIV test result. The HIV test could have been conducted during testing for TB or there may be documented evidence of admission in HIV care such as registration in the pre-ART register or ART register.

HIV-negative TB patient refers to any clinically diagnosed or bacteriologically confirmed case of TB with a negative result for HIV testing done during the time of TB diagnosis. If an HIV negative patient is later found as HIV positive during the course of treatment for TB, they should be reclassified as HIV positive.

HIV status unknown TB patient implies TB patients that are clinically diagnosed or bacteriologically proved to be TB positive, but their HIV status is unknown due to lack of HIV test result or documented evidence of registration in any HIV care centers. If at a later time the HIV status of the patient is determined, he/she is reclassified appropriately.

2.6 Clinical symptoms of tuberculosis

In case of severe Pulmonary TB the following classic symptoms appear: Persistent cough, lasting at least 3 weeks, cough with blood in sputum (hemoptysis), loss of appetite and weight, fatigue, shortness of breath, swelling in the neck, low grade fever, night sweats, chest pain and abnormalities on chest x-ray (e.g., upper lobe infiltrates, cavitation).TB usually affects the lungs but in certain cases it may affect other parts of the

bodies showing different symptoms. Depending on the anatomical location of the infection symtoms may include:

1 Persistently swollen lymph nodes, or “swollen glands”
2 Abdominal pain
3 Joint or bone pain
4 Confusion
5 A persistent headache
6 Seizures
7 Blood in your urine

The most significant for successful TB control lies in the identification and successful treatment of TB patients with a smear positive pulmonary TB. A person is believed to have Pulmonary TB if he presents with cough persisting for two weeks or more despite using antibiotics and irrespective of sputum production. Thus, presumptive TB refers to any patient who has symptoms or signs of TB. They should be confirmed using GeneXpert or Sputum microscopy. In fact, any patient with cough persisting for two weeks or more even in the absence of other symptoms should undergo GeneXpert or sputum microscopy testing. Additionally, contacts of microbiologically confirmed TB patients, people living with HIV, malnourished people, diabetics, patients on immune-suppressants or steroids and cancer patients should be screened regularly for sign and symptoms of TB.

2.7 Diagnosis of tuberculosis

Latent TB infections are usually asymtomatic but if a person suspects of being exposed to the organism he/she may undergo the following screening test which would confirm wheather or not the organism is active.

1. Immunological diagnosis includes ALS assay, Tuberculin skin test, Mantoux skin test Transdermal patch.
2. Blood tests include adenosine deaminase test, Nucleic acid amplification tests (NAAT), and Interferon-γ release assays (IGRA).
3. Microbial tests include sputum, laryngeal swab, gastric washing, bronchoscopy, and PCR analysis. WHO recommended test include Xpert MTB/RIF, Xpert Ultra and

Truenat assays. Radiography diagnosis includes chest X-ray and CT chest imaging, FDG PET/CT tests are performed to identify any abnormalities in the lungs (Islam, et al., 2017).

2.8 Prevention & control of tuberculosis

Tuberculosis is an airborne disease that spreads when an infected person coughs, releasing tiny droplets containing the bacterial organisms into the air. It is not spread by sharing utensils, food, drinks, by touching, or having sex. Thus, the following preventive measures can prevent and control TB.

1. Early diagnosis and treatment
2. Using mask i.e. covering the mouth and nose when coughing or when close to a TB patient, this could aswell prevent the spreading of many other airborne disease.
3. TB patients must ware mask and limit contact with others until he/she is confirmed to be non contegious.
4. Getting vaccinated.
5. Proper disposal of tissues used while sneezing and coughing.
6. Educating the general public about TB
7. Proper ventilation where a TB patient stays
8. Beining isolated i.e staying indoor when infected with TB reducing exposure of the organism to healthy individuals.
9. Using respiratory hygienes when infected with TB
10. Health care providers must follow infection control procedures to prevent passing on the infection from one person to another.

2.9 Treatment for tuberculosis

When a person has TB disease (active organism multiplying in the body) his immune system is weak and as a result cannot stop the organism from growing in the body. At this condition the patient is very contagious and can spread the infection to others. It is very important to take proper treatment and finish the course as prescribed or else high chances that the organism would get resistant to the given drugs and as a result the treatment procedure would become expensive and difficult to cure. TB disease can be

treated by taking various drugs for about 6 to 9 months. More than 20 drugs are used for the treatment of tuberculosis disease. The treatment given for TB patients are as follows.

New TB patients:

Whether bacteriologically confirmed or clinically diagnosed, all patients with drug-sensitive tuberculosis (DS TB) will undergo the usual treatment regimen, which consists of 4 medications (HRZE) during the first 2 months (Intensive Phase) and 2 drugs (HR) for the following 4 months (Continuation Phase). In some cases of EP-TB, such as CNS TB, skeletal TB, and disseminated TB, the treatment may be prolonged at the discretion of the treating physician.

Previously Treated TB patients:

Drug Susceptibility Testing (DST) will be performed on every patient, and the regimen will be chosen based on the DST results. All previously treated pulmonary and extra-pulmonary TB patients who have had their bacteriology verified will receive the Cat.1 regimen, which is 2EHRZ/4HR, if the results of the DST demonstrate that the patient is sensitive to both rifampicin and isoniazid. In some cases of EP-TB, such as CNS TB, Skeletal TB, and Disseminated TB, the treatment may be prolonged based on the treating physician's clinical judgment. All patients with pulmonary TB who have received prior therapy and have a clinical diagnosis (PT Cases) will be prescribed a 4-drug regimen for 6 months (6HRZE). Patients with TB who undergo drug susceptibility testing and whose results indicate that Rifampicin is susceptible, but Isoniazid is resistant (Hr-TB) or that the data are unavailable are prescribed a 5-drug regimen along with the antibiotic levofloxacin for a period of six months. Patients exhibiting other patterns of resistance must be handled as necessary. There are two phases to the treatment of drug-sensitive tuberculosis:

Intensifying phase (IP): For the first two months of (4FDC) treatment, this is given daily. During the intensive phase (IP), the goal of combining four medications is to quickly eliminate the actively expanding bacillary population. Drug resistant mutants will no longer emerge as a result of this phase's removal of naturally occurring mutants that

are resistant to drugs. The contagious patients quickly stop being contagious (within approximately two weeks of treatment initiation).

The continuation phase (CP), which is given for four months (2FDC), is crucial for getting rid of the residual bacterial population, mostly persistent ones that are largely to blame for relapses. The CP may be extended past 4 months in some exceptional circumstances. Depending on the category, the medications are given every day for the remainder of the treatment period. The status of resistance to at least rifampicin, and preferably isoniazid, should be determined by a fast molecular test or drug susceptibility testing for previously treated (PT) patients who are suitable for retreatment. The patient is started on a 6-month course of 5 medicines (4 FDC + Levofloxacin) if rifampicin sensitivity, but isoniazid resistance is found (Hr-TB)/H DST uncertain. However, an MDR-TB regimen is necessary if rifampicin resistance is found. However, if rifampicin resistance is detected, an MDR-TB regimen should be prescribed according to recent drug resistant TB treatment guidelines. The standardized treatment regimen for each diagnostic category in adult patients is summarized in the table below.

Table 2.2- Standardized treatment regimen for each diagnostic category (adult)

<table>
<tr><th rowspan="2">TB diagnostic category</th><th rowspan="2">Type of Patient</th><th colspan="2">Treatment regimen</th></tr>
<tr><th>Intensive phase (Daily)</th><th>Continuation Phase (Daily)</th></tr>
<tr><td rowspan="4">New Cases (never been treated for TB or have taken ATT for < 1 month)</td><td>Bacteriologically positive PTB patients</td><td rowspan="4">2 (HRZE)</td><td rowspan="4">4 (HR)</td></tr>
<tr><td>Bacteriologically negative PTB patients</td></tr>
<tr><td>Extra-pulmonary TB*</td></tr>
<tr><td>TB/HIV co-infected</td></tr>
<tr><td rowspan="4">Previously Treated Cases (received ≥ 1 month of ATT in the past) **</td><td>If no resistance to TB drugs (both H and R sensitive P and EP TB Cases)</td><td colspan="2">6 HRZE</td></tr>
<tr><td>Clinically diagnosed PTB</td><td colspan="2">6 HRZE</td></tr>
<tr><td>Complicated EP cases (TB meningitis, Neurological TB, Bone TB, non-resolving lymph node)</td><td colspan="2">12 HRZE-Lfx</td></tr>
<tr><td>If Rif susceptible and INH resistant or unknown in bacteriologically confirmed PTB & EP-TB</td><td colspan="2">6 (H)REZ- Lfx</td></tr>
</table>

** Treatment for certain EP TB may be prolonged till 12 months if non-resolving lymph nodes at 6 months; 12 months in case of CNS, TB meningitis, bone TB etc.*

2.10 Risk factors associated with tuberculosis

Tuberculosis is an airborne disease and can affect anyone who inhales the organism. But it completely depends on the patient what the progression of the disease would be from exposure to tubercle bacilli (latent Tb) to the development of active TB disease. These two stages (infection phase to Active TB disease) are governed by several exogenous and endogenous risk factors. Some of them are given below:

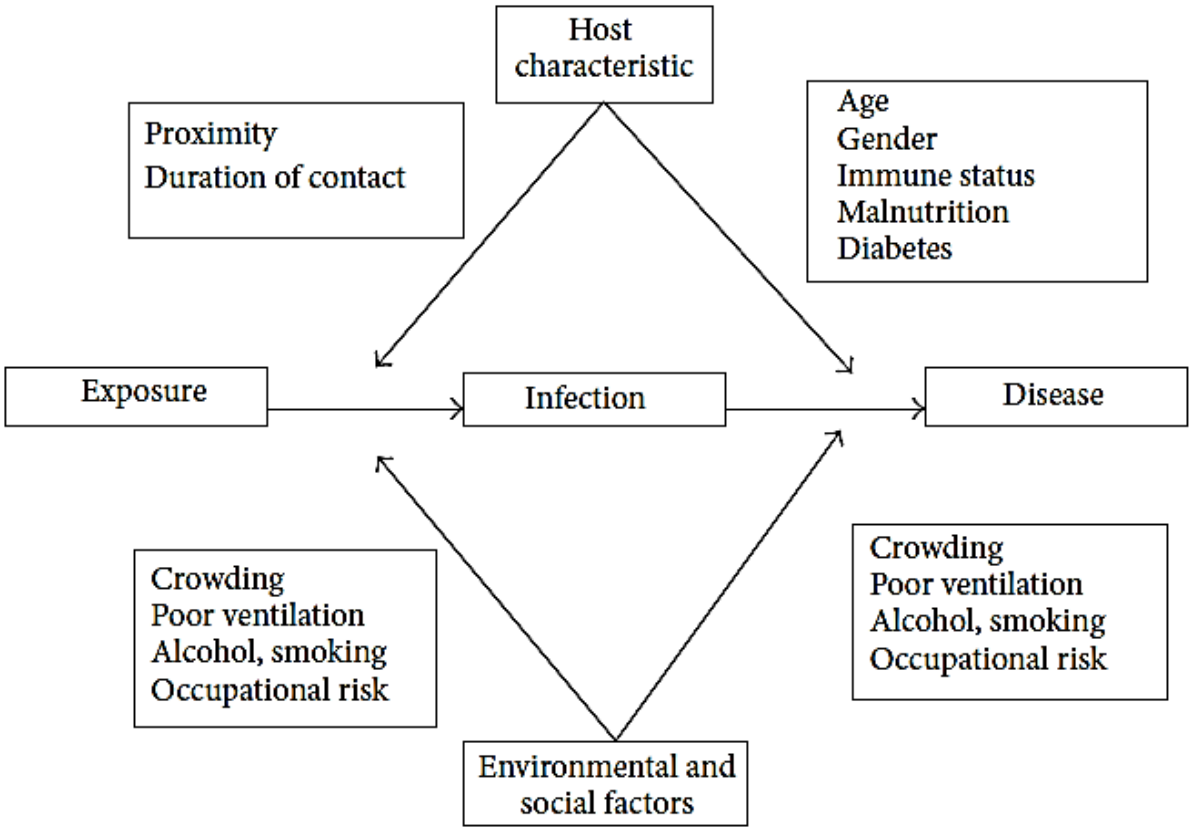


Figure 2.7: Risk factors associated with Tuberculosis infection and disease.

2.10.1 Factors related to the Index Case

Bacillary Load- The concentration of tubercle bacilli in the sputum of a TB patient is positively correlated with the severity of the disease. Many experiments in different countries have shown that smear negative patients are expected to have reduced number of bacilli than smear positive patients, but the infecting dose of *M. tuberculosis* bacilli can be as little as one to ten bacilli. So, smear negative patients are also contagious but

the prevalence of infection and disease is higher among contacts with smear positive patients (Hobby, et al., 1973; Menzies, 1997; Singh, et al., 2005).

Proximity to an Infectious Case- Staying in close contacts with TB patients such healthcare workers are at high risk of becoming infected with *Mycobacterium tuberculosis.* TB can be transmitted in very short time to many people at the same time if the air gets infected with the bacilli. This transmission very quickly leads to endemic situation especially in nontraditional locations, where poverty, overcrowding, drug abuse, being homeless, poor ventilation and high infection pressure are key factor which increase casual transmission of TB (Golub, et al., 2001) (Marais, et al., 2005).

2.10.2 Factors related to patient condition

Immunosuppressive Conditions- HIV patients are the most potent immunosuppressive and are at very high risk for developing active TB disease. HIV can exacerbate the severity of TB disease where the coinfection with Tb accelerates HIV replication in affected organs including lungs and pleura (Corbett, et al., 2003). Individuals with immune-mediated inflammatory disorders (IMID) are also known to be at increased risk of developing active TB, especially after the use of tumor necrosis factor (TNF)—alpha inhibitors to treat a variety of autoimmune disease (Winthrop, 2006).

Malnutrition- Nutrition deficiency (both micro and macro deficiency) causes an impaired immune response with further increases the risk of TB. Since TB itself leads to severe malnutrition due to loss in appetite and changes in metabolic processes (Cegielski & McMurray, 2004) (Chandra & Kumari, 1994).

Age- Children are at higher risk of contracting TB infection and disease compared to adults. Studies have shown that majority of children (< 2 years age) get infected from household sources, whereas children above 2 years get infected from the community (Marais, et al., 2004).

Diabetes- The chances for a person with diabetes to develop active TB is three times compared to a normal individual. About 15% of TB cases in the world is linked to diabetes. Diabetes directly hampers the immune responses thereby accelerating the proliferation of TB. In these patients there is a decrease in production of IFN-γ and other

cytokines which stops T-cell immunity and lessens chemotaxis in neutrophils which in turn increases the risk of developing active TB (Martens, et al., 2007).

Healthcare Workers- TB transmission occurs through very tiny droplet nuclei aerosolized by patients with infectious pulmonary TB and inhaled by other persons. Since healthcare worker in close association with these patients they are highly exposed to the organisms. This occupational exposure can be minimized by clinician, adequate infection control measures by hospital authorities, and early identification of latent tuberculosis infection by occupational and public-health specialists (de Vries, et al., 2006).

2.10.3Socioeconomic and Behavioral Factors

Socioeconomic Condition- It has been observed in many studies that Asia having lower socio-economic status is associated with increased risk of TB. Rapid urbanization in developing countries and poor socioeconomic status of individuals has shown to have great influence on a person's susceptibility to develop TB. Burden of poor socioeconomic conditions lead to malnutrition, low education, unemployment, living in crowded areas, low income, poverty, smoking, indoor air pollution, and alcohol use have all increased the risk of TB disease (Jiamsakul, et al., 2018).

Tobacco Smoke- Smoking damages the lungs and also has a bad impacts on the body's immune system, making them two-and-a-half times more susceptible to TB infection. There is a negative impact of smoking on TB as it not only increases the chances of acquiring TB infection but also increases the developing of TB disease. More than 20% of global TB incidence are attributed to smoking. It is predicted that 18 million additional cases of TB would be found by 2050. Moreover, continuing smoking after being diagnosed with TB infection can lead to severe TB outcomes(Alavi-Naini, et al., 2012).

Alcohol- Alcohol consumption, particularly heavy consumption is a risk factor for TB disease (Lönnroth, et al., 2008). The reason behind this is because alcohol alters the immune system's signaling molecules that are responsible for producing cytokines (Szabo, 1997).

Indoor Air Pollution- In the developing countries more than 80% use solid fuel for cooking purpose. But people living in poor socioeconomic conditions still use firewood

and biomass smoke to cook food. Smoke from biomass combustion causes chronic pulmonary disease due to polluted hazardous smoke particle that deposits deep into the alveoli causing considerable damage to the lunch which worsen due to further infection with TB disease(Boman, et al., 2003).

Other risk factors that are related to health system issue such as delaying diagnosis and treatment increases the duration of infection which may develop active TB disease leading to further transmission to healthy individuals(Golub, et al., 2006). Therefore, awareness programs should be made to educate the public regarding TB disease and their associated risk factors to minimize the number of cases.

2.10.4 Factors related to animal exposure

Mycobacterium bovis is the main cause of zoonotic tuberculosis (zTB), a type of tuberculosis that affects humans. The Mycobacterium tuberculosis complex, or MTC, which includes M. caprae and M. orygis, can also be the cause (WHO, 2021). (van Ingen, et al., 2012). Bovine TB, often known as bTB, is a chronic TB disease that affects cattle, but it can also infect goats and other mammalian species and have an adverse effect on these animals' ability to produce milk and meat (LoBue, et al., 2010). (Higino, et al., 2011). Direct contact with infected animals, airborne transmission, or consumption of tainted raw milk or meat are all ways that humans can contract zTB (Grange & Yates, 1994). Occupational risks for zTB include certain groups like veterinarians, farmers, cattle handlers, slaughterhouse employees, and butchers (Islam, et al., 2021). 2019 saw an estimated 11,400 deaths and 140,000 new cases of zTB in humans worldwide (Islam,, et al., 2021). In Bangladesh and the rest of Southeast Asia, there were 43,400 cases and 2,020 fatalities (WHO, 2021). However, the true extent of zTB's burden is unknown and is probably greatly underestimated, particularly in low- and middle-income countries (LMICs), where there is a paucity of epidemiologic data (Wedlock, et al., 2002). The national tuberculosis program in Bangladesh has understated the effects of zoonotic TB on human health (DGHS, MOH&FW, 2017). According to estimates, the prevalence of bTB in animals as a whole ranges from 2 to 11.3%. (Mahmud, et al., 2014). In compliance with the World Organization for Animal Health's requirements, Bangladesh sends disease information on the existence of zTB (MTC) in cattle on a regular basis (six

monthly or yearly) (World Organization for animal Health, 2019). These yearly studies made clear that the illness is widespread among animals. Both human health and cattle output are impacted by zTB. Transmission can occur when human populations come into contact with cattle directly or closely. Reduced milk and meat output and increased poverty in marginalized populations are indirect effects on animal health (Liverani, et al., 2013).

2.11 DOTS

Political commitment, microscopy services, drug supply, surveillance and monitoring systems, adoption of highly effective regimens, and direct observation of therapy are the five main components of the Directly Observed Therapy Short Course (DOTS). Misunderstandings have arisen as a result of discrepancies in how "DOTS" is defined by WHO and interpreted by numerous observers. Although the abbreviation DOTS, which stands for Directly Observed Therapy Short course, is commonly used by the World Health Organization to refer to the five DOTS components, many professionals only use the phrase to refer to direct monitoring of therapy. The two main goals of DOTS are to guarantee that TB patients finish their treatments until they are cured and to stop the spread of drug resistance in the community. The fundamental criticism of DOTS, however, is justified because several adequately done randomized, controlled studies of directly observed therapy, including or excluding the other components, have failed to demonstrate any positive outcomes. The fundamental problem is that comparing contemporary directly monitored therapy to earlier self-administered, underfunded programs is very hard to do. The attention given to patients in the control (non-directly observed therapy) arm automatically improves from the earlier non-trial service state as soon as a study is established. One worrying finding is that, even with direct observation therapy, cure rates in certain trials fell below 70%. DOTS is the greatest method for TB control because there aren't any new medications or adjuvant therapies that might drastically shorten the course of treatment to less than 6 months (Davies, 2003).

2.12 Other related studies

Study 1- In order to look into how TB infection control methods are being implemented in these hospitals, Chen et al. (Chen, et al., 2016) carried out a cross-sectional study in

Zhejiang province, China. This survey comprised 88 hospitals in total. During the study period, all management, administrative, environmental, and personal infection control methods were evaluated. Some steps, such reducing wait times, evaluating TB infection control on a frequent basis in high-risk locations, and providing a separate waiting space for patients with suspected TB, were occasionally overlooked. Although only 44 (50%) hospitals made sure the N95 respirators were a good fit, 85 (97%) hospitals had them on hand. A dedicated sputum collection space and annual respirator fit testing were more prevalent in hospitals with more staff and higher admission rates for TB patients. At conclusion, infection control procedures required to be reinforced even further, particularly in medical facilities with lower rates of TB patient admission.

Study 2- To make TB diagnosis and treatment easier, the Bangladesh National Tuberculosis (TB) Control Program used a number of measures. One of the main tactics used by BRAC's (Bangladesh Rural Advancement Committee, a non-governmental development organization) TB control program was "Advocacy, Communication and Social Mobilization" (ACSM). Paul et al. carried out a study to evaluate the knowledge and attitudes of the key community members (KCMs) who participated in ACSM in BRAC TB control zones, including cured TB patients, community leaders, private medical practitioners, drug merchants, village doctors, and healthcare staff. For the quantitative approach, a multistage random sampling strategy was used and a total of 432 people participated in this study. For the qualitative approach 42 of the 432 participants were interviewed in-depth. Although BRAC workers were more knowledgeable as compared to KCMs, there was still gaps in knowledge among BRAC community health workers especially for child TB. For KCMs, varying levels of knowledge and mixed attitudes about TB were found. Furthermore, presence of stigma that young girls with TB have lower chances of getting married were also found. Such issues need to be addressed and resolved in future ACSM activities (Paul, et al., 2015).

Study 3- This study was conducted in South Africa where the incidences of tuberculosis has been gradually increasing. Malangu& Mngomezulu (Malangu & Mngomezulu, 2015) attempted to describe and compare the tuberculosis infection control measures implemented by facilities in Ugu and Uthungulu health districts of Kwazulu-Natal

province in South Africa. Data for this cross-sectional survey was collected from healthcare workers at 52 health facilities using self-administered questionnaires and site visit observations. Majority (80%) of the facilities surveyed complied to only 48.6 % (18 out of 37) of the overall aspects of TB infection control. These aspects included administrative, environmental, clinical and occupational health measures. Owing to this inadequate compliance nosocomial incidences of tuberculosis has been reported among healthcare workers in both districts.

Study 4- This study was conducted among pediatric pulmonary tuberculosis patients in South Delhi, India. A retrospective analysis of 1028 children who were diagnosed with pulmonary tuberculosis and treated according to the DOTS strategy was conducted and the outcomes of these children were evaluated. Although the cure rate of new cases and relapsing cases were very similar, treatment completion rates were significantly higher for new cases as compared to relapsing cases. Overall success rate was 95.4% for new cases and 82.6% for relapse cases. Overall default, failure and death rates in the study were low suggesting DOTS to be a highly efficient strategy in treatment of tuberculosis among pediatric patients (Sharma, et al., 2008).

CHAPTER THREE- MATERIALS AND METHODS

3.1 Description of the study area

The district of Chattogram is an administrative region of the Chattogram Division that is located in southeastern Bangladesh. Being a large port city and is considered as the commercial capital of Bangladesh. The geographical diversity of Chattogram is very different from other districts in the country owing to its mountains, valleys, seas and forests. The district is bounded in the north by Feni district as well as the Indian state of Tripura, in the south by Cox's Bazar district, on the east by Bandarban, Rangamati and Khagrachhari districts; and on the west by Noakhali district and the Bay of Bengal.

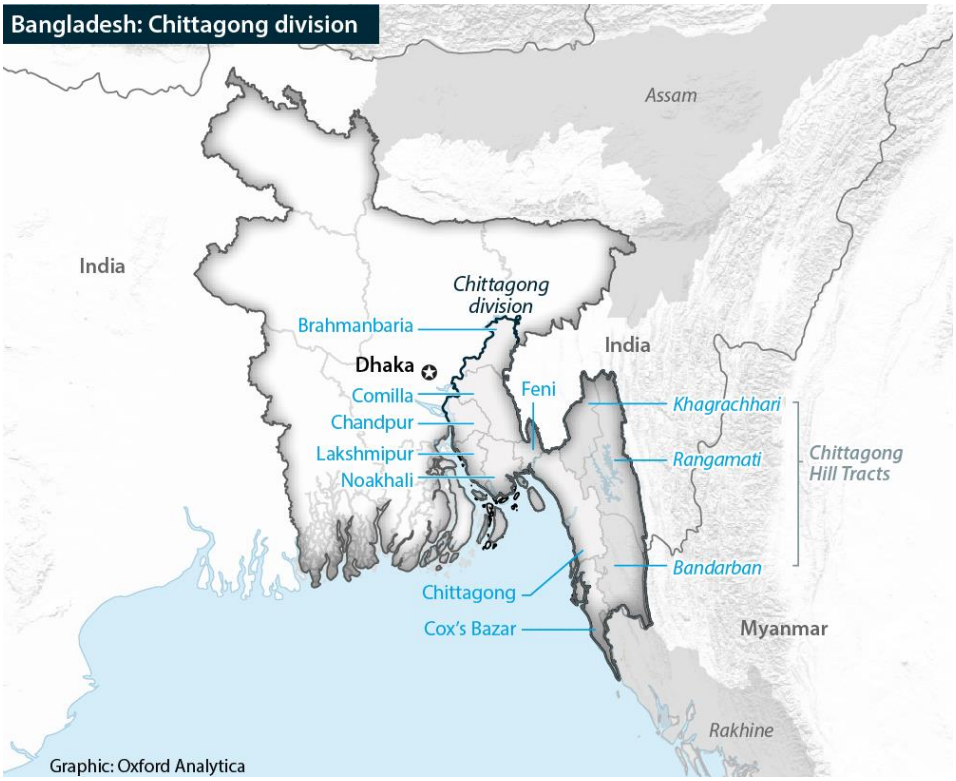


Figure 3.1: Map of Chattogram

The entire district has an area of 5,263 km^2 with a population of 6,913,375 (Portal, 2021). The Chattogram metropolitan area currently has a population of about 5 million (World Population Review, 2021). It is placed between the Chittagong Hill Tracts and the Bay of Bengal, lying at the banks of the Kornophuli River. A high degree of religious and ethnic diversity exists within Chattogram despite having an overwhelming Bengali Muslim majority. Minorities include Bengalis of other faiths such as Hindus, Christians and Buddhists. The district has a tropical monsoon climate with temperatures between 21°C to 30°C. It is also known for its rich biodiversity with hills and jungles laden with flowing river streams and elephant reserves. Economically, Chattogram contributes to a substantial share of Bangladesh's national GDP making up about 12% of the nation's GDP (The Chittagong chamber of commerece and industry, 2021). About 75% of the country's total export and 80% of total import occurs through the city of Chattogram.

DOTS corner for the treatment of tuberculosis patients is located in at least 65 different locations within the Chattogram metropolitan area (ICDDRB, 2018). Data was collected from a single DOTS corner located at Bandartila, Chattogram.

3.2 Study Design

The study was a retrospective observational study that was conducted in the city of Chattogram. Only cases of pulmonary tuberculosis (PTB) were included in the study. All cases of extra pulmonary tuberculosis and known cases of drug resistant tuberculosis were excluded.

3.3 Study period

Data was collected for this study over a period of two years from January 2020 to end of December 2021.

3.4 Sample size calculation

Sample size was determined according to(Thrusfield & Brown, 2017), using the estimated prevalence of 50%. The following formula was used.

$$n = \frac{(1.96)^2 \text{Pexp}\ (1-\text{Pexp})}{d^2}$$

where:

n = required sample size;

P_{exp} = expected prevalence;

d = desired absolute precision.

Since the expected prevalence of 50% is tobe estimated with a desired absolute precision of ± 5(i.e., the limits of the associated 95% interval are 25%and 35%), then:

P_{exp} =0.50,

d =0.05

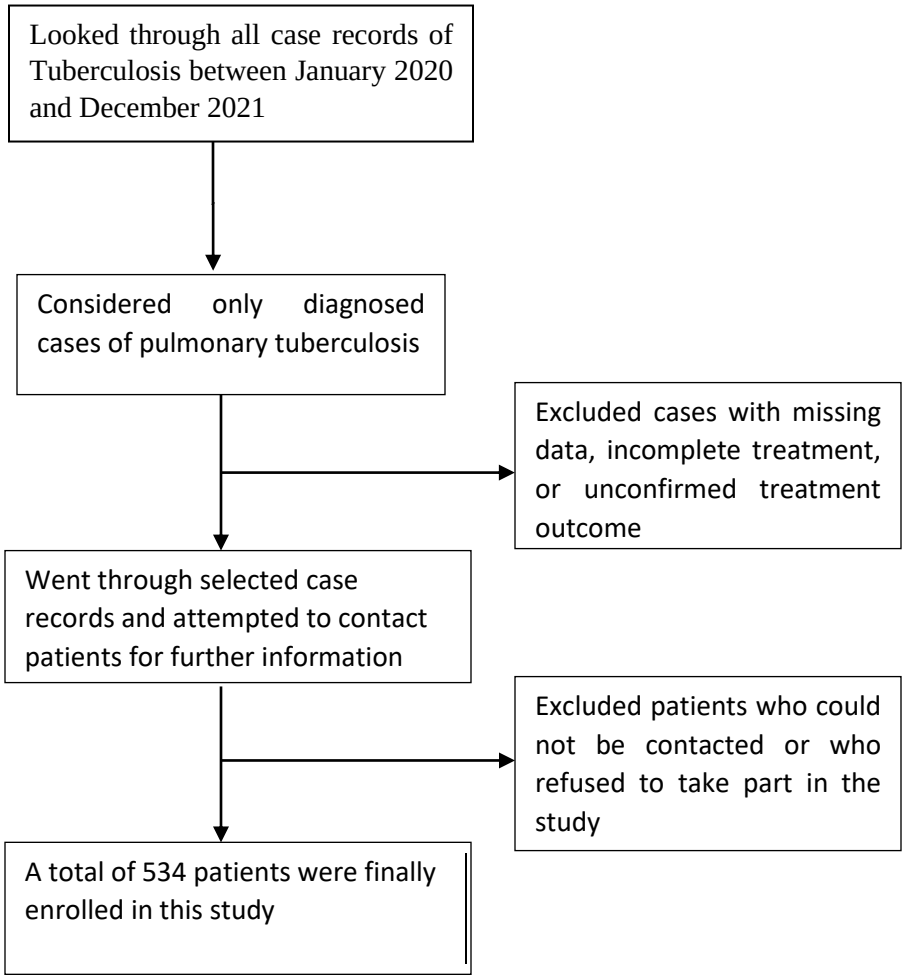
Substituting these values in the formula:

$$n = \frac{(1.96)^2 x\ 0.5\ (1-0.5)}{(0.05)^2} = 384$$

To avoid bias and other unwanted errors, 534 patients were enrolled in this study.

3.5 Collection of data

After obtaining permission from the ethical review committee of CVASU, all cases between the aforementioned period were browsed through for data collection. Only patients that were diagnosed as pulmonary tuberculosis were considered for this study. Diagnosis was made by Chest Xray findings, Sputum positive for AFB and GeneXpert testing. Following this, exclusions were made based on treatment outcome. Only patients who completed treatment and had a known outcome (cured or treatment failure) were included. Data was collected from their case record forms. Further questions on their exposure history were obtained through phone calls using contact numbers on their case record forms. Any incomplete data were discarded. A total of 534 patients were finally enrolled in this study. The data collection procedure is summarized in the flow chart in the following page.



3.6 Operational definition

The operational definitions have been set based on the national guidelines for tuberculosis infection control(DGHS & WHO, 2021).

Case definition: Any patient who has been diagnosed as a case of pulmonary tuberculosis either bacteriologically (sputum smear or culture positive, GeneXpert positive) or clinically (Chest X ray abnormalities) were considered as cases.

Pulmonary Tuberculosis (PTB): Refers to the disease affecting the lung parenchyma. PTB is divided in to two types bacteriologically confirmed (smear positive and Xpert positive cases) and smear negative pulmonary cases.

Smear positive- Patient with at least one sputum specimen positive for acid fast bacillus

Xpert positive- Patient with clinical symptoms of TB having at least two sputum specimens negative for AFB and found positive on Xpert by detection of MTB that is rifampicin susceptible.

X-ray- Both sputum and Xpert are negative for PTB, but chest X ray findings are consistent with active TB and the diagnosis is made by a qualified physician.

Category of TB treatment:

Category 1- Treatment with 4 drug combination (HRZE) for two months followed by 2 drug combination (HR) for four months

Retreatment- Based on gene X pert results the following is given

In case of X pert positive- Treatment with 4 FDC with Levofloxacin for 6 months according to weight of patient.

In case of Xpert negative- Treatment with 4 FDC for 6 months

Child- Treatment with 3 drug combination (HRZ) for two months followed by 2 drug combination (HR) for four months.

Treatment outcome:

Cured- Any pulmonary TB patient with a bacteriologically confirmed TB at the beginning of treatment who becomes smear or culture- negative in the last month of treatment and on at least one previous follow up occasion.

Treatment failure-

- A TB-patient whose sputum smear or culture is positive at month 5 or later during treatment or
- A patient who was initially smear negative, and was found smear positive at the end of the second month of treatment.

3.7 Data analysis

Data was initially recorded on a data record sheet and was manually compiled on to a Microsoft excel spreadsheet. The data was then analyzed using STATA/IC 1 (StataCorp 4905, Lakeway Drive, College Station, Texas 77845, USA).

3.7.1 Descriptive analysis

Prevalence of treatment failure was calculated by dividing number of patients who had a positive test for PTB despite receiving treatment by the total number of patients who received treatment expressing the result as a percentage. Prevalence of different diagnostic methods and provided treatments were also done in a similar way.

3.7.2 Risk factor analysis

For each of the independent variables, a univariate analysis was conducted against the dependent variable for treatment outcome of the study subjects. Chi square test was done to identify significant risk factors for predicting patient outcome. A p- value of <0.05 was considered as statistically significant. The results were presented in tables with frequency and Odds Ratio at 95% confidence intervals (CI). A student's t-test was used for continuous variables.

CHAPTER 4- RESULTS

The study was conducted retrospectively using data from pulmonary tuberculosis patients collected from a single center in Chattogram district. Out of 534 patients who completed their treatment, 524 (98%) patients were cured, while 10 (2%) patients had treatment failure.

4.1 Demographic characteristics of the patients

Among the total number of patients in this study, there were 332 (62.2%) male and 202 (37.8%) females. Majority of the study subjects were adults (95.8%) and belonged to lower socioeconomic class (93.6%). Most of them were married (92.1%) and lived in nuclear families (95.1%). In case of type of dwelling, more than half of the respondents (56.7%) lived in slums. As for location of residence, most of the respondents resided in EPZ area (49.6%) followed by Potenga (29.2%), Bandar (6.2%), Sadarghat (4.9%), Pahartoli (4.1%), Doublemooring (2.3%), and so on. The demographic characteristics of the study participants are depicted below in **Figure 4.1**.

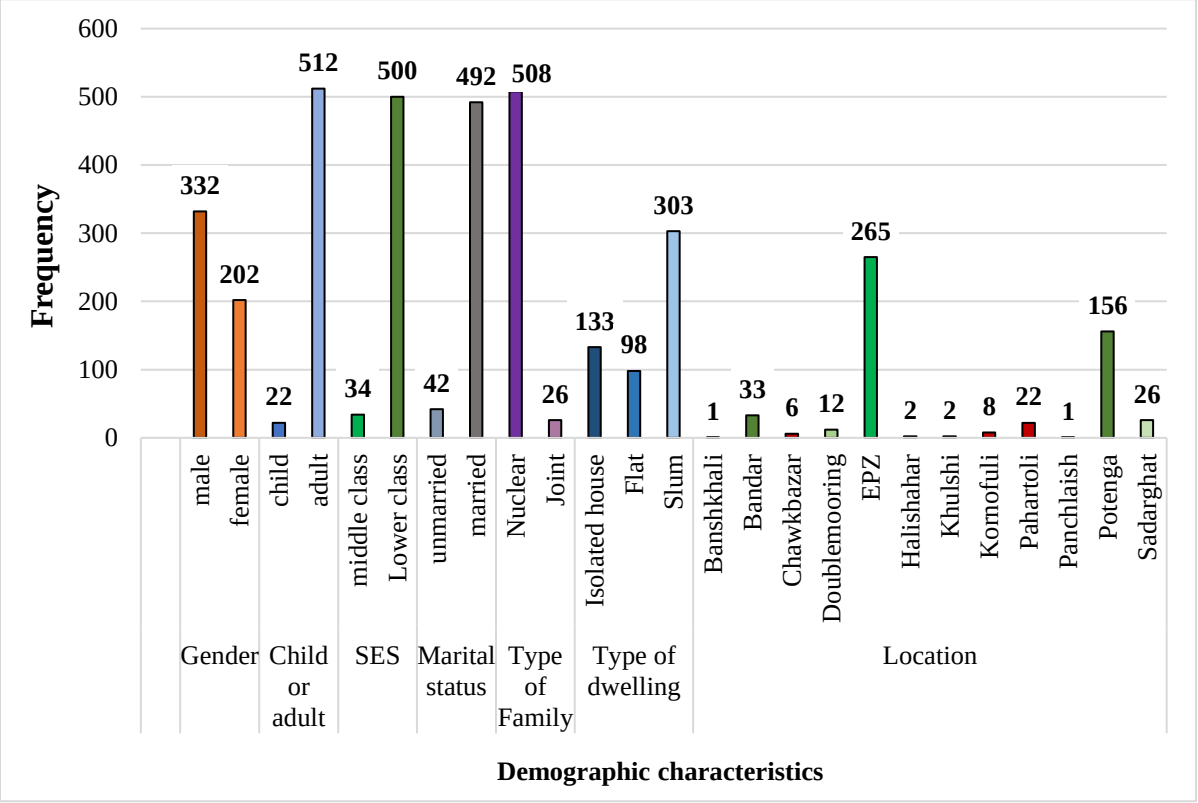


Figure 4.1- Demographic characteristics of all patients (N=534)

After completion of treatment, it was found to have failed in ten patients. An equal number of male and female had treatment failure (50%). In case of type of dwelling, most cases of treatment failure lived in isolated houses (40%) and most cases belonged to nuclear families (90%). All cases of treatment failure were adults and were married (100%). Most of them belonged to lower class (90%).**Figure 4.2** below displays the demographic characteristics of the patients who had treatment failure.

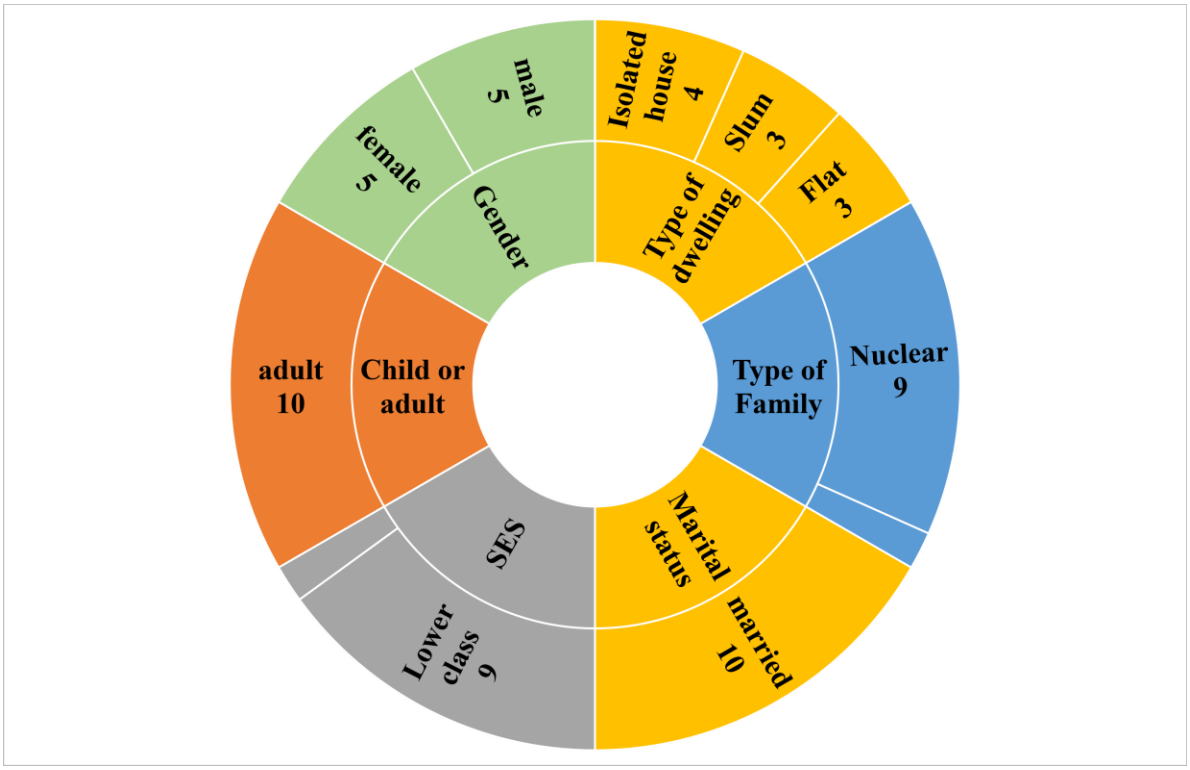


Figure 4.2- Demographic characteristics of patients of treatment failure (N=10)

Table 4.1: Univariate association between treatment outcome and demographic characteristics of the patients

Variable	Category	Treatment outcome		Total (%)	p- value	Odds Ratio [95% CI]
		Failed (%)	Cured			
Gender	male	5 (1.51%)	327 (98.49%)	332 (62.17%)	.5146	1.66 [0.46 to 6.04]
	female	5 (2.48%)	197 (97.52%)	202 (37.83%)		0.60 [0.17 to 2.19]
Child or adult	child	0 (0%)	22 (100.00%)	22 (4.12%)	1	N/A
	adult	10 (1.95%)	502 (98.05%)	512 (95.88%)		
SES	Middle	1 (2.94%)	33 (97.06%)	34 (6.37%)	0.485	0.60 [0.11 to 11.32]
	Low	9 (1.80%)	491 (98.20%)	500 (93.63%)		1.65 [0.09 to 9.19]
Marital status	Unmarried	0 (0%)	42 (100.00%)	42 (7.87%)	1	N/A
	married	10 (2.03%)	482 (97.97%)	492 (92.13%)		
Type of family	Nuclear	9 (1.77%)	499 (98.23%)	508 (95.13%)	0.3956	2.22 [0.12 to 12.50]
	Joint	1 (3.85%)	25 (96.15%)	26 (4.87%)		0.45 [0.08 to 8.48]
Type of dwelling	Isolated house	4 (3.01%)	129 (96.99%)	133 (24.91%)	0.2757	0.49 [0.14 to 1.94]
	Flat	3 (3.06%)	95 (96.94%)	98 (18.35%)	0.4013	0.52 [0.14 to 2.43]
	Slum	3 (0.99%)	300 (99.01%)	303 (56.74%)	0.1099	3.12 [0.86 to 14.62]
Location (Thana)	Banshkhali	0 (0%)	1 (100.00%)	1 (0.19%)	1	N/A
	Bandar	1 (3.03%)	32 (96.97%)	33 (6.18%)	0.4746	0.59 [0.11 to 10.96]
	Chawkbazar	0 (0%)	6 (100.00%)	6 (1.12%)	1	N/A
	Doublemooring	0 (0%)	12 (100.00%)	12 (2.25%)	1	N/A
	EPZ	4 (1.51%)	261 (98.49%)	265 (49.63%)	0.7516	1.49 [0.42 to 5.88]
	Halishahar	0 (0%)	2 (100.00%)	2 (0.37%)	1	N/A
	Khulshi	0 (0%)	2 (100.00%)	2 (0.37%)	1	N/A
	Kornofuli	1 (12.50%)	7 (87.50%)	8 (1.50%)	0.1412	0.12 [0.02 to 2.40]
	Pahartoli	0 (0%)	22 (100.00%)	22 (4.12%)	1	N/A
	Panchlaish	0 (0%)	1 (100.00%)	1 (0.19%)	1	N/A
	Potenga	4 (2.56%)	152 (97.44%)	156 (29.21%)	0.488	0.61 [0.17 to 2.43]
	Sadarghat	0 (0%)	26 (100.00%)	26 (4.87%)	1	N/A
Total		10 (1.87%)	524 (98.13%)	534 (100.00%)		

The table above displays the demographic profile of the study subjects. Although no significant differences in demographics were found among cases who were cured and cases for whom treatment had failed, the odds of being cured were slightly raised with some of the demographic factors. In case of gender, males have a higher odd of getting cured with an odds ratio of 1.65; 95% CI: 0.09 to 9.19. As for socioeconomic status, people with a lower income are more likely to be cured (OR=1.65;95% CI: 0.09 to 9.19). Patients from nuclear families (OR=2.22; 95% CI: 0.12 to 12.50) and patients living in slums (OR=3.12; CI: 0.86 to 14.62) have higher odds of being cured from the disease.

4.2 Association of other variables with treatment outcome

A students t-test was conducted to identify any significant difference between three different continuous variables, namely, age of the study subjects, duration of previous treatment and number of family members. The results are shown in **Table 4.2**.

Table 4.2: Association of age, duration of previous treatment and number of family members with treatment outcome.

Variable	Treatment	N	Mean± SD	Median [IQR]	Min	Max	P- value
Age (in years)	Cured	524	29.8± 16.7	27.0 [16.0;43.0]	1	67	0.7791
	Failure	10	30.4± 13.4	30.0 [22.0;43.0]	9	47	
	Total	534	29.8 ±16.6	27.0 [16.0;43.0]	1	67	
Duration of previous treatment (in months)	Cured	524	1.7 ± 1.7	1.0 [1.0;1.0]	1	8	0.2158
	Failure	10	1.0 ± 0	1.0 [1.0;1.0]	1	1	
	Total	534	1.6 ±1.7	1.0 [1.0;1.0]	1	8	
Number of family members	Cured	524	6.0 ±1.4	6.0 [5.0;7.0]	1	11	0.1053
	Failure	10	6.8 ± 1.7	7.0 [6.0;7.8]	4	10	
	Total	534	6.0 ±1.4	6.0 [5.0;7.0]	1	11	

On comparing mean age, duration of previous treatment and number of family members among cured TB cases vs cases of treatment failure, no significant difference was found among any of the parameters. The mean age for patients who were cured from PTB was 29.8± 16.7 years, and that for treatment failure cases was 30.4± 13.4 years. The mean duration of treatment was 1.7 ± 1.7 months for cured patients and 1.0 ± 0 for patients with treatment failure. Among family members, the average family members were 6.0 ±1.4 people among patients who were cured and 6.8 ± 1.7 people among patients whose treatment failed.

4.3 Prevalence of risk factors and its association with treatment outcome

The prevalence of a variety of risk factors were evaluated among the study subjects. Smoking was the most prevalent risk factor among the study subjects and was present in 243 (45.5%) study subjects. Other common risk factors were previous history of anti-TB treatment (15.7%), comorbidities like diabetes (14.8%), malnourishment (13.3%), immunosuppressive therapy (12.7%), contact with domestic animals (6.7%), consumption of raw milk (5.6%), and history of contact with infected people (4.5%). **Figure 4.3** below illustrates the presence of these risk factors among the study population.

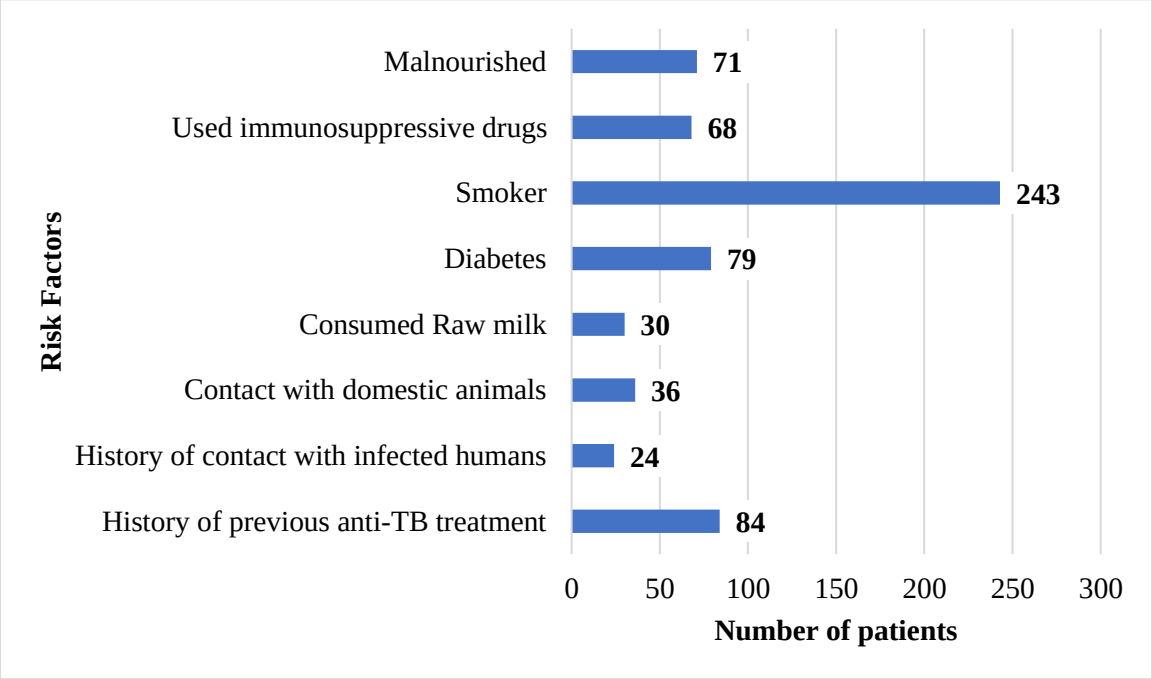


Figure 4.3- Presence of risk factors among the TB patients (N=534)

To identify any association between the risk factors and treatment outcome of the study population, a univariate analysis was conducted with treatment outcome being the dependent variable. The results are summarized in **Table 4.3**.

Table 4.3: Association of risk factors with the treatment outcome among the patients (N=534)

Variable	Category	Treatment outcome		Total	p-value	OR [95% CI]
		Failure	Cured			
History of previous anti-TB treatment	Yes	1 (1.19%)	83 (98.81%)	84 (15.73%)	1	1.69 [0.31 to 31.44]
	No	9 (2.00%)	441 (98.00%)	450 (84.27%)		0.59 [0.03 to 3.20]
History of contact with infected humans	Yes	1 (4.17%)	23 (95.83%)	24 (4.49%)	0.371	0.41 [0.07 to 7.78]
	No	9 (1.76%)	501 (98.24%)	510 (95.51%)		2.42 [0.13 to 13.71]
Contact with domestic animals	Yes	0 (0%)	36 (100%)	36 (6.74%)	1	N/A
	No	10 (2.01%)	488 (97.99%)	498 (93.26%)		
Consumed Raw milk	Yes	1 (3.33%)	29 (96.67%)	30 (5.62%)	0.442	0.53 [0.09 to 9.89]
	No	9 (1.79%)	495 (98.21%)	504 (94.38%)		1.90 [0.10 to 10.61]
Diabetes	Yes	2 (2.53%)	77 (97.47%)	79 (14.79%)	1	0.64 [0.03 to 3.45]
	No	8 (1.76%)	447 (98.24%)	455 (85.21%)		1.57 [0.29 to 29.23]
Smoker	Yes	6 (2.47%)	237 (97.53%)	243 (45.51%)	0.359	0.51 [0.11 to 1.85]
	No	4 (1.02%)	287 (98.62%)	291 (54.49%)		1.37 [0.63 to 2.93]
Used immunosuppressive drugs	Yes	0 (0%)	68 (100%)	68 (12.73%)	0.624	N/A
	No	10 (2.15%)	456 (97.85%)	466 (87.27%)		
Malnourished	Yes	0 (0%)	71 (100.0%)	71 (13.30%)	0.373	N/A
	No	10 (2.16%)	453 (97.84%)	463 (86.70%)		
Total		10 (1.87%)	524 (98.13%)	534 (100%)		

As observed in the table above, no significant association was found between any of the risk factors and the treatment outcomes. However, presence of some risk factors can increase the likelihood of treatment failure. Patients with a history of receiving treatment previously for T.B were more likely to be cured (OR=1.69; 95% CI: 0.31- 31.44). Similarly, patients with no history of contact with infected humans were more likely to be cured (OR= 2.42; 95% CI: 0.13 to 13.71). Patients who did not consume raw milk were

more prone to be cured (OR= 1.90; 0.10 to 10.61), while smokers (OR= 1.37; 0.63 to 2.93) were less likely to be cured. Non-diabetics (OR= 1.57; 0.29 to 29.23) were more likely to be cured after completion of treatment for TB as compared to diabetics.

4.4 Method of diagnosis of the patients

In the present study, patients of pulmonary tuberculosis were diagnosed by four different methods.Out of the total 534 cases, 253 (48%) cases were bacteriologically confirmed where 95(18%) cases had a positive smear test and 158 (30%) cases had MTB DNA detected on Gene Xpert test; the remaining 281 (52%) cases were diagnosed clinically. Among them, 273 (51%) cases were confirmed by chest X-rays that showed features suggestive of PTB. **Figure 4.4** is a pie chart that exhibits the various methods in which the patients were diagnosed.

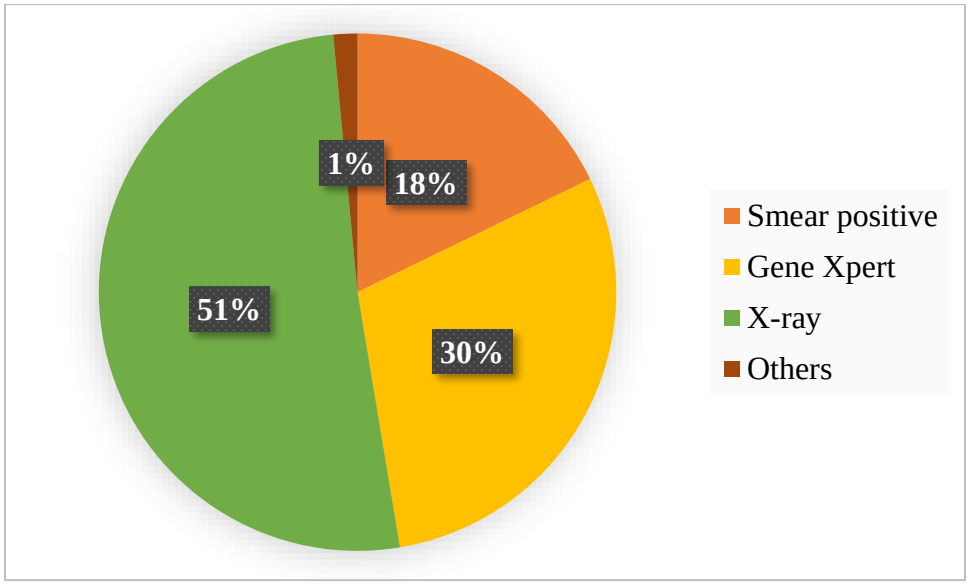


Figure 4.4- Mode of diagnosis of patients (n=534)

A chi-squared test was conducted to identify any association between the method of diagnosis and the patient's treatment outcome. The results are shown in **Table 4.4.**

Table 4.4: Association of the method of patient diagnosis with treatment outcome (N=534)

Method	Treatment outcome		Total	P- value	OR [95% CI]
	Failure	Cured			
Smear positive	1 (1.05%)	94 (98.95%)	95 (17.79%)	1	1.97 [0.36- 36.50]
Gene Xpert	5 (3.16%)	153 (96.84%)	158 (29.59%)	0.1701	0.41 [0.11- 1.50]
X-ray	4 (1.47%)	269 (98.53%)	273 (51.12%)	0.5369	1.58 [0.45- 6.25]
Others	0 (0%)	8 (100.00%)	8 (1.50%)	1	N/A
Total	10 (1.87%)	524 (98.13%)	534 (100.00%)		

As observed in the table above, patients diagnosed with chest X-ray (OR= 1.58; 95% CI: 0.45- 6.25) and smear test positive (OR= 1.97; 95% CI: 0.36- 36.50) had higher odds of getting cured as compared to patients diagnosed using Gene Xpert.

4.5 Treatment of the patients with Pulmonary TB

Based on the treatment regimen, 455 (85.2) patients received treatment as new TB patients, 77 (14.4%) were grouped as retreatment cases and 2 cases (0.4%) were treated under the guidelines for children. As for total duration of treatment, 531 (99.4%) patients had taken treatment for 6 months. Only three (0.56%) patients received treatment for a short duration of 2 months due to adverse drug reactions. During treatment, 17 (3.2%) patients skipped medications in between while 517 (96.8%) did not. **Figure 4.5** shows the frequency distribution of cases based on category of treatment and patient's treatment related behavior.

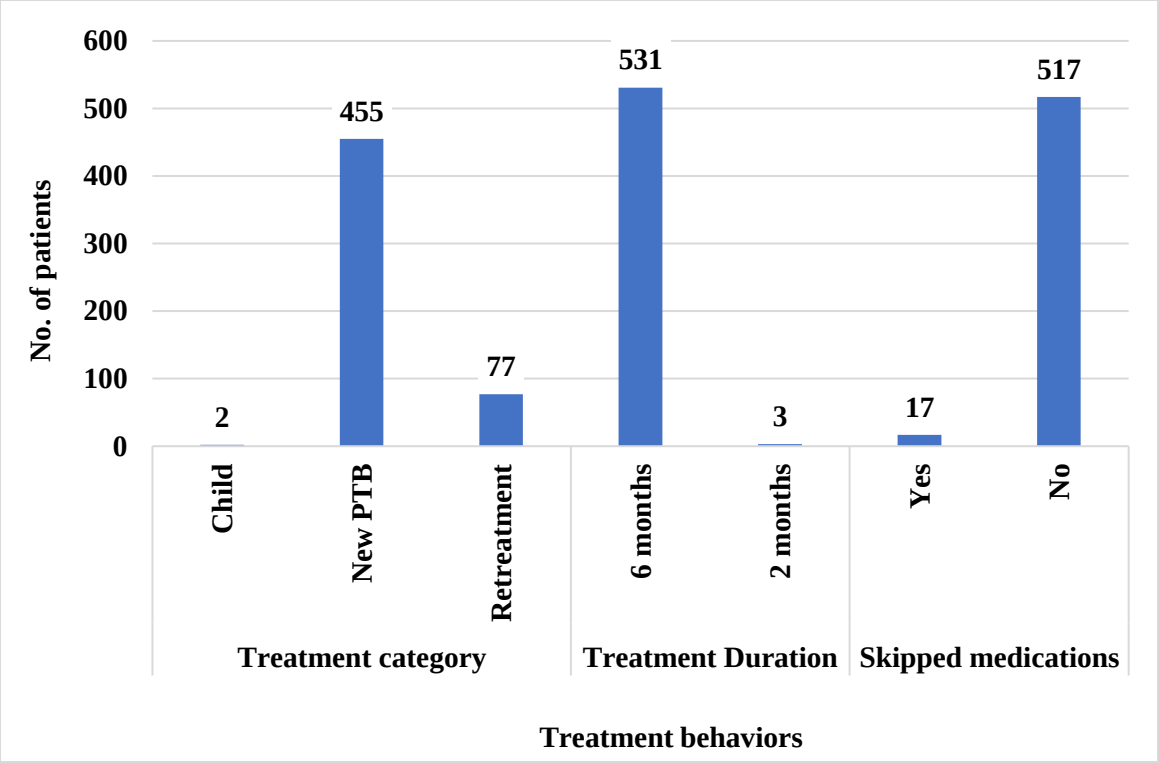


Figure 4.5- Treatment category and treatment behavior of the study subjects

To further analyze an association between the treatment behaviors and categories of treatment against treatment outcome, a Chi squared test was conducted. A significant association was found between shorter duration of treatment ($p<0.001$) and history of skipping medications during treatment ($p=0.037$) against treatment outcome. On observing odds ratio, the odds of getting cured were higher (OR=1.53; 95% CI: 0.28 - 28.36) among patients who were being re-treated for the disease after treatment failure. Again, patients who did not skip medications were more likely to be cured (OR= 8.48; 95% CI:1.21 - 37.60). The results are summarized in **Table 4.5**.

Table 4.5: Association of treatment category, duration and non-compliance with treatment outcome

Variable	Category	Treatment outcome		Total	P- value	OR [95% CI]
		Failure	Complete			
Treatment category	Child	0 (0%)	2 (100.00%)	2 (0.37%)	1	N/A
	New PTB	9 (1.98%)	446 (98.02%)	455 (85.21%)	1	0.64[0.03-3.45]
	Retreatment	1 (1.30%)	76 (98.70%)	77 (14.42%)	1	1.53 [0.28 - 28.36]
Total duration of treatment	6 months	7 (1.32%)	524 (98.68%)	531 (99.44%)	***<0.0001***	N/A
	2 months	3 (100.00%)	0 (0%)	3 (0.56%)		
Skipped medication	Yes	2 (11.76%)	15 (88.24%)	17 (3.18%)	***0.037***	0.12 [0.03 - 0.82]
	No	8 (1.55%)	509 (98.45%)	517 (96.82%)		8.48 [1.21 - 37.60]
Total		10 (1.87%)	524 (98.13%)	534 (100.00%)		

CHAPTER 5- DISCUSSION

Any tuberculosis (TB) control or intervention program's success depends on its ability to comprehend the dynamics of TB transmission there. However, there is scarcity of data in high disease burdened countries like Bangladesh on the various risk factors that predict treatment outcome among TB patients, and this supports the need for this research. This study was undertaken to determine the prevalent risk factors that are associated with treatment failure among patients of pulmonary tuberculosis (PTB) and hence provide an idea on what measures can promote TB infection control and reduce the risk of treatment failure among the patients.

A total of 534 patients with mean age of 29.8 ±16.6 years and male: female ratio of 4.28:1 were enrolled in this study. The mean age of patients in the present study was consistent with another Chinese study (Zhu, et al., 2018), where ages between 25-34 years and 15-24 years were reported to have the highest percentage of TB cases. However, another study from DOTS corner in Sylhet (Sagir, et al., 2018) showed a higher mean age of 42.1 ±12.8 years as compared to our study. Since that study only included adults aged 18 years or more, such a variation in mean age could be expected, especially since our study also included children thus shifting the mean age to a lower value. As for gender, male predominance is a common observation in many studies (Jimenez-Corona, et al., 2006); (Banu, et al., 2013); (Miller, et al., 2021) .The reason for this is probably due to the fact that men are usually positioned in social networks such that they contact more people or social groups as compared to women (Miller, et al., 2021).

In the present study, more than half of the respondents (56.7%) lived in slums. The high prevalence of TB among slum dwellers has also been reported in another study conducted in Dhaka, where a low BMI and history of cough were suggested screening methods among slum dwellers to suspect cases of PTB (Banu, et al., 2013). One reason for the high prevalence in slum areas is the lack of adequate knowledge, negative attitude and poor practices regarding spread of tuberculosis among this population (Bam, et al., 2014). Additionally, barriers for health seeking practices such as cost, prevailing stigma on

TB,lack of information on service sites and unavailability of accompanying person results in most slum dwellers suffering from the disease rather than seeking treatment.

In our study, smoking was the most prevalent risk factor among the study subjects and was present in almost half the study subjects. Smoking was associated with tuberculosis in many studies prior to this (Ferrara, et al., 2012) (Kolappan, et al., 2007)(Alcaide, et al., 1996) with some studies reporting that even passive smoking increases the risk of PTB (Altet, et al., 1996). The odds of getting cured among non-smokers in this study was 1.37 times that of smokers. This finding is similar to another case-control study by Aguilaire et al (2019) (Aguilar, et al., 2019), where the risk of treatment failure among smokers is high despite adjusting for other factors such as age. These findings suggest that smoking has a strong influence on TB and is a major barrier towards treatment success. Therefore, smoking cessations are an effective way to decrease treatment failure and drug resistance (Khan, et al., 2020). In case of diabetes mellitus, the odds of getting cured among non-diabetics was 1.57 times the odds of getting cured among diabetics. This is similar to another study by Mboussa et al (2003) (Mboussa, et al., 2003) where treatment failure and death were more frequent among diabetics. One other study from India (Viswanathan, et al., 2014) showed that treatment failure for PTB among diabetic patients were more common but death from PTB among non-diabetics was more common. Our study also showed that the consumption of raw milk increased the likelihood of developing treatment failure. Consumption of unpasteurized milk was reported to be associated with the development of TB especially in the pediatric population (Attah, et al., 2018). Since cases of tuberculosis are not spoigilotyped to differentiate *M. Tuberculosis* from *M. Bovis*, it is difficult to distinguish between the two based on only clinical features or a conventional AFB testing (Lan, et al., 2016). Nevertheless, no study was found directly implicating consumption of raw milk with treatment failure.

Our study showed a significant association between shorter duration of treatment ($p<0.001$) and history of skipping medications during treatment ($p=0.037$) against treatment outcome. According to WHO recommendations, the minimum treatment requirement is 6 months (Silva, et al., 2020). However, in our study, three patients took

treatment for only two months following which their sputum smear came back positive for AFB. This finding is highly suggestive to continue the treatment regimen strictly for a duration of at least 6 months. Adherence to such rules will reduce treatment failure rates. Similarly, non-compliance as a significant risk factor for treatment failure among TB patients was found in other studies (Morsy, et al., 2003). In such cases, reaching out to patients through outreach programs if they have become non-compliant can reduce chances of treatment failure (Schluger, et al., 1995).

On comparing age against treatment outcome, mean age for patients who were cured from PTB was lower than the mean age for treatment failure cases. This finding agrees with the findings in another study conducted in Zimbabwe (Ncube, et al., 2017) where treatment success for all forms of TB cases decreased with increasing age. Older TB patients may be more vulnerable to physical impairment, which could prolong the time it takes for the mycobacterium bacilli to be cleared. This is likely owing to waning immunity. These results contrasted with those from Uganda (Morsy, et al., 2003) and Egypt (Namukwaya, et al., 2011) which showed no differences in age. The present study showed mean duration of treatment for treatment failure cases was lower than the mean duration of treatment for cured patients. While studies have associated noncompliance with treatment failure (Yasin, et al., 2016), it was not found to be the reason in our study. These patients had a smear positive test even after two months of treatment and were already at risk of treatment failure. According to one study, national TB programs usually perform sputum smear microscopy after two months of tuberculosis treatment. As a result, TB control programs view patients who test positive for tuberculosis after two months of treatment as being at risk for treatment failure (Becerra, et al., 2000). The average number of family members were sightly raised among patients with treatment failure in our study, as compared to patients who were cured. This is due to the chance of over-crowding in houses with large families, thus decreasing the proximity between family members and enhancing disease spread (Morens, et al., 2004). Additionally, low socio-economic status, poor nutrition, lack of access to health care services and health education, can result in family members becoming a source of re-infection rather than a support and care giver for the diseased individual. According to a study in Iran (Adineh, et al., 2014), patients with a family history of tuberculosis have a significantly higher

chance of treatment failure. While family history of most of our patients could not be verified partially owing to recall bias and mostly because most of their family members have never approached health services despite, there is a possibility that patients of treatment failure have undiagnosed family members living close to the patient.

CHAPTER 6- CONCLUSION

Interventions like strengthening the diagnosis of pulmonary TB further, putting active case finding and targeted communication programs into place to reduce patient level delays, increasing the public-private mix to increase access to TB services, utilizing rapid diagnostics, and offering social protection to vulnerable populations are required to stop the spread of PTB in Bangladesh. The countries' progress towards reaching the End TB targets can be accelerated by these strategies. Among patients seeking treatment for tuberculosis, presence of certain risk factors such as smoking, diabetes, previous TB history with drug non-compliance, socioeconomic status could be used to predict treatment failure.

The effectiveness of tuberculosis treatment will be improved by early detection of patients with the aforementioned risk factors and rigorous case management. Patients who test positive for cancer on a smear after two months of treatment require closer monitoring. To perform drug susceptibility testing and routine drug monitoring in cases of non-conversion at the second month of therapy, the national referral laboratory's capability needs to be improved. Younger patients with lower BMIs should receive greater attention during follow-up since they are more likely to be non-compliant.

CHAPTER 7- LIMITATIONS

The current study was not without limitations.

- Since the sample was collected randomly only few cases of treatment failure were found thus failing to give an accurate comparison.
- Most of the risk factors did not show a high level of significance since the number of treatment failure patients were very low as compared to the number of successful treatment cases. Hence odds ratio were considered in these cases.
- Only one center was considered in this study thus failing to represent the entire city.

CHAPTER 8- RECOMMENDATIONS AND FUTURE PERSPECTIVES

Conducting a case-control study using patients with treatment failure as cases and patients who were cured as controls would give us a better idea on the associated risk factors and treatment variations that can help predict the outcome of a PTB patient receiving treatment for the diseases. Since treatment failure rates were very low, and the study was conducted with data collection from only one DOTS corner for a specified period of time, sufficient number of treatment failure cases were not available. Hence, for future studies, involvement of multiple centers within the same city can yield better results and provide a more accurate picture of the situation of PTB in Chattogram city. Implementing the FAST strategy (Find cases Actively, Separate safely and Treat effectively) in future studies can help diagnose cases in a short duration and identify unsuspected cases. However, ensuring financial resources, stakeholder engagement and laboratory capacity are important for sustainability and scalability. Additionally, dedication of health care workers in controlling TB infection at hospital settings rather than just focusing on patient management can curb the spread of disease from unknown carriers. The management of TB patients must prioritize TB prevention through infection control. To implement infection control efficiently, it is necessary to set up an infection control committee, train healthcare professionals, and appropriately monitor and evaluate infection control activities.

To successfully prevent and control the spread of bovine tuberculosis, it is essential to educate patients who have had contact with animals about the risk factors for zoonotic transmission of the disease through training and media campaigns, improve meat hygiene through better abattoir services, and induce behavioral changes regarding the consumption of raw meat and raw milk.

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Data Collection sheet

Case # :

Name:

Age: **Gender:** **Contact No:**

Address:

Religion: **Occupation:**

1. **Patient's education level**
   1. Illiterate 2. PSC 3. SSC 4. HSC 5.Bachelor 6. Masters ☐
2. **Socioeconomic status** 1. Upper class 2. Middle class 3. Lower class ☐
3. **Location** 1. Urban 2. Semi urban 3. Rural ☐
4. **Marital status** 1. Single 2. Married 3. Divorced 5. Separated 4. Widowed ☐
5. **Type of Family** 1. Nuclear family 2. Joint family ☐
6. **Number of family members** ☐
7. **Type of dwelling** 1. Isolated house 2. Flat 3. Slum ☐
8. **Contact with domestic animals** 1. Yes 2. No ☐
   7.1 Type of animal _____
9. **Any family members or close contacts previously diagnosed with TB?** 1. Yes 2. No ☐
10. Did you consume raw milk or milk products (eg Ghee, yoghurt)? 1. Yes 2. No ☐
11. Do you have Diabetes? 1. Yes 2. No ☐
12. Do you take immunosuppressive drugs 1. Yes 2. No ☐
13. Are you malnourished? 1. Yes 2. No ☐
14. Do you/ did you ever smoke? 1. Yes 2. No ☐
15. Did you hear about TB prior to Illness? 1. Yes 2. No ☐
16. How does TB spread?
    - 10.1 Cough 1. Yes 2. No ☐
    - 10.2Sneezing 1. Yes 2. No ☐
    - 10.3 Talking 1. Yes 2. No ☐
    - 10.4 Spitting 1. Yes 2. No ☐
    - 10.5 Close contact 1. Yes 2. No ☐

17. Is TB curable? 1. Yes 2. No

18. Is it ok to skip medications for TB? 1. Yes 2. No

19. Do people behave differently towards you after your diagnosis? 1. Yes 2. No

20. How long did you have symptoms before seeking treatment? _____ days/ months.

21. Did you use masks at work/ home after being diagnosed with PTB? 1. Yes 2. No

22. Did your close contacts have their sputum tested for PTB? 1. Yes 2. No

23. Did any of your close contacts Test positive for PTB after your diagnosis? 1. Yes 2. No

24. Did you take time off work during your disease? 1. Yes 2. No

25. Did you skip any medications during your treatment? 1. Yes 2. No

26. If yes to question 12, then why?_____

National Tuberculosis Control Programme

TB 01

Directorate General of Health Services, Bangladesh

Treatement Card (Front page)

TB Registration No:

e-TB Manager Registration No.:

Name & Address of Health Institution/DOTS Center.

Name : _____

Father's/Husband's name: _____

Sex: M ☐ F ☐ Age : _____ BCG: no scar. ☐ Scar seen ☐

Occupation: _____ Phone. No.: _____

Address (in full) : _____

Name & Address of contact person: _____

_____ Phone. No.: _____

Name & address of person providing DOT: _____

Pulmonary		Extra Pulmonary, Site	
Bacteriologically Confirmed	Clinically Diagnosed (Ψ)	Bacteriologically Confirmed	Clinically Diagnosed (Ψ)
Smear positive ☐ X-pert positive ☐ Culture positive ☐	Diagnosed by : X-Ray ☐ Others ☐	Smear positive ☐ X-pert positive ☐ Culture positive ☐	Diagnosed by : X-Ray ☐ Others ☐

New	☐	Previously Treated	
Treatment History Unknown	☐	Relapse	☐
Transfer in	☐	Treatment after failure	☐
		Treatment after loss to follow up	☐
		Others	☐

* Refd by:						
Graduate PP	GFS	VD	Gov. Hospital	TB Patient	CHCP
Non Graduate PP	NGFS/SS	CV	Provate Hospital	Self	Other Specify

H/O Previous Anti TB Treatment ☐ Yes ☐ No; If yes Duration: ☐

H/O Contact : ☐ No ☐ Yes: TB/DR-TB

1. Intensive PHASE--Prescribed regimen and dosages

Frequency: Daliy

Tick Category and indicate number of tablets per dose and doses of S (gms):

CAT 1 ☐ CAT 2 ☐ CHILD ☐

4FDC ☐ 4 FDC ☐ 3FDC ☐

☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
R	H	Z	E	R	H	Z	E	S	R	H	Z	E	S	

Enter ☑ in the appropriate box to indicate the date when the drugs have been swallowed under direct observation: enter ⊟ if swallowed but not supervised: enter ⊡ when not taken ****IPT=isoniazid preventive therapy

Month	Date	Result of sputum examination				Weight (kg)
		Smear 1	Smear 2	Lab No.	*****X-pert result	
0						
2						
3						
5						
6/8						

TB/HIV/IPT		
	Date	Result
HIV Test		
**CPT Start		
***ART start		
****IPT start		

**CPT=Co-trimoxazole preventive Therapy. ***ART=Anti retro viral therapy

Month/Year	Day																													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

* PP = Private Practitioner, GFS= Govemment field staff, NGFS= Non Govt. Field staff, SS=Shebika, VD= Village Doctor, CV=Community volunteer, CHCP=Community Health Care Provider

*****X-pert result

T=MTB detected Rif resistance not detected; RR=MTB detected Rif resistance detected; TI=MTB detected Rif resistance indeterminate; N=MTB not detected, I=invalid/ no result/ error.

(Ψ) Please keep evidence in favour of diagnosis

TB 01

Tuberculosis Treatment Card (Back page)

PRESCRIBED REGIMEN AND DRUG DOSAGES

the appropriate box

CAT1

2FDC

CAT2

3FDC

Child

2FDC

R H

R H E

R H

Enter ☑ in the appropriate box to indicate the date when the drugs have been swallowed under direct observation: enter — if swallowed but not supervised: enter O when not taken

Month/ Year	Day																													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

Treatment outcome

Date of decision _____

- ☐ Cured
- ☐ Treatment complete
- ☐ Died
- ☐ Treatment failure
- ☐ Lost to follow up (defaulted)
- ☐ Transferred out
- ☐ Not evaluated

Types of drug reaction (if any):

Remarks (if any): _____

_____

_____

_____

_____

Signature of Medical Officer