ADDIS ABABA UNIVERSITY
COLLEGE OF NATURAL AND COMPUTATIONAL SCIENCES
DEPARTMENT OF ZOOLOGICAL SCIENCES

TRENDS IN MULTI-DRUG-RESISTANT TUBERCULOSIS CASES AT ST. PETER'S SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

BY: HAYLEYESUS BIRHANU MEHAMED

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Addis Ababa, Ethiopia

ADDIS ABABA UNIVERSITY
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Trends in Multi-Drug-Resistant Tuberculosis Cases at St. Peter's Specialized Hospital, Addis Ababa, Ethiopia

By: Hayleyesus Birhanu

Advisor: Hassen Mamo (Prof.)

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APPROVAL SHEET

ADDIS ABABA UNIVERSITY

This is to certify that the Thesis is prepared by Hayleyesus Birhanu, entitled: "'Trends in Multi-drug-Resistant Tuberculosis cases at St. Peter's Specialized Hospital, Addis Ababa, Ethiopia'', and submitted in partial fulfillment of the requirements for the awards of the degree of masters of science (M.Sc.) in Biology.

Approved by Board of Examiners

Hassen Mamo (Prof.)	____________	____________
Advisor	Signature	Date
Tegenu Gelana (PhD)	____________	___________
Examiner	Signature	Date
Bezawork Afework (PhD)	____________	____________
Chairperson	Signature	Date

Declaration

I hereby declare that this thesis is my original work and has not been presented for a degree in any other university and that all sources of materials used for the thesis have been duly acknowledged.

Declared by:	Confirmed by:
Name: Hayleyesus Birhanu	Advisor name: Prof. Hassen Mamo
Signature: __________	Signature: __________
Date: __________	Date: __________

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List Of Abbreviations/Acronyms

AFB	Acid Fast Bacilli
AIDS	Acquired Immuno deficiency Syndrome
AMR	Antimicrobial Resistance
ART	Anti-Retroviral Treatment
CI	Confidence Interval
CXR	Chest Radiograph
DOTs	Directly Observed Treatment, Short-Course
DR	Drug Resistant
EC	Ethiopian Calendar
EP	Extra Pulmonary
EPTB	Extra Pulmonary Tuberculosis
FMOH	Federal Ministry of Health
GC	Gregorian Calendar
HIV	Human Immuno deficiency Virus
LMICs	Low- and Middle-Income Countries
MDR-TB	Multi-drug-Resistant Tuberculosis
MOH	Ministry of Health
MTB	Mycobacterium Tuberculosis
OR	Odd Ratio
PPM	Public-Private/Public-Public Mix

Pre-XDR	Pre-Extensively-drug- Resistant
PTB	Pulmonary Tuberculosis
RIF	Rifampicin
RR-TB	Rifampicin-Resistant Tuberculosis
SARS-COV2	Severe Acute Respiratory Syndrome - Corona virus - 2
SPSS	Statistical Package for Social Sciences
SSM	Sputum Smear microscopy
TB	Tuberculosis
TBL	Tuberculosis Leprosy
TPT	Tuberculosis Preventive Therapy
UHC	Universal Health coverage
UI	Uncertainty interval
UNHLM	United Nations High-Level Meeting
UN	United Nations
WHO	World Health Organization
XDR	Extensively Drug Resistant
XDR-TB	Extensively Drug Resistant Tuberculosis

ABSTRACT

Tuberculosis (TB) is an infectious bacterial disease caused by ***Mycobacterium tuberculosis*** **(**MTB**)** that commonly affects the lungs. This Study was conducted to investigate the trend of multi-drug-resistant (MDR)-TB at St. Peter's Specialized Hospital in Addis Ababa, Ethiopia, February 2016 - February 2023. Data were collected using a step-by-step record review method. SPSS version 26 and Excel Microsoft were used to analyze the data using Descriptive statistics, such as frequencies and percentages of different variables. Bivariate and binary logistic regression analysis was done to compute the crude and adjusted odds ratio. P-values less than 0.05 with corresponding 95% confidence intervals (CI) were considered statistically significant. A total of 600 MDR-TB patients received for treatment at the study Hospital during the study years of which 352 (58.7%) were male and 248(41.3%) were female. Majority of the cases were 'new' cases and most of the total patients 439(73.17%) were from Addis Ababa, followed by Oromia Region 90(15.0%). Among the MDR-TB patients, 446(74.3%), 109(18.2%), and 45(7.5%) had pulmonary TB (PTB), Extra-Pulmonary TB (EPTB), and both PTB and EPTB, respectively. The majority of the patients (38.33%) were in the age group 25–34, followed by 22.5% in the age group 15–24. The highest specific MDR-TB prevalence of 122 was detected in 2018, while the lowest prevalence of MDR-TB was in 2016. The overall treatment outcome was classified as cured 183(30.5%), completed in 180(30.0%), died in 79(13.2%), ongoing treatment 65(10.8%), lost follow-up 38(6.3%), treatment failure 39(6.5%) and transferred out 16(2.7%). The successful treatment outcomes (cured or completed) were 363(60.5%), and the unsuccessful treatment outcomes were 237(39.5%). There was a significant association between HIV positivity and MDR-TB treatment outcomes ($p<=0.001$). Patients with a history of contact with MDR-TB cases also had significantly different treatment outcomes compared to those without such contact histories ($p<=0.001$). However, there was no significant association between residence and treatment outcome ($p>=0.157$). Overall, an increasing trend of MDR-TB cases was observed. TB patients should take the prescribed drug according to the physician's procedure carefully, which is very important to reduce the development of antibiotic-resistant bacteria in general.

Key words/phrases: trend analysis, tuberculosis, pulmonary TB, Extra-pulmonary TB, MDR-TB, treatment outcome**.**

1: INTRODUCTION

1.1 Background of the study

Tuberculosis (TB) is an infectious disease that is a vital cause of afflicted health and one of the main causes of death at global. Until the corona virus (COVID-19) pandemic, TB was the leading cause of death from a single infectious agent, ranking above Human Immuno Deficiency Virus (HIV)/Acquired Immuno Deficiency Syndrome (AIDS) (WHO, 2022). Drug-Resistant (DR)-TB continues to be a public health hazard. Resistance to isoniazid and rifampicin – the two most effective first-line drugs is of greatest concern; resistance to both drugs is defined as Multi-DR-TB (MDR-TB). Both MDR-TB and Rifampicin-Resistant-TB (RR-TB) require treatment with second-line drugs (WHO, 2021).

TB continues to be a significant public health problem in the World Health Organization (WHO) African Region, with a dominant number of cases and mortality. Despite making up only 15% of the world's population, the region accounted for 23% of new TB cases and 31% of TB-related deaths in 2021 (WHO, 2023). Approximately 25% of people worldwide either have *Mycobacterium Tuberculosis* ***(***MTB***)*** infection or are at risk of getting the illness. Furthermore, because TB is a disease of the impoverished, a large portion of the TB disease burden is carried by Low and Middle-Income Countries (LMICs) (Cohen *et al.*, 2019). Because of this, these nations require even more intensive TB preventive initiatives that work with their limited resources in order to make a major difference in case identification, diagnosis, and treatment possibly saving lives (WHO, 2023).

TB is a major public health problem posing significant deleterious health impacts by affecting the productive segment of the population and resulting serious burden to the health system and exploiting the individual/household economy. Despite the 42% of decline in the annual TB incidence from 369 cases per 100,000 populations in 1990 to 177 per 100,000 populations in 2016, the Ethiopia remains to be among the 30 countries reported with high burden of TB, TB/HIV and DR-TB for 2015 to 2020. TB related mortality is highlighted in the top ten reported causes of death among hospital admissions, with annual estimated death rate of 26 per

100,000populations in 2015 according to Federal Ministry of Health (FMOH) Report (FMOH, 2018). In Ethiopia, TB is a main public health problem. The nation is still among the 22 high TB burden countries with high number of missed and infectious TB cases in the community. TB is among the top ten causes of admission and deaths in adults in Ethiopia (Setegn Eshetie *et al*., 2017; Amare Deribew *et al*., 2018).

1.2 Statement of the Problem

Globally, TB is a severe public health concern. Every year approximately 9 million people develop TB a transmitted infection, usually of the lungs and about two million people die from the disease. TB can be cured by taking a lot of powerful antibiotics daily for at least six months. Ethiopia is one of the 30 nations with the highest rates of HIV, TB and MDR-TB. From 22 nations with a high TB burden, Ethiopia ranked seventh in the world (FMOH, 2018; WHO, 2017).

TB in Ethiopia that was excessively impacts populations in low resource environment. Ethiopia is among the countries with a dominant incidence of TB, MDR-TB, and TB/HIV, with a predicated 151 and 1.4 TB and MDR-TB cases per 100,000 people, correspondingly. According to the WHO's 2019 global TB report, MDR/RR-TB was expected to be present in 0.71% of Ethiopia's new TB cases and 16% of its retreatment TB cases (WHO, 2019).

St. Peter’s Specialized Hospital is a well-known for TB facility. Because of this, people from different parts of the country visit this hospital for MDR-TB treatment. Some of them recover from this infectious disease and leave the hospital, where some patients die of by this widespread disease. In addition, after the COVID-19 outbreak, the focus of the health care system was on this new pandemic.

In spite of efforts to control this fatal disease, the prevalence and mortality rates still rise gradually, affecting especially economically productive age group. Up to date information on TB, its diagnosis, and treatment outcome is important for its control and management. This study, aimed to investigate the trend of MDR-TB in St. Peter’s Specialized Hospital.

1.3 Objectives of the Study

1.3.1 General objective

The general objective of this study was to assess MDR-TB Cases at St. Peter's Specialized Hospital, Addis Ababa, Ethiopia from February 2016 to February 2023.

1.3.2 Specific Objectives

The specific objectives of this study were:

- To determine the treatment status of MDR-TB patients.
- To estimate the trend of MDR-TB for the last 7 years.
- To determine MDR-TB distribution by sex and age.
- To determine MDR-TB distribution by patient address.
- To determine the association between dependent and independent variables.

1.3.3 Limitations of the study

This research has some limitations. The major limitation of this study is related to the use of retrospective secondary data, which is restricted to information recorded in the hospital. The other limitation is that since it was a hospital-based study, it would not have been representative of the general population.

2: LITREATURE REVIEW

2.1. Global Prevalence of MDR-TB

Globally, the estimated number of people who developed MDR-TB or RR-TB (MDR/RR-TB) each year was relatively stable between 2015 and 2020, but it increase in 2021. There were an approximated 450 000 incident cases (95%) in 2021, up 3.1% from 437 000 (95%) in 2020. In 2021, the estimated proportion of people with TB who had MDR/RR-TB was 3.6% (95% UI: 2.7–4.4%) among new cases and 18% (95% UI: 11–26%) among those previously treated (WHO, 2022).

Three countries accounted for 42% of the estimated global number of people who developed MDR/RR-TB in 2022: India (27%), the Philippines (7.5%) and the Russian Federation (7.5%). The highest proportions (>50% of previously treated cases with MDR/RR-TB) are found in the Russian Federation and in several countries in Eastern Europe and Central Asia (WHO, 2023).

DR-TB, both RR and MDR, is a growing burden, affecting 450 000 and 77 000 people in the Africa region respectively. Of these cases 53% were from Nigeria and South Africa (WHO, 2023).

Ethiopia is still among the 22 high TB burden countries with high number of missed and infectious TB cases in the community (WHO, 2017). The prevalence and incidence of TB in Ethiopia in 2014 were 211 and 214 per 100,000 populations respectively (WHO, 2015). Increasing the trends of MDR-TB (2% among new cases in 2006 vs 4.5% among new cases in 2016) is a serious public health challenge for the country (WHO, 2015; Setegn Eshetie *et al*., 2017).

TB is one of the world's leading causes of death and a significant contributor to poor health. Prior to the COVID-19 pandemic, TB was the most common infectious disease-related cause of mortality, surpassing HIV/AIDS (WHO, 2021).

One- quarter of the world's population is thought to be infected by the respiratory infection MTB, which has caused more fatalities throughout human history than any other microbe (Chandra *et al*., 2021). There are two types of drug resistance: primary resistance and secondary resistance. When patients come into contact with and become infected with a DR strain, primary resistance occurs. When patients take TB medicine, inadequate regimens, drug malabsorption, and poor adherence to treatment all contribute to the development of acquired resistance, also known as secondary resistance. While acquired resistance is the cause of most MDR-TB infections, a prior study found that in most high-burden settings, transmission rather than resistance acquisition occurred during therapy (Kendall *et al*., 2015).

DR-TB is a man-made disease that is mostly the product of human mistake due to poor supply management, low-quality anti-TB medications, and inadequate or improper treatment. HIV further exacerbates the situation (Fantahun Biadglegne *et al*., 2014).The most recent WHO study states that TB is Second only to HIV as the leading infectious disease killer and is the main cause of mortality for HIV-positive individuals. Despite the availability of effective medications for nearly additional 50 years, TB continues to be a leading cause of illness and mortality worldwide. According to the (WHO, 2017) study, there were an estimated 10.4 million new cases of TB worldwide, with 6.2 million men, 3.2 million women, and 1 million children affected.

2.2. TB Pathogenesis

Infection starts when MTB from aerosols or sputum undergoes phagocytosis in the lung reaching tissue-resident alveolar macrophages and dendritic cells. MTB then go through a transient period of unrestricted intracellular replication, during which infected cells leave to local draining lymph nodes. Once there, MTB can affect other areas of the lungs by infecting other host cells. With the onset of cellular immunity, a local pro-inflammatory response leads to the recruitment of additional monocytes and lymphocytes, which in turn cluster around the infected macrophages, forming what is known as a granuloma. Granuloma is a pathological hallmark of TB, and it is thought that MTB continue in a prolonged state of delayed or arrested replication at this site. If MTB multiplies too much, the granuloma will not be able to control the infection and MTB will eventually pass to other organs, including the brain. At this stage, MTB can enter the bloodstream or re- enters the respiratory tract to be released causing new infections (Yan *et al*., 2022).

PTB frequently develops slowly, without a definite date of onset. The disease has a wide spectrum of manifestations ranging from skin positivity with negative X-rays to far advanced TB. Ordinarily, until the disease is moderately or far advanced, as shown by changes on the roentgenogram, signs are slightest and often attributable to other causes, such as excessive smoking, hard work, pregnancy, or other conditions (Lyon and Rossman, 2017).

EPTB can occur through hematogenous, lymphatic, or localized bacillary dissemination from a primary source, such as PTB, and affects the brain, eye, mouth, tongue, lymph nodes , spine, bones, muscles, skin, pleura, pericardium, gastrointestinal, peritoneum, and the genitourinary system as main and/or disseminated disease .Risk factors involved in the development of EPTB are chiefly increasing age, concurrent HIV infection and alcoholism, co-morbidities such as chronic renal disease, diabetes mellitus or immune suppression (Dias *et al*., 2016).

Anyone can get TB, regardless of their age or gender. Adult men carry the heaviest burden of the disease, accounting for 56% of all TB cases in 2020, compared to adult women's 33% and children's 11%. Men experience the disease at a higher rate than women do, and there are greater gaps in case detection and reporting for men, according to data from national TB prevalence surveys (WHO, 2021). The high incidence of TB in LMICS is caused by a number of factors, including limited access to health care facilities, inadequate TB prevention and control systems, crowded living quarters, workplace hazards, individuals' poor nutritional status, a high prevalence of HIV, other comorbidities, and drug addiction (Churchyard *et al*., 2014). MTB strains become resistant to antibiotics as a result of spontaneous gene changes that reduce the bacterium's susceptibility to the most used anti-TB medications. The effectiveness of anti-TB therapy may be impacted by these genes, which may encode drug targets or processes of drug metabolism (WHO, 2020).

2019 saw an increase from 64% in 2018 to 69% of notified TB patients having a recorded HIV test result. 86% of TB patients in the WHO African Region, where the prevalence of HIV-associated TB is highest, had a recordable HIV test result. A total of 456 426 cases of TB and HIV co-infection were recorded, and 88% of those patients were receiving antiretroviral medication (WHO, 2020).

Around 84% of TB fatalities among HIV-negative persons worldwide in 2020 and a total of 85% of TB deaths among both HIV-negative and HIV-positive people happened in the WHO African and South-East Asia regions, respectively. India was responsible for 38% of all TB fatalities worldwide among HIV-negative persons and 34% of all TB deaths worldwide among both HIV-positive and HIV-negative people. 53% of deaths among HIV-negative people were caused by men, 32% by women, and 16% by children under the age of 15. 50% of TB deaths among HIV-positive individuals were caused by men, 40% by women, and 9.8% by children (WHO, 2021).

MDR-TB is now a serious threat to global health security, adding to the growing burden of Antimicrobial Resistance (AMR). In 2018, there were about one-half a million new cases of RR-TB, but only one in three cases was reported by countries to have been treated. Globally, 3.4 percent of new TB cases and 18 percent of previously treated cases had MDR- or RR-TB (WHO, 2019).

RR or MDR-TB is an estimated 3.3% of new cases of TB and 17.7% of those that have already been treated. AMR-is the largest cause of death globally, and DR-TB is a danger to the security of global health (FMOH, 2021). Ethiopia is one of the least developed nations in the world and one of the nation's most severely afflicted by TB outbreaks. The government reported 117,705 TB cases in 2018, 28,600 deaths (3600 of whom were co-infected with TB and HIV), and only 11% of the $93 million annually required for TB care and control was provided domestically (WHO, 2018).

2.3. Transmission of Tuberculosis

MTB, the bacillus that causes TB, spreads when TB patients discharge bacteria into the air, such as when they cough. Although the disease primarily affects the lungs, Extra Pulmonary TB (EPTB) can also affect other places (WHO, 2020). MTB is dispersed in airborne droplet nuclei, which have a diameter of 1 to 5 microns. when people with pulmonary or laryngeal TB illness cough, sneeze, shout, or sing, infectious droplet nuclei are produced. These tiny particles may float in the air for several hours, depending on the surroundings. MTB is spread by inhaling droplet nuclei that contain the disease, which travel through the respiratory system and land in the lungs' alveoli to cause infection (FMOH, 2021).

As obligate aerobes, the tubercle bacilli thrive in places of the body with abundant oxygen. People with pulmonary TB (PTB) eject the bacilli while coughing, sneezing, and talking, which allows them to spread the disease from one person to another via aerosols (Shi *et al*., 2018; Wang *et al*., 2017). Although TB mostly affects the lungs, up to one-third of cases also include other body regions. People with TB can spread the disease to others by coughing, sneezing, singing, or talking when they are contagious. Up to 4.000 droplets can be produced by a single cough. Most infections, also referred to as latent TB, are asymptomatic. According to estimates, up to 10% of infected individuals could develop active TB over the course of their lifetime and, if untreated, up to 50% of patients could pass away (Nicas *et al*., 2005).

2.4. Diagnosis of TB

Sputum smear microscopy (SSM), a quick molecular test that was initially recognized by the WHO in 2010, and culture-based approaches, which take a few weeks to produce findings but are still the gold standard for TB diagnosis, are among the diagnostic tests for the disease. Rapid testing, culture techniques, and sequencing technologies can be used to identify TB that is resistant to first- and second-line anti-TB medications (WHO, 2021).

TB screening is the practice of conducting tests, examinations, or other procedures that should be used on risky groups to identify persons who appear to be healthy but may have active TB (Lonnorth *et al*., 2013). When it comes to resource availability, cost, and predicted yield, the combination of symptom inquiry and chest radiograph (CXR) is the most effective strategy for TB screening (Vanthoog *et al*., 2012). Since Gene Xpert simultaneously detects Rifampicin (RIF's) resistance and MTB, it is the best rapid diagnostic test currently on the market (Arora and Dhanashree, 2020).

SSM and Xpert MTB/RIF are the two frequently used confirmatory tests for active TB. However, the majority of clinicians rely on the results of a CXR and a questionnaire about symptoms to make the diagnosis of active TB. Patients who do not improve following a brief course of broad-spectrum antibiotics should have another evaluation for possible concealed TB (Steingart *et al*., 2006). According to the WHO recommendations, bacteriological confirmation of TB and testing for DR utilizing quick molecular tests, culture techniques, or sequencing technologies are required for the diagnosis of MDR/RR-TB (WHO, 2020).

2.5. Treatment of TB

The 1940s saw the invention of the first efficient medication therapies. Currently, a 6-month regimen of four first-line drugs isoniazid, RIF's, ethambutol, and pyrazinamide is advised for those with drug-susceptible TB illness (WHO, 2021).

TB is treatable and avoidable. A 6-month treatment regimen can effectively treat 85% of persons who have TB disease, and regimens of 1-6 months can be used to treat TB infection. To guarantee that everyone who has an illness or infection may receive these medicines, universal health coverage (UHC) is required. Through multi-sectoral effort to address TB determinants such poverty, undernutrition, HIV infection, smoking, and diabetes, the number of persons getting infection and developing disease (and thus the number of deaths caused by TB) can also be decreased. Fewer than 10 cases and less than 1 death per 100,000 people per year are the limits of TB sickness in some nations. Research innovations are required, such as a new vaccination. Global levels already attained in these low-burden nations (WHO, 2021).

Progress toward the TB treatment and preventive targets set at the United nations (UN) high-level meeting on TB could be slowed or reversed, particularly in countries with a high TB burden, as a result of additional strain on health facilities brought on by the COVID-19 epidemic and effects on care-seeking behavior (WHO, 2020).The use of second line anti TB medications, which are more toxic and ineffective, is necessary for the treatment of DR-TB, particularly MDR-TB, which is time demanding and expensive (WHO, 2019).

2.6. TB epidemiology in Ethiopia

The WHO objective of 68% for TB case detection was not met by Ethiopia (FMOH, 2017), and the rate is even lower for women and children. 117,705 TB cases were reported, out of an anticipated 172,000 cases. PTB accounted for more than two thirds of all TB cases in the nation; EPTB cases burdened the country at 31%, double the global proportion (WHO, 2018).

Ethiopia makes up 3% of the 3 million TB cases that the international health system misses each year. An estimated 35% (56,164) of incidence cases of TB were missed in 2016. It is thought that the majority of missing cases tend to focus on underprivileged, vulnerable, and impoverished areas. In addition to having an impact on epidemiology, addressing the missed cases also raises concerns about equity and human rights (FMOH, 2017).

2.7. Trends of TB Cases notifications

Geographically, the WHO areas of South-East Asia (45%), Africa (23%) and the Western Pacific (18%) had the highest percentage of TB cases in 2021. The Eastern Mediterranean (8.1%), the Americas (2.9%) and Europe (2.2%) had lower percentages. Eight of the 30 high-burden countries-India (28%), Indonesia (9.2%), China (7.4%), the Philippines (7.0%), Pakistan (5.8%), Nigeria (4.4%), Bangladesh (3.6%), and the Democratic Republic of the Congo (2.9%) accounted for more than two thirds of the estimated global total of incident cases. These 30 high-burden countries accounted for 87% of all estimated incident cases worldwide (WHO, 2022).

An estimated 10.0 million individuals (9.0–11.1 million) worldwide contracted TB in 2018. With an anticipated 1.2 million deaths (range, 1.2–1.3 million) among HIV-negative persons and 251 000 deaths (range, 223 000–281 000) among HIV-positive people, it was the highest cause of death from a single infectious agent (WHO, 2019).

The TB incidence rate defined as the number of new cases per 100,000 people annually rose by 3.6% between 2020 and 2021 after declining by roughly 2% annually for the most of the previous two decades (WHO, 2022). In the world, 24% of cases and 32% of deaths occurred in the African continent. It comprised nations with some of the worst TB epidemics globally, particularly those where the general population has a high HIV prevalence (Law and Floyd, 2020).

With a high number of cases and fatalities, TB is a serious public health issue in the African Region. The region accounted for 23% of new cases of TB and 31% of TB -related deaths in 2021, although making up only 15% of the world's population. This translates to an estimated 500 000 deaths and 2.5 million TB cases. About 20% of newly reported cases of TB were among individuals with HIV/AIDS. The region's TB death rate is still high, with a few nations having substantial disease loads. For example, 48% of all TB deaths in the African Region were expected to have occurred in 2021 in the Democratic Republic of the Congo, Nigeria, and South Africa (WHO, 2023).

Ethiopia is currently ranked third in Africa and eighth overall among the 22 nations with the highest TB burden. An estimated 164 cases of all TB types per 100,000 people result in an annual mortality rate of 27.5 cases per 100,000 people (FMOH, 2016 and WHO, 2018). TB is Ethiopia's third-leading cause of hospital fatalities and the eighth-leading reason of hospital admissions; according to a 2011 FMOH report (Kebede Abebaw *et al*., 2014).

The table below shows the prevalence, incidence and Mortality estimates of TB in Ethiopia from 1990-2011

Table 2-1: Prevalence, incidence and mortality estimates of tuberculosis in Ethiopia: 1990 – 2011

Year	**Prevalence rate**	**Incidence rate**	**Mortality rate**
1990	425	367	49
1995	480	419	48
2000	430	421	41
2005	333	342	29

2006	314	324	27
2007	296	308	25
2008	280	293	23
2009	265	280	21
2010	251	261	20
2011	237	258	18

Source: REVISED STRATEGIC PLAN TUBERCULOSIS, TB/HIV, MDR-TB, AND LEPROSY PREVENTION AND CONTROL 2006-2013 EC (2013/14 – 2020).

2.8. TB control in Ethiopia

After a successful pilot program with the creation of the first integrated TB and Leprosy Prevention and Control Program handbook, Ethiopia adopted the Directly Observed Treatment Short-Course (DOTS) method in 1997. Activities for TB/HIV collaboration were piloted in 2004 and then ramped up nationally. In later years, the Private/Public-Public Mix(PPM) DOTS, Community TB Care, and MDR-TB programs were also piloted and incorporated into the TB-Leprosy (TBL) and TB/HIV control program (FMOH, 2017).

Ethiopia has accepted the post-2015 Global End TB Strategy and the United Nations High-Level Meeting (UNHLM) objectives, committed to stepping up the fight to end the TB epidemic by 2035, and integrated its National TB Strategic Plan with the National Health Sector Transformation Plan. Between 2015 and 2035, the National Terminate TB Strategy seeks to end the TB epidemic by lowering TB-related fatalities by 95% and incident TB cases by 90%(FMOH, 2017c).Effective TB control programs require early and accurate diagnoses in order to enhance treatment, minimize transmission, and manage the emergence of DR. In order to control TB, laboratories and laboratory networks are essential. They provide testing for diagnosis, surveillance, and treatment monitoring at all levels of the healthcare system (Ridderhof *et al.*, 2007; Steingart *et al.*, 2007).

The struggle to control TB disease is made more difficult by the epidemiology of TB transmission and the emergency of DR-TB. Therefore, if infectious cases are identified and properly treated, appropriate diagnosis and treatment of TB contribute to lowering the burden of TB (Sintayehu Fekadu *et al*., 2015).The growth of DR to more anti-TB medications, which results in MDR, pre-extensively drug-resistant (Pre-XDR), and extensively drug-resistant (XDR) TB, poses a challenge to TB control today (WHO, 2019and WHO, 2018).The current Severe Acute Respiratory Syndrome - Corona virus – Two (SARS-CoV-2) 2019 pandemic, commonly known as COVID-19, has had a significant negative impact on TB prevention and control (WHO, 2020).

2.9. COVID-19 Pandemic time and the access to TB Services

In early 2020, in response to the emergence and global spread of SARS-CoV-2, many countries went into lockdown, as well as implementing other restrictions to curb the spread of infection. The effects on TB services were immediate, and severe. On the one hand, people's ability to access TB diagnosis and treatment services were suddenly curtailed, due to lockdown-imposed lack of transportation, "stay-at-home" messaging from public health authorities, fear of visiting health facilities, and increased stigma due to common symptoms between TB and COVID-19 (Sahu *et al*., 2022).

COVID-19 may have complicated TB patients' treatment in addition to lowering the number of TB diagnoses by causing drug stock outs and inadequate treatment support. It is anticipated that such disruption may impact the outcomes of TB therapy by raising the probability of treatment interruption and delay as well as decreasing treatment adherence (Hussen Mohameed *et al*., 2020). By 2022, 202 nations and territories representing more than 99% of the global population and TB cases had submitted combined data to WHO on a number of predetermined metrics. Following the start of the COVID-19 pandemic, nations are now able to notify WHO on TB on a monthly or quarterly basis (Falzon *et al*., 2023).

3: MATERIALS AND METHODOLOGY

3.1. Description of the study area

The study was conducted at St. Peter's Specialized Hospital in Addis Ababa, Ethiopia. St. Peter's Specialized Hospital was established in the June 1961 Gregorian Calendar (GC). It is a governmental hospital under the FMOH. St. Peter's Specialized Hospital is currently located in Gulele Sub City, Woreda 01. Due to their extensive experience in the management of TB, St. Peter's Specialized Hospital has been selected as the facility that would provide treatment and follow-up to avoid TB. This hospital treats both inpatients and outpatients. St. Peter's Specialized Hospital provides various services, especially in TB diagnosis and treatment. It helps as a referral TB hospital in Addis Ababa, Ethiopia, and has a vision to become a Center of Excellence for the diagnosis and treatment of TB in East Africa.

The location map and a front view of the study place are shown in the figure below respectively.

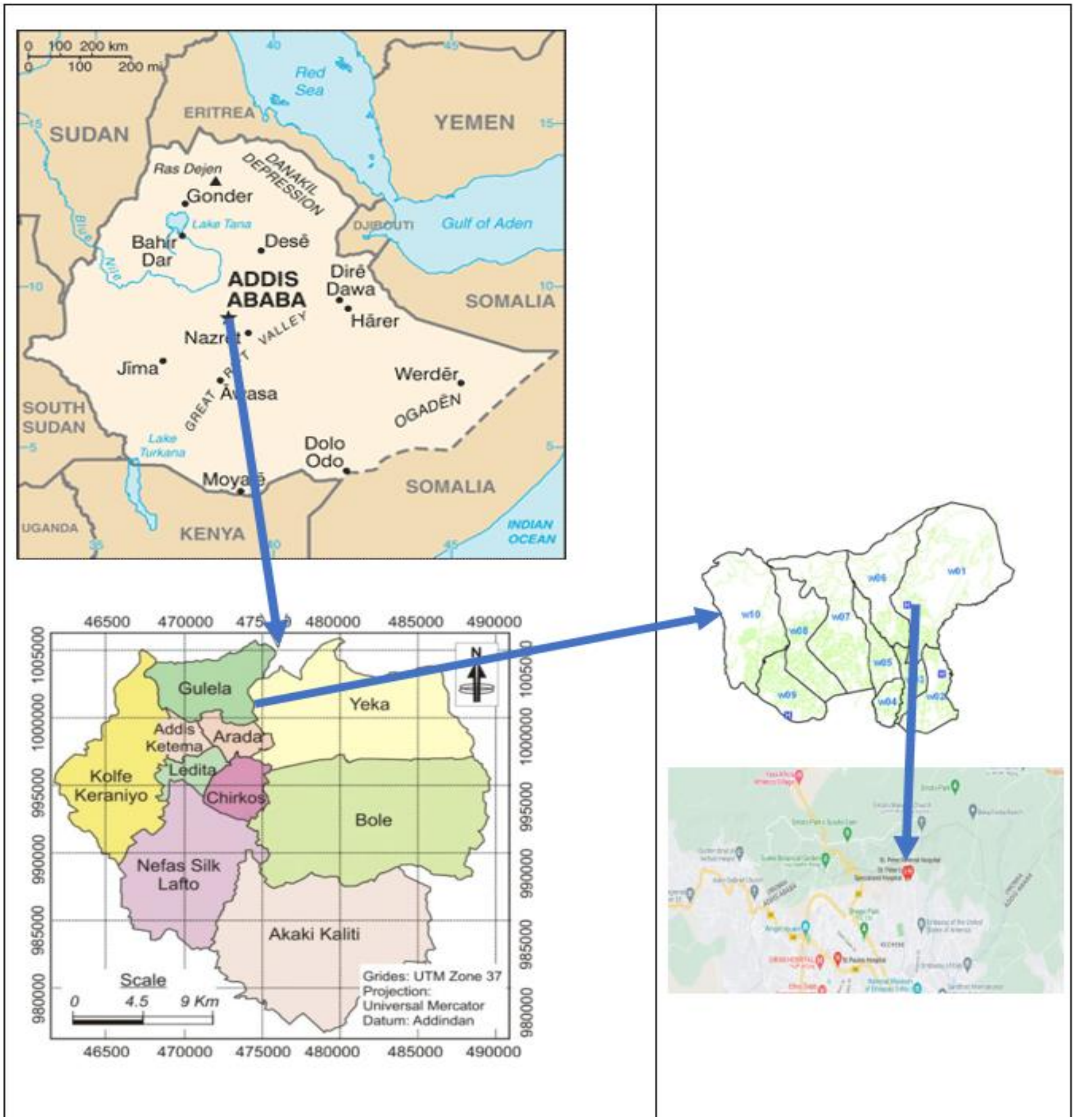

Figure 3-1: Map of the study area (Source, internet).

Figure 3-2: St. Peter’s Specialized Hospital and MDR Ward (Source, Hayleyesus)

3.2. Operational definition

MDR-TB It is a form of TB that is resistant to at least two of the most effective first-line drugs used to treat TB: isoniazid and rifampicin.

PTB is a bacterial infection that mostly affects the lungs. It’s caused by the bacterium MTB.

EPTB: Any case of TB that has been confirmed by clinical or microbiological means to impact organs other than the lungs, including the belly, genitourinary system, pleura, lymph nodes, skin, joints, and bones, or meninges.

PTB, smear-positive

When a patient has MTB in their sputum or other respiratory secretions, it is known as smear-positive PTB. Acid-fast bacilli (AFB) staining is used to detect MTB in sputum or other respiratory secretions in patients with smear-PTB.

PTB, smear-negative

Smear-negative PTB is defined as when a TB test did not detect the presence of MTB bacteria in the sputum sample under a microscope.

Previously treated: those who after taking anti-TB medication one or more than one month had a relapsed TB diagnosis.

New TB: Cases of TB that have not had prior treatment are referred to as new cases. This can include newly discovered primary infections as well as latent TB that have reactivated.

Relapse: Patients who were thought to be cured or to have completed their therapy after completing their most recent cycle of treatment

Treatment after failure: This term describes a patient's status after their most recent therapy session if, in compliance with national protocol, they were considered treatment failures.

Treatment after lost to follow-up: refers to patients who were deemed lost to follow-up at the conclusion of their most recent TB treatment course and are now scheduled to get a full course of TB therapy.

Others: describes patients who do not fit any of the previously listed criteria or who have previously had TB treatments but whose results are uncertain or lack documentation after their most recent course of treatment.

Transfer in: A patient who starts therapy in one reporting unit and is moved to another to finish

Cured: a PTB patient who has been previously smear- or culture-negative at least once, received bacteriological confirmation of the illness at the beginning of treatment, and completed treatment as required by national policy.

Treatment completed; A TB patient who did not exhibit any signs of resistance to treatment but who did not have any records indicating that sputum or culture results during the last month of treatment were negative, either because the tests were not run or the information is not available.

Died; A patient with TB who passed away either during treatment or before it began (after registering).

Lost to follow-up (LTFU);A patient is considered LTFU if they were registered at a TB treatment center or reporting unit but did not start anti-TB therapy for eight weeks or if their treatment was stopped for eight weeks or longer.

Treatment success: A sum of cured and completed treatment.

Unsuccessful treatment outcome: treatment failure, lost to follow up, death, and not evaluated are considered as unsuccessful TB treatment outcomes.

First Line drugs: The main medications used to treat PTB are called first-line treatments. They constitute the mainstay of TB treatment and are efficient against MTB. Primary first-line medications consist of: Rifampicin (RIF), Isoniazid (INH), Ethambutol (EMB), Pyrazinamide (PZA), and streptomycin.

Second-line TB drugs: When first-line medications are not successful in treating TB, usually because of drug resistance or intolerance, second-line medications are utilized. These medications are often only used in cases of DR-TB, such as extensively DR-TB (XDR-TB) or MDR-TB. Primary second-line medications consist of: bedaquiline (Bdq), linezolid (Lzd), moxifloxacin (Mfx), levofloxacin (Lfx), clofazimine (Cfz), cycloserine (Cs), para-amino salicylic acid.

Long term regimen-For MDR/RR-TB patients, long-term regimens are used. These last for at least 18 months and can be made to order or standardized. These regimens usually comprise a minimal quantity of second-line TB medicines that are considered beneficial based on patient history or drug-resistance patterns.

A shorter MDR-TB regimen is a 9–12 month, largely consistent treatment plan for MDR/RR-TB. Its length and makeup closely align with the regimens for which documented data has been collected across multiple contexts.

Individualized regimens: Individualized regimens are recommended for patients whose TB disease is caused by MTB strains that exhibit widespread drug resistance such as XDR-TB;

patients who do not meet the requirements for, or did not respond well to, the aforementioned 6- or 9-month regimens; and patients who are intolerant to significant components of the aforementioned regimen.

3.3. Study Period

The study was conducted from February 2016 to February 2023.

3.4. Research Design

The research method used was retrospective data extraction from patient medical records. The research method was a cross-sectional design to assess the Trend of MDR-TB at St. Peter's Specialized Hospital, Addis Ababa, Ethiopia, from February 2016 to February 2023 to form a data base for retrospective data; both qualitative and quantitative methods were used.

3.5. Study Population

The study population was MDR-TB patients who started treatment for TB in St. Peter's Specialized Hospital from February 2016 to February 2023. The medically registered file was reviewed. The estimated study population was 600.

All the 600 MDR-TB patients that visited the St. Peter's Specialized Hospital charts, both males and females, young and old were sorted out to form the data base for this analysis using Microsoft Excel and SPSS (Statistical Package for Social Science).

3.6. Sampling technique and sample size determination

3.6.1. Sampling technique

The sampling technique used for selections in this study was that each individual of MDR-TB patients who visited St. Peter's Specialized Hospital from February 2016 G.C. to February 2023 G.C using medical records, the MDR-TB treatment card, and the bacteriological reports.

3.6.2. Sample size determination

The sampling unit for this study was the individual patient. This means that each individual in the population has an equal chance of being selected for the sample. Therefore, all individuals who started treatment for MDR-TB in St. Peter's Specialized Hospital from February 2016 to February 2023 were taken as a sample size.

3.7. Study variables

3.7.1. Dependent variables

The dependent variables are the treatment outcomes, which are categorized as treatment completed, cured, on treatment, treatment failed, transfer out, lost follow-up treatment, and died. When a sputum smear test results in a bacteriological negative result during the final month of treatment, the patient is deemed to be "cured." A patient is considered to be "treatment completed" if they finish their treatment without receiving a negative bacteriological test in the final month of their care or on at least one prior occasion. A patient is considered to be in treatment failure if, at the end of five months or after, they continue to test positive for the disease. If a patient passes away for whatever cause while receiving care, that patient is deemed "dead." If a patient is moved to another medical facility, they are referred to as "transferred out."

Consequently, the treatment outcomes in this study were divided into two categories: successful treatment outcomes (which included cases that were cured and completed) and unsuccessful outcomes, their care or on at least one prior occasion.

3.7.2. Independent variables

Socio-demographic factors: Age, Sex, residence, HIV Status, length of treatment, MDR Contact history, other illness, use of second line drugs.

3.8. Data collection methods

To achieve the stated objectives, the study employed secondary data sources to seek sufficient information. The secondary data source collected was based on a medical registration chart obtained through document analysis.

The study looked at the medical records of all the patients who went to St. Peter's Specialized Hospital from February 2016 to February 2023, except for those with missing information.

TB data was collected from a checklist that contains a medical record number to ensure the confidentiality of patient results**.** Age, sex, residence, HIV status, and TB Type were taken from the patient's medical care card.

A data collection form was completed that recorded each patient's personal and demographic profile. The most important variables driving the thesis were age, sex, treatment outcome, residence, HIV status, MDR-contact history and length of treatment.

3.9. Data Analysis

Data analysis means looking at data to understand it better. Logic and reasoning were used to carefully study each part of the information gathered. The analysis is just one part of the many things that need to be done to do a thesis experiment.

The study was analyzed using Microsoft Excel and SPSS software version 26. The collected Data was checked for consistency and completeness and entered into SPSS software version 26. Descriptive analysis, figures and tables were all developed to support the analysis. Binary logistic regressions were employed to measure the association among variables. The Crude odd ratios, adjusted odd ratio, P-Value were computed. P-value less than 0.05 with corresponding 95% confidence interval (CI) were considered statistically significant.

3.10. Ethical consideration

Ethical clearance was obtained from the research ethical review committee office of St. Peter's Specialized Hospital, Addis Ababa, Ethiopia.

4: RESULTS

4.1. Sociodemographic Characteristics

Among 600 MDR-TB cases, 352(58.7%) were males and 248(41.3%) were females. The mean age of the patients was28, ranging 3-87 years old. The majority of the patients 38.33% were in the age group 25-34, followed by 22.5% age group 15-24. The majority of the patients 439(73.17%) were from Addis Ababa 90(15.0%) followed by Oromia region (Table 4.1). Regarding the annual distribution, the retrospective data shows highest MDR-TB Cases 122(20.33%) in the year 2018, 105(17.75%) in 2021 and 101(16.83%) in the year 2022. The lowest MDR-TB Cases 19(3.16%) was observed in the year 2016.

Table 4-1: Sociodemographic characteristics of MDR-TB patients at St. Peter's Specialized Hospital, February 2016 to February 2023

Variables	Frequency	Percent
Age (year)		
0-14	17	2.83
15-24	135	22.5
25-34	230	38.33
35-44	119	19.84
45-54	48	8.0
55-64	30	5.0
≥65	21	3.5
Sex		
Male	352	58.7
Female	248	41.3
Residence		
Addis Ababa	439	73.17
Oromia	90	15.0
Amhara	36	6.0
Former SNNPR	21	3.5
Benishangul-Gumuz	4	0.67
Gambella	4	0.67
Tigray	3	0.5
Afar	3	0.5
Total	600	100.0

SNNPR =Southern Nations, Nationalities, and Peoples Region.

4.2. Clinical characteristics

4.2.1. MDR-TB Category

PTB, EPTB, and both PTB and EPTB were the different types of TB. The gathered retrospective data was arranged below to depict the distribution and trend of TB types at St. Peter's Specialized Hospital over the previous seven years. Retrospective data obtained between February 2016 and February 2023 was used to examine the case notification pattern. Thus, during the course of the study, 600 individuals received an MDR-TB diagnosis (table 4-2). Among MDR-TB patients, 446(74.3%), 109(18.2%), and 45(7.5%) had pulmonary tuberculosis (PTB), EPTB, or both PTB and EPTB.

Table 4-2: Trend of MDR-TB types among MDR-TB patients at *St. Peter's* Specialized Hospital, February 2016 to February 2023. N=600

	MDR-TB type			
Year	**PTB, n (%)**	**PTB & EPTB, n (%)**	**EPTB, n (%)**	**Total, n (%)**
2016	18(94.7)	1(5.3)	-	19(100)
2017	45(76.3)	5(8.5)	9(15.2)	59(100)
2018	101(82.8)	7(5.7)	14(11.5)	122(100)
2019	57(75.0)	8(10.5)	11(14.5)	76(100)
2020	56(68.3)	11(13.4)	15(18.3)	82(100)
2021	82(78.1)	8(7.6)	15(14.3)	105(100)
2022	72(71.3)	3(3.0)	26(25.7)	101(100)
2023	15(41.7)	2(5.6)	19(52.8)	36(100)
Overall	**446(74.3)**	**45(7.5)**	**109(18.2)**	**600(100)**

N=number of patients, - = not recorded, PTB=Pulmonary tuberculosis, EPTB=Extra-pulmonary tuberculosis, MDR-TB = Multi-Drug-Resistant Tuberculosis.

Based on the data shown in the table, it can be noticed that the number of MDR-TB cases increased from 19 in 2016 to 59 in 2017. There was also an increase from 2017 to 122 in 2018, with a subsequent reduction in MDR-TB cases starting in 2019.

4.2.2. HIV status of MDR-TB patients

HIV status in MDR-TB patients is an essential factor in controlling and treating both illnesses. Treatment for MDR-TB can be made more difficult by HIV infection and vice versa. The Retrospective data obtained between February 2016 and February 2023 was used to examine the distribution of HIV and Analysis result was shown below (table 4-3).

Table 4-3: Distribution of MDR-TB patients by HIV status

Age	**Positive, n** (%)	**Negative, n (%)**
0-14	4(23.53)	13(76.47)
15-24	55(40.74)	80(59.26)
25-34	73(31.74)	157(68.26)
35-44	60(50.42)	59(49.58)
45-54	28(58.33)	20(41.67)
55-64	10(33.33)	20(66.67)
≥65	8(38.1)	13(61.9)
Total	**238(39.67)**	**362(60.33)**
Gender		
Male	144(40.9)	208(59.1)
Female	94(37.9)	154(62.1)
Total	**238(39.67)**	**362(60.33)**

Out of the study population (n=600), 238(39.67%) were HIV positive, whereas 362(60.33%) were negative. 94(37.9%) of the group of people who tested positive for HIV were female, and 144(40.9%) were male. This suggests that the rate of HIV positivity among MDR-TB patients was greater in men than in women. The age groups between 45 and 54 years old (58.33%) and between 35 and 44 years old (50.42%) had the largest percentage of MDR-TB patients affected by HIV.

4.2.3. MDR-TB contact histories of patients

Healthcare professionals can find more people who might have been exposed MDR-TB by looking into who the MDR-TB patient has been in close contact with. This is crucial for the early detection and treatment of dormant TB or early cases of active MDR-TB. From A total of 600 people included in the study; 160(or 26.67% of the population) had a history of MDR-TB contact, and 440 (73.33%) had never had MDR-TB (table 4.4).

Table 4-4: Distribution of MDR-TB patients by MDR Contact history

Age	**Positive, n** (%)	**Negative, n (%)**
0-14	3(17.65)	14(82.35)
15-24	38(28.15)	97(71.85)
25-34	61(26.52)	169(73.48)
35-44	29(24.37)	90(75.63)
45-54	18(37.5)	30(62.5)
55-64	6(20)	24(80)
≥65	5(23.80)	16(76.2)
Total	**160(26.67)**	**440(73.33**
Gender		
Male	87(24.7)	265(75.3)
Female	73(29.4)	175(70.6)
Total	**160(26.67)**	**440(73.33**

According to the above table, the age group between 45-54 years old, with 18(37.5%) and 15-24 years old, with 38(28.15%), had the highest proportion of patients with a history of previous MDR-TB contact. Based on Gender, there were 87(24.7%) males and 73(29.4%) females. This suggests that a larger percentage of female MDR-TB patients had a history of MDR-TB than male MDR-TB patients.

4.2.4. Use of second line drugs for MDR-TB

When the traditional first-line medications, isoniazid and rifampicin, are no longer effective owing to resistance, a regimen of second-line treatments is used to treat MDR-TB. According to table 4.5 Out of the study population (n=600), 128(21.33) were Used second line drug, 472(78.67) were not used second line drug. Among the MDR-TB patients, 77(21.88%) were males and 51(20.56%) were female used second line drug.

Table 4-5: Use of second line drug for MDR-TB

Age	**Use of second line**, **n** (%)	**Not used second line drug, n (%)**
0-14	2(11.76)	15(88.24)
15-24	33(24.44)	102(75.56)
25-34	41(17.82)	189(82.18)
35-44	29(24.37)	90(75.63)
45-54	13(27.08)	35(72.92)
55-64	5(16.67)	25(83.33)
≥65	5(23.80)	16(76.19)
Total	128(21.33)	472(78.67)
Gender		
Male	77(21.88)	275(78.12)
Female	51(20.56)	197(79.44)
Total	128(21.33)	472(78.67)

4.2.5. MDR-TB Registration Group

The trends of the registration group of MDR-TB are summarized in the table below. According to the table below the majority of MDR-TB Patients were new cases.

Table 4-6: The distribution of MDR-TB cases at St. Peter's Specialized Hospital (2016-2023).

Registration group	Frequency	Percent
New	270	45.0
Relapse	195	32.5
After failure of first-line treatment	93	15.5
After failure of second-line treatment	25	4.2
After lost-to-follow-up	17	2.8
Total	600	100.0

Out of the 270 newly recorded cases for MDR-TB, 164 had successful TB treatment outcomes, and the remaining 106 had failure treatment outcomes.

There were 195 relapse instances total that were registered for MDR-TB; of these, 120 had effective TB treatment outcomes, while the remaining 75 had unsuccessful TB treatment outcomes.

4.2.6. MDR-TB treatment regimen

Among the MDR-TB patients, 404(67.3%), 165(27.5%), 31(5.17%) used long-term regimen, short term and individualized regime in drug usage respectively.

Table 4-7: The distribution of MDR-TB cases by Treatment Regimen

Age	**Long term, n** (%)	**Short term, n (%)**	**Individualized, n (%)**	**Total, n (%)**
0-14	14(82.35)	3(17.647)	0	17(100)
15-24	92(68.15)	37(27.407)	6(4.44)	135(100)
25-34	144(62.608)	73(31.739)	13(5.65)	230(100)
35-44	82(68.907)	30(25.210)	7(5.88)	119(100)
45-54	38(79.17)	7(14.58)	3(6.25)	48(100)
55-64	21(70)	8(26.67)	1(3.33)	30(100)
≥65	13(61.90)	7(33.33)	1(4.76)	21(100)
Total	**404(67.33)**	**165(27.5)**	31(5.17)	600(100)
Gender				
Male	232(65.91)	106(30.11)	14(3.98)	352(100)
Female	172(69.355)	59(23.790)	17(6.855)	248(100)
Total	**404(67.33)**	**165(27.5)**	31(5.17)	600(100)

The age category was based on WHO.

Patients with MDR-TB may change from a long-term regimen to individualized regimen because of the side effects of drug, not good treatment response and patient health.

4.3. Trend of MDR-TB by Age Groups

The overall trend of MDR-TB patients are categorized by age group and are presented in the figure below. According to the below figure the majority of age group that infected with MDR-TB cases were in age group 25-34.

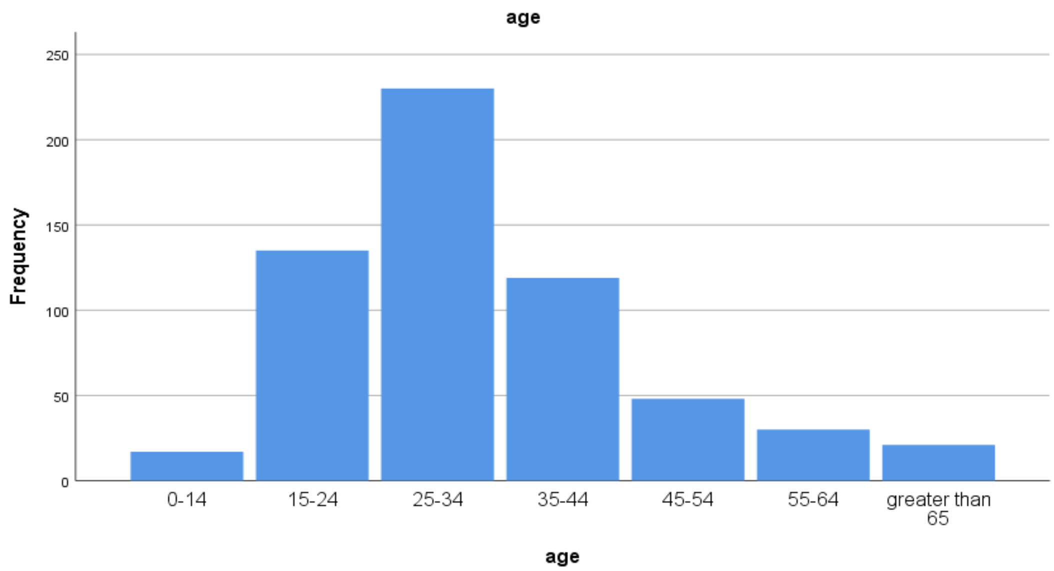

Figure 4-1: MDR-TB categories by age group from 2016-2023.

4.4. Treatment outcomes

From the 600-MDR-TB cases, 363 cases (60.5%) of patients received satisfactory treatment (Table 4-8). Of them, 183 (30.5%) were cured, 180 (30.0%) were treatment completed. Whereas 237 cases (39.5%) did not respond to treatment.

The highest rate of cured outcome was 67(54.9%) in 2018, while the lowest was 13(15.9%) in 2020. All years had recorded deaths, with 2016 having the highest death rate at 11(57.9%) in 2016 and the lowest treatment failure rate at 12 (20.4%) in 2017.

Table 4-8: Trend of treatment outcomes of **MDR-TB** cases from 2016-2023

Year	Treatment outcomes (new, previously exposed)							
	TC, n (%)	C, n (%)	DI, n (%)	OT, n (%)	LFT, n (%)	F, n (%)	TO, n (%)	Total, n (%)
2016	-	-	11(57.9)	-	5(26.3)	2(10.5)	1(5.3)	19(100)
2017	8(13.6)	12(20.3)	10(16.9)	-	15(25.42)	12(20.4)	2(3.38)	59(100)
2018	28(23.0)	67(54.9)	9(7.37)	-	10(8.2)	5(4.09)	3(2.45)	122(100)
2019	20(26.3)	34(44.7)	13(17.1)	-	1(1.3)	5(6.6)	3(4)	76 (100)
2020	49(59.8)	13(15.9)	10(12.2)	1(1.2)	3(3.7)	2(2.4)	4(4.8)	82(100)
2021	40(38.1)	29(27.6)	11(10.5)	15(14.3)	2(1.9)	7(6.6)	1(1.0)	105(100)
2022	29(28.7)	18(17.8)	13(12.9)	36(35.6)	-	4(4.0)	1(1.0)	101(100)
2023	6(16.7)	10(27.7)	2(5.6)	13(36.1)	2(5.6)	2(5.6)	1(2.7)	36 (100)
Total	180(30.0)	183(30.5)	79(13.2)	65(10.8)	38(6.3)	39(6.5)	16(2.7)	600(100)

TC=Treatment completed, C=cured, DI=Died, OT=on treatment, LFT=Lost-to-follow-up, F=failed, TO=transfer out, N=number of patients. - = not recorded.

Using the chi square test, the correlation between the years was examined; as a result, the years 2019, 2020, and 2021 were shown to be significantly correlated with the outcomes of TB treatment, whereas the remaining years did not exhibit any significant correlation. In 2019 and 2020, the chi square values were 21.121, and the P value was 0.0006. These findings showed a strong relationship between the outcomes of TB treatment and the years 2019 and 2020 (table 4.9).

The results of TB therapy showed a substantial association in 2020 and 2021, with chi square points of 6.65 and a P value of 0.0099, respectively.

Table 4-9: Chi square test for inter annual changes of Successful treatment outcome from 2017-2023.

Year	C, n	TC, n	Expected frequency		Chi square points		Chi square value	p-value
			For C,n	ForTC,n	For C,n	For TC,n		
2017	8	12	6.261	13.739	0.483	0.22	0.851	0.3563
2018	28	67	29.739	65.261	0.102	0.046		
2018	28	67	30.604	64.396	0.222	0.105	0.902	0.3422
2019	20	34	17.396	36.604	0.39	0.185		
2019	20	34	32.121	21.879	4.574	6.715	21.121	0.0000
2020	49	13	36.879	25.121	3.984	5.848		
2020	49	13	42.122	19.878	1.123	2.38	6.65	0.0099
2021	40	29	46.878	22.122	1.009	2.138		
2021	40	29	41.043	27.957	0.027	0.039	0.162	0.6873
2022	29	18	27.957	19.043	0.039	0.057		
2022	29	18	26.111	20.889	0.32	0.4	2.833	0.0923
2023	6	10	8.889	7.111	0.939	1.174		

TC=Treatment completed, C=cured *N=number of patients.*

4.4.1. Factors associated with treatment outcomes

Several significant characteristics were identified as being linked with treatment results for MDR-TB patients at the study place during the study period. Successful treatment outcomes were substantially correlated with HIV-negative cases (p=0.001). In addition, patients without a history of contact with MDR-TB cases saw considerably better treatment outcomes than patients with a history of contact (p=0.001). There is a substantial correlation between the patient's age greater than 65 and the course of treatment (p=0.015). Furthermore, the use of second-line medications was not substantially linked with treatment outcomes (p=0.388). On the other hand, there was no statistically significant correlation (p=0.604) between the particular treatment regimen employed and the outcome of MDR-TB treatment. Furthermore, the patients' location of residence, had no significant effect on their treatment outcomes (p>=0.157). Overall, HIV status, previous MDR-TB contact, patient age, and the use of second-line medications seemed to have a significant impact on the outcomes of MDR-TB treatment; treatment regimen and residential location did not show any significant relationships with treatment outcomes (Table 4-10).

Table 4-10: Bivariate and Multivariate Analysis to identify Factors associated with treatment outcome among MDR-TB patients at St. Peter's specialized hospital, February 2016 to February 2023.

Variable	Treatment outcome		COR (95% CI)	AOR (95% CI)	P-value
	Successful, n (%)	Unsuccessful, n (%)			
Sex					
Male	205(58.24)	147(41.76)	1	1	
Female	158(63.7)	90(36.3)	1.259(0.901, 1.759)	1.169(0.777, 1.759)	0.453
HIV status					
Positive	96(40.33)	142(59.67)	1	1	
Negative	267(73.76)	95(26.24)	4.157(2.932,5.894)	4.028(2.737, 5.929)	0.001
MDR-contact history					
Yes	60(37.5)	100(62.5)	1	1	
No	303(68.87)	137(31.13	3.686(2.525, 5.381)	3.49(2.287,5.325)	0.001
Use of second line					
Yes	62(48.43)	66(51.57)	1	1	
No	301(63.78)	171(36.22)	1.874(1.263, 2.779)	1.233(0.766,1.984)	0.388
TB type					
PTB	268(60.09)	178(39.91)	1.471(0.761, 2.842)	1.595(0.752, 3.383)	0.223
EPTB	64(58.7)	45(41.3)			
Both PTB and EPTB	31(68.89)	14(31.11)	1.557(0.745,3.255)	2.209(0.947, 5.150)	0.067
Treatment regimen					
Short-term regime	97(58.79)	68(41.21)	1	1	
Long-term regimen	247(61.13)	157(38.87)	1.006(0.475, 2.130)	1.271(0.547, 2.953)	0.576

Individualized	19(61.3)	12(38.71)	1.110(0.506,2.437)	2.142(0.879, 5.220)	0.094
Address					
Addis Ababa	264(60.13)	175(39.87)	1.32(0.119, 14.732)	0.575(0.046, 7.254)	0.669
Oromiya	53(58.9)	37(41.1)	1.39(0.122, 15.969)	0.542(0.042, 7.076)	0.640
Amhara	28(77.78)	8(22.22)	0.57(0.046, 7.143)	0.227(0.016,3.273)	0.276
Former SNNP	10(47.61)	11(52.39)	2.2(0.172,28.137)	1.088(0.073,16.229)	0.951
Benishangul	3(75)	1(25)	0.67(0.25,18.059)	0.082(0.003,2.604)	0.157
Gambela	2(50)	2(50)	2(0.090,44.350)	1.189(0.041,34.217)	0.919
Tigray	1(33.33)	2(66.67)	4(0.134,119.230)	4.458(0.132,150.629)	0.405
Afar	2(66.67)	1(33.33)	1	1	
Age					
0-14	13(76.47)	4(23.53)	1	1	
15-24	87(64.44)	48(35.56)	1.79(0.554,5.805)	1.302(0.369,4.602)	0.682
25-34	151(65.65)	79(34.35)	1.7(0.537,5.387)	1.402(0.408,4.819)	0.592
35-44	64(53.79)	55(46.21)	2.79(0.861,9.064)	2.078(0.585,7.378)	0.258
45-54	21(43.75)	27(56.25)	4.17(1.188,14.693)	2.620(0.666,10.304)	0.168
55-64	20(66.67)	10(33.33)	1.62(0.42,6.29)	1.271(0.292,5.537)	0.749
Greater than 65	7(33.33)	14(66.67)	6.5(1.537,27.486)	6.917(1.459,32.792)	0.015

AOR=Adjusted odd ratio, COR=Crude odd ratio, CI=Confidence interval, N= *number of patients.*

5: DISCUSSION

In this study, MDR-TB affected men more than women. It was exactly the same as the research done in Ethiopia's capital, Addis Ababa (Tadesse Fikadu, 2015). Likewise, comparable to the study carried out in the Amhara national regional state of Ethiopia, which had 243(40.1%) females and 363(59%) male participants (Daniel Mekonnen *et al*., 2014). Men may be more prone to acquired resistance since they spend so much time outside, which could explain the higher tendency of MDR-TB in this population.

Approximately 73.2% of the study populations in Addis Ababa were beginning treatment at the time of the study. In a similar manner, Addis Ababa accounted for 80.7% of the MDR-TB patients in a thesis conducted at St. Peter's Specialized Hospital (Tsegaye Tulu and Mesfin Haile, 2015). This might be the hospital, which was regarded as a top-register MDR-TB treatment center in Addis Ababa.

Sex was not significantly linked to MDR-TB in this investigation, which was consistent with a case control study conducted at St. Peter's Specialized Hospital (Abdulhalik Workicho *et al*., 2017). It is comparable to a case control research that was carried out in Serbia (Stosic, 2018).

HIV positivity was substantially related with a poorer treatment result in this investigation, as it was in a case-control study in St. Peter's Specialized Hospital (Abdulhalik Workicho *et al*., 2017), in Tigray Region, Ethiopia: A case-control study (Kidane Zereabruk *et al*., 2024). Similar to a study carried out in Ethiopian University Hospital, this study shown that HIV positive TB patients were substantially associated with unsuccessful treatment outcomes (Minaleshewa Biruk *et al*., 2016). In contrast to a Serbian study, a case control's HIV status had no discernible impact on the success of TB treatment (Stosic, 2018). HIV impairs the immune system, which makes it more difficult for the body to fight MDR-TB. This could be the reason why HIV positivity is linked to worse outcomes from TB treatment.

According to this study, having a history of MDR-TB contact was substantially more likely to result in a poor treatment outcome than not having a history of contact (p=0.000). A-case–control study in Addis Ababa, Ethiopia (Ezra Shimeles *et al*., 2019) and a thesis conducted in St. Peter's

Specialized Hospital (Abdulhalik Workicho *et al*., 2017) both found that prior MDR-TB therapy was substantially associated with p=0.00. This might be patients that are early contact with MDR-TB delays for diagnosis.

The statistics showed in table 4-2 shows that there was a very significant trend in TB cases among patients who visited St. Peter's Specialized Hospital between February 2016 and February 2023.This may be because, at the time of admission to the center, the majority of these individuals were already ill and had begun exhibiting clinical signs and symptoms of the illness. The trend indicates that there was an increase in MDR-TB patients from 19 in 2016 to 59 in 2017, and then there was an increase in MDR-TB patients from 2017 to 122 in 2018, a decline in MDR-TB patients from 122 to 76 in 2019, and 82, 105, 101, and 36 MDR-TB patients in 2020, 2021, and so on. The majority of them were new cases. However, there are also relapses after failure of the first line and after losing follow-up cases seen during the Seven -year period. The highest specific MDR-TB trend of 122 was detected in the year 2018, while the lowest prevalence of MDR-TB was in the year 2016.

Similar to a study done in Addis Ababa, Ethiopia, 219 individuals, or 89.4% of the total, had PTB. Of the 446 patients in this study, or 74.3%, had PTB (Genanew Kassie *et al*., 2023). Additionally, Wolayta Sodo, Southern Ethiopia found that only 34.1% of patients had EPTB, while the majority of patients (65.9%) had PTB (Melese Yeshambaw *et al*., 2021). Given that MTB prefers the lung and that oxygen is necessary for bacterial metabolism, this could be the case.

The majority of MDR-TB patients were between the ages of 25 and 34, accounting for 38.3%. Comparable to research done at St. Peter's Specialized Hospital, the majority of MDR cases (39.75%) happened in people between the ages of 25 and 34 (Tsegaye Tulu and Mesfin Haile, 2015). Comparable to a study carried out from specific TB treatment beginning clinics in Ethiopia, which found that 40.7% of participants were in the 25–34 age groups (Biniyam Dagne *et al*., 2021). According to a similar thesis done in South Africa, most patients were between the ages of 25 and 34 (Weyer *et al*., 2007). This suggests that the productive age group is impacted by MDR-TB. However, this infectious bacterial disease also affects other age groups.

The overall treatment success rate of MDR-TB patients in this study is 60.5%, which is comparable to a study conducted in Ethiopian University Hospital that found that 60.1% of patients had successfully completed their treatment (Minaleshewa Biruk *et al*., 2016). It is also very close to a study conducted in Addis Ababa, Ethiopia, which found that 66.1% of patients completed their treatment (Genanew Kassie *et al*., 2023). The treatment outcome of this study was higher than the studies conducted in Debre markos referral hospital, North West Ethiopia, which found that the treatment outcome was 59.3% (Esmael Ahmed *et al*., 2014). It is unlikely to be lower than the study conducted in ALERT hospital Addis Ababa, Ethiopia, which found that the treatment success rate was 76.9% (Netsanet Aragaw *et al*., 2021) and the investigation carried out in Ethiopia: a 10-year retrospective cohort study national treatment success rate of 75.7% (Habteyes Tola *et al*.,2021).

6: CONCLUSION AND RECOMMENDATION

6.1. Conclusion

The results showed that adult patients, particularly those over twenty, reported the most. It is at this point in life in that country that an individual takes full responsibility for himself or herself to earn a positive living. The highest specific MDR-TB trend of 122 was detected in the year 2018, while the lowest trend of MDR-TB was in the year 2016.

The treatment success rates of TB patients treated at St. Peter's Specialized Hospital were successful (60.5 %) and the unsuccessful MDR-TB treatment outcomes were 39.5.An increasing trend of MDR-TB cases was observed and PTB was the most common TB type.

HIV status of patients and their prior contact with TB drugs are significantly associated with unfavorable MDR-TB treatment outcome.

6.2. Recommendations

Based on the conclusion, the following recommendations are forwarded.

- Creating more awareness about the diagnosis, transmission, trend, control, and treatment of TB through mass media and education.
- TB patients should take the prescribed drug according to the physician's procedure carefully.
- Creating advanced diagnostic facilities and increase the use of Gene Xpert MTB/RIF for the early detection of MDR-TB.
- Early diagnosis of TB is important for HIV patients to lower Unsuccessful treatment outcome.
- People living with HIV should receive regular TB screening, particularly for latent TB infection, Antiretroviral therapy (ART) can reduce the HIV viral load and improve immunological function.

- Enhance surveillance and monitoring data collection and analysis to track patterns in MDR-TB patients, spot outbreaks, and guide public health measures.

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APPENDIX

ቅዱስ ጴጥሮስ ሆስፒታል
KIDUS PETROS HOSPITAL

RESEARCH & EVIDENCE GENERATION DIRECTORATE; THE RESEARCH ETHICAL REVIEW COMMITTEE OFFICE (RERCO) OF SPSH; ETHICAL CLEARANCE LETTER

Title: Assessment on the prevalence of Tuberculosis at St.Peter Hospital, Addis Ababa, Ethiopia: A retrospective study.

Principal Investigator: Mr. Hayleyesus Birhanu

Project type: For Partial Fulfillment of the requirements for graduate DEGREE of Master of Science in Biology at Addis Ababa University

Protocol/Version no: V5681/29/11/2022.

The office of RERCO of SPSH has reviewed the research proposal with the above title on the day of 29/Nnvember/2022 & passed the following decision.

- **Approved**
- Approved with recommendation
- Approved on condition
- Disapproved

This decision is valid for consecutive 12 months taking this decision date as day one, & the proposal should be implemented as presented to the office with the incorporated comments. If there is any plan to make changes in any part of the approved protocol, it is obligatory to inform the office to have another review. It is the researcher duty to inform & submit a summary of each and every activity of the study every three months to the office & finally submit the final completed work of the research to the office.

Regards

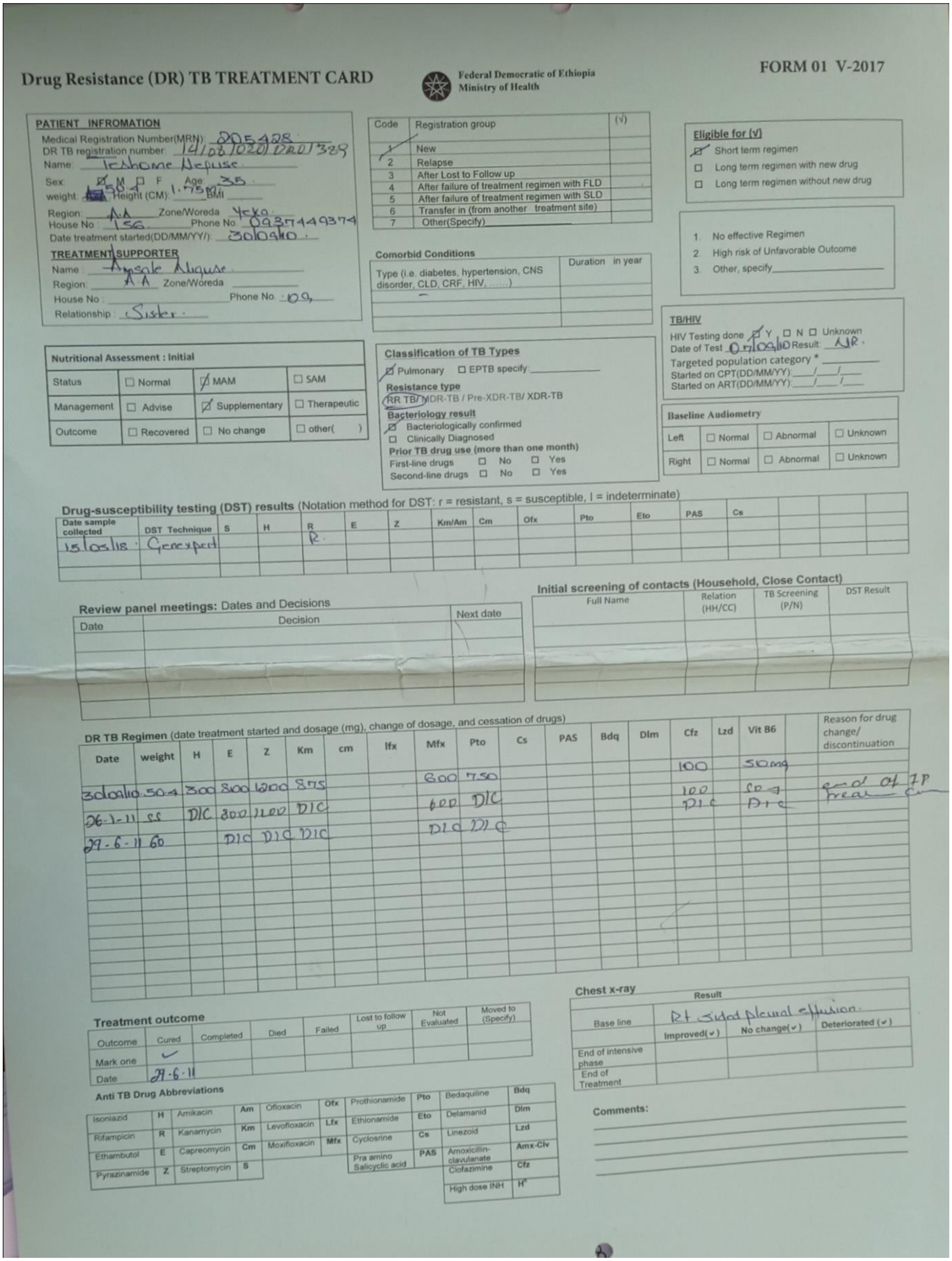
Dr. Million Molla Sisay
Research & evidence Generation Directorate director

Cc

Academic, Research & Training Directorate

CamScanner

Appendix 1**: Ethical clearance from St. Peter's Specialized Hospital** (Source, Hayleyesus).



Drug Resistance (DR) TB TREATMENT CARD

Federal Democratic of Ethiopia
Ministry of Health

FORM 01 V-2017

PATIENT INFROMATION
Medical Registration Number(MRN): 205428
DR TB registration number: 14/08/2020/DRDT329
Name: Teshome Nefuse
Sex: ☑ M ☐ F Age: 35
weight: 50.4 Height (CM): 1.75 BMI
Region: AA Zone/Woreda: Yeka
House No: 156 Phone No: 0937449374
Date treatment started(DD/MM/YY): 30/09/10

TREATMENT SUPPORTER
Name: Amsale Aligue
Region: AA Zone/Woreda
House No: Phone No: 09
Relationship: Sister

Code	Registration group	(√)
1	New	✓
2	Relapse	
3	After Lost to Follow up	
4	After failure of treatment regimen with FLD	
5	After failure of treatment regimen with SLD	
6	Transfer in (from another treatment site)	
7	Other(Specify)	

Eligible for (√)
☑ Short term regimen
☐ Long term regimen with new drug
☐ Long term regimen without new drug

1. No effective Regimen
2. High risk of Unfavorable Outcome
3. Other, specify

Comorbid Conditions	Duration in year
Type (i.e. diabetes, hypertension, CNS disorder, CLD, CRF, HIV, ...)	
–	

TB/HIV
HIV Testing done ☑ Y ☐ N ☐ Unknown
Date of Test 07/09/10 Result NR
Targeted population category *
Started on CPT(DD/MM/YY): / /
Started on ART(DD/MM/YY): / /

Nutritional Assessment : Initial			
Status	☐ Normal	☑ MAM	☐ SAM
Management	☐ Advise	☑ Supplementary	☐ Therapeutic
Outcome	☐ Recovered	☐ No change	☐ other( )

Classification of TB Types
☑ Pulmonary ☐ EPTB specify
Resistance type
RR TB/ MDR-TB / Pre-XDR-TB/ XDR-TB
Bacteriology result
☑ Bacteriologically confirmed
☐ Clinically Diagnosed
Prior TB drug use (more than one month)
First-line drugs ☐ No ☐ Yes
Second-line drugs ☐ No ☐ Yes

Baseline Audiometry			
Left	☐ Normal	☐ Abnormal	☐ Unknown
Right	☐ Normal	☐ Abnormal	☐ Unknown

Drug-susceptibility testing (DST) results (Notation method for DST: r = resistant, s = susceptible, I = indeterminate)

Date sample collected	DST Technique	S	H	R	E	Z	Km/Am	Cm	Ofx	Pto	Eto	PAS	Cs			
15/05/18	Genexpert			R												

Review panel meetings: Dates and Decisions

Date	Decision	Next date

Initial screening of contacts (Household, Close Contact)

Full Name	Relation (HH/CC)	TB Screening (P/N)	DST Result

DR TB Regimen (date treatment started and dosage (mg), change of dosage, and cessation of drugs)

Date	weight	H	E	Z	Km	cm	lfx	Mfx	Pto	Cs	PAS	Bdq	Dlm	Cfz	Lzd	Vit B6	Reason for drug change/ discontinuation
														100		50mg	
30/09/10	50.4	300	800	1200	875			800	750					100		50	end of IP treat...
26-1-11	55	D/C	800	1200	D/C			600	D/C					D/C		D/C	
29-6-11	60		D/C	D/C	D/C			D/C	D/C								

Treatment outcome

Outcome	Cured	Completed	Died	Failed	Lost to follow up	Not Evaluated	Moved to (Specify)
Mark one	✓						
Date	29-6-11						

Chest x-ray	Result		
Base line	Rt sided pleural effusion.		
	Improved(✓)	No change(✓)	Deteriorated (✓)
End of intensive phase			
End of Treatment			

Anti TB Drug Abbreviations

Isoniazid	H	Amikacin	Am	Ofloxacin	Ofx	Prothionamide	Pto	Bedaquiline	Bdq		
Rifampicin	R	Kanamycin	Km	Levofloxacin	Lfx	Ethionamide	Eto	Delamanid	Dlm		
Ethambutol	E	Capreomycin	Cm	Moxifloxacin	Mfx	Cyclosrine	Cs	Linezoid	Lzd		
Pyrazinamide	Z	Streptomycin	S			Pra amino Salicyclic acid	PAS	Amoxicillin-clavulanate	Amx-Clv		
								Clofazmine	Cfz		
								High dose INH	H^{h}		

Comments:

Appendix 2: MDR-TB Patient Treatment Card (Source, Hayleyesus).

Appendix 3: Sample Data collected Format number 1

Data collected format for the Retrospective Study from St. Peter's Specialized Hospital.

NO	MRN	Sex	Age	Treatment started date	Address (U or R)	TB type (Site of TB)	HIV Test Result	Other illness	Gene Xpert Rif Assay	Treatment outcome	Year
1	314546	Male	61	14/1/2013	Addis Ababa	pul	Negative		R	Cured	2013
2	315113	Male	36	21/1/2013	Addis Ababa	Pul	Negative		R	Cured	2013
3	075491	Male	40	13/2/2013	Oromiya	Both	Positive		R	on treatment	2013
4	315429	Male	23	17/2/2013	Addis Ababa	Pul	Negative	Severe malnutrition	R	Completed	2013
5	315383	Male	50	26/2/2013	Addis Ababa	Pul	Positive		R	Died	2013
6	315584	Female	23	5/2/2012	Addis Ababa	Pul	Negative		R	Completed	2013
7	315708	Male	37	27/2/2013	Oromiya	EP	Positive		R	on treatment	2013
8	315444	Male	30	28/2/2013	Addis Ababa	PU	Negative		R	Completed	2013
9	315270	Female	87	1/3/2013	Addis Ababa	Pul	Negative	'	R	Died	2013
10	267350	Female	32	8/3/2013	Addis Ababa	EP	Negative		R	Completed	2013
11	344125	Male	35	13/3/2013	SNNP	Pul	Negative		R	on treatment	2013
12	104239	Female	12	15/3/2013	Addis Ababa	PUL	Negative		R	Completed	2013
13	315300	Male	30	17/3/2013	Addis Ababa	Pul	Negative		R	Completed	2013

14	315301	Female	25	18/3/2013	Amhara	Pul	Negative		R	Cured	2013
15	315448	Male	41	19/3/2013	Addis Ababa	Pul	Negative		R	Completed	2013
16	315745	Male	70	20/3/2013	Addis Ababa	Pul	Negative		R	Cured	2013
17	315541	Female	28	22/3/2013	Amhara	Both	Negative		R	Died	2013
18	316117	Male	33	25/3/2013	Oromiya	pul	Positive		R	Failed d/c	2013
19	316018	Female	25	26/3/2013	Addis Ababa	Both	Negative		R	Cured	2013
20	315974	Male	40	29/3/2013	Addis Ababa	Pul	Negative	Severe malnutrition	R	Completed	2013
21	316019	Male	17	30/3/2013	Oromiya	EP	Negative		R	Failed	2013
22	316479	Male	28	7/4/2013	Addis Ababa	PUL	Negative		R	Completed	2013
23	316161	Female	60	8/4/2013	Addis Ababa	Pul	Negative		R	Died	2013

Appendix 4: Sample Data collected Format number 2

Data collected format for the Retrospective Study from St. Peter's Specialized Hospital.

NO	Prior-TB Drug use		AFB microscopy	Resistance Type	Registration Group	Treatment Regimen	MDR-contact history	last date For treatment
1	Yes	No	Positive	RR	Relapse	Long term regime	No	6/8/2014
2	No	No	Unavailable	RR	New	Long term regime	No	28/8/2014
3	Yes	Yes	Negative	RR	Relapse	Short term regime	No	9/5/2015
4	Yes	Yes	Positive	RR	After lost to follow up	Long term regime	yes	14/10/2014
5	Yes	No	Unavailable	RR	Relapse	Long term regime	No	5/8/2013
6	No	Yes	Positive	RR	New	Long term regime	yes	6/12/2014
7	No	No	Negative	RR	New	Long term regime	No	On treatment
8	No	No	Negative	RR	New	Long term regimen	No	13/10/2014
9	No	No	Unavailable	RR	New	Individualized regimen	No	12/10/2013
10	Yes	No	Unavailable	Clinically	After failure of first line Rx	Long term regimen	No	11/4/2014
11	Yes	No	Positive	RR	Relapse	Long term regime	No	On treatment

12	Yes	No	Negative	Clinically	Relapse	Long term regimen	No	18/11/2014
13	Yes	No	Negative	RR	Relapse	short term regimen	No	25/1/2014
14	Yes	Yes	Positive	RR	Relapse	Long term regimen	No	18/3/2015
15	Yes	No	Negative	RR	New	Long term regimen	No	2/2/2015
16	No	No	Positive	Clinically	Relapse	Short term regime	No	19/1/2015
17	Yes	No	Negative	RR	Relapse	Long term regimen	No	23/1/2014
18	Yes	No	Negative	RR	New	Long term regimen	No	24/4/2014
19	Yes	No	Positive	Clinically	Relapse	Long term regimen	No	11/12/2014
20	Yes	No	Unavailable	RR	After failure of first line Rx	Long term regimen	No	11/12/2014
21	Yes	Yes	Negative	RR	New	Long term regimen	Yes	23/12/2015
22	No	No	Negative	RR	Relapse	Long term regimen	No	10/11/2014
23	No	No	Negative	RR	New	Long term regimen	No	5/12/2013

Appendix 5: Picture during the data collection time at St. Peter's Specialized Hospital (Source, Hayleyesus).