



COLLEGE OF MEDICINE AND HEALTH SCIENCES

DEPARTMENT OF MEDICAL LABORATORY SCIENCES

**THREE YEAR PREVALENCE TREND ANALYSIS OF RIFAMPICIN
RESISTANT PULMONARY TUBERCULOSIS IN BUTAJIRA GENERAL
HOSPITAL, SOUTHERN ETHIOPIA**

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WOLKITE UNIVERSITY

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SCIENCES

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WOLKITE, ETHIOPIA

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List of Abbreviations

AFB - Acid Fast Bacilli

IUATLD - International Union Against Tuberculosis and Lung Disease

MDR - Multi-Drug Resistance

PTB - Pulmonary Tuberculosis

TB - Tuberculosis

SNNPR - South National Nationality People Region

SPSS - Statistical package for the social sciences

XDR - Extensively drug-resistant

WHO - World Health Organization

Abstract

Background: Multi-drug resistant TB (MDR TB) is caused by an organism that is resistant to at least isoniazid and rifampin, the two most potent TB drugs. Ethiopia is highly afflicted by the TB pandemic, multi-drug resistant TB (MDR TB) and is ranked among the top 30 high TB burden countries worldwide.

Objective: To determine three year prevalence trend analysis of rifampicin resistant pulmonary Tuberculosis in Butajira General Hospital.

Method: Retrospective study was conducted to determine three year prevalence trend analysis of Rifampicin resistant Tuberculosis by reviewing the MDR TB registration laboratory logbook at Butajira General Hospital from February 2019 - February 2022 GC. For all patients, geneXpert were done for the detection of MDR PTB cases. All the socio-demographic data, year, month and MDR PTB data were collected using a predesigned data collection sheet from April to June, 2022. SPSS version 25 software was used for data analysis.

Result: Data of 4196 presumptive TB patients were identified, of which 526 (12.5%) were positive for pulmonary TB and 3670 (87.5%) were negative for pulmonary TB. Overall prevalence of Rifampicin resistant tuberculosis among the participants was 46(8.9%). MDR-TB was more prevalent in the age group 15-34 years (19,41.3%), age groups 45- 65 years (14,30.4%) and males ,32(69.6%). In the years from 2019 to 2022, the trend of MDR-TB was 7(15.2%), 23(50.0%) and 16(34.8%) respectively, demonstrating a decreasing trend though inconsistent.

Conclusion: The trend of MDR-TB proportion in Butajira, Eastern Ethiopia, is fluctuating in the past three years (2019 - 2022), it increase slightly in the first year and decreased slightly in the last one year. Productive age (15 – 34 and 35 – 45)) groups and males were significantly at the greater prevalence of TB and MDR-TB, highlighting the importance of strengthening sustainable TB care and prevention interventions toward these groups of people.

Keywords: MDR PTB, TB, RR TB, Trend

CHAPTER ONE

1. Introduction

1.1 Background

Tuberculosis (TB) is a disease caused by bacteria that are spread from person to person through the air and also known as chronic air borne infectious disease. TB usually affects the lungs, but it can also affect other parts of the body, such as the brain, the kidneys, or the spine [1]. In most cases, TB is treatable and curable; however, persons with TB can die if they do not get proper treatment. Multi-drug resistant TB (MDR TB) is caused by an organism that is resistant to at least isoniazid and rifampin, the two most potent TB drugs. These drugs are used to treat all persons with TB disease [2].

Drug-susceptible TB and drug-resistant TB are spread the same way. TB bacteria are put into the air when a person with TB disease of the lungs or throat coughs, sneezes, speaks, or sings. These bacteria can float in the air for several hours, depending on the environment. Persons who breathe in the air containing these TB bacteria can become infected. TB is not spread by, shaking someone's hand, sharing food or drink, touching bed linens or toilet seats, sharing toothbrushes, kissing and etc [1].

Resistance to anti-TB drugs can occur when these drugs are misused or mismanaged. Examples include when patients do not complete their full course of treatment; when health-care providers prescribe the wrong treatment, the wrong dose, or length of time for taking the drugs; when the supply of drugs is not always available; or when the drugs are of poor quality [1, 2].

Drug resistance is more common in people who do not take their TB medicine regularly, do not take all of their TB medicine as told by their doctor or nurse, develop TB disease again, after having taken TB medicine in the past, come from areas of the world where drug-resistant TB is common and have spent time with someone known to have drug-resistant TB disease [3].

The most important thing a person can do to prevent the spread of MDR TB is to take all of their medications exactly as prescribed by their health care provider. No doses should be missed and treatment should not be stopped early [3]. Patients should tell their health care provider if they are having trouble taking the medications. If patients plan to travel, they should talk to their health care providers and make sure they have enough medicine to last while away [2].

The general symptoms of TB disease include feelings of sickness or weakness, weight loss, fever, and night sweats [2]. The symptoms of TB disease of the lungs may also include coughing, chest pain, and coughing up blood. Symptoms of TB disease in other parts of the body depend on the area affected [1, 2].

Globally around 8.6 million new TB cases in 2012 were reported and 1.3 million die every year as a result of TB. Ethiopia, having experienced a major increase in the burden of TB, presents one of the most serious public health challenges [4]. Ethiopia is highly afflicted by the TB pandemic and is ranked second after Nigeria in Africa and seventh among the 22 high TB burden countries worldwide [5].

1.2 Statement of the problem

Multi-drug resistant (MDR) TB has become a major public health problem and presents new barriers to the control of TB. Drug-resistant TB is a man-made problem, largely being the consequence of human error as a result of poor supply management and quality of anti-TB drugs and inadequate or improper treatment, which is further exacerbated by human immunodeficiency virus (HIV). Poor infection control practice has also been identified as a major contributing factor for the spread of drug-resistant TB [5]. Nearly half a million cases of MDR-TB emerge every year, but only 3% of them get treatment globally and 110,000 die annually [6]. The World Health Organization's (WHO's) 2010 Global MDR-TB report estimated that there were 440,000 MDR-TB cases and 150,000 deaths due to MDR TB worldwide in 2008. China and India accounted more than half of the MDR-TB worldwide [7].

According to a WHO/IUATLD (World Health Organization/International Union Against Tuberculosis and Lung Disease) survey of 20 countries with the highest rates of MDR-TB among previously treated cases, 14 were in the European Region [8]. In Africa 69,000 MDR-TB cases

were reported in 2008 [5]. Extensively drug-resistant TB (XDR-TB) has been reported worldwide and an estimated 9.6% of MDR-TB cases are XDR-TB [2].

In some countries, it is becoming increasingly difficult to treat MDR-TB. Treatment options are limited and expensive, recommended medicines are not always available, and patients experience many adverse effects from the drugs. In some cases even more severe drug-resistant TB may develop. Extensively drug-resistant TB, XDR-TB, is a form of multi-drug resistant TB with additional resistance to more anti-TB drugs that therefore responds to even fewer available medicines. It has been reported in 117 countries worldwide [9].

Ethiopia is one of the 27 high MDR-TB countries; it is ranked 15th with more than 5000 estimated MDR-TB patients each year [6]. According to the WHO report, the prevalence of MDR-TB has been 2.8% in newly diagnosed patients; it is reportedly even higher in patients who have previously received anti-TB treatment 21% [5, 10]. Published studies on MDR-TB are increasingly available worldwide, but accurate data on drug-resistant TB in Ethiopia in South Nation and Nationality People Region (SNNPR) in Gurage zone is limited.

Upon this statement of problem, this review provides a comprehensive and up-to-date assessment of the status of the MDR-TB epidemic in Ethiopia, following up on a series of reports on anti-TB drug-resistance previously reported by WHO. Therefore, the purpose of this research was determined three year prevalence trend analysis of Multi-Drug Resistance Tuberculosis (MDR TB) in Butajira General Hospital, Southern Ethiopia.

1.3 Significance of the study

As it is clearly described in the statement of problem and literature review, reports on the prevalence of MDR TB is high in developing countries like Ethiopia. This study can provide information about the trend analysis of prevalence of MDR PTB infection in Butajira General Hospital. Also, it may provide base line information on the prevalence of MDR PTB to the concerned governmental and service institution and describe socio-demographic characteristic of the infection. Furthermore, this study initiates other researchers on the topic to determine the magnitude of the problem and implement solution to reduce.

CHAPTER TWO

2. Literature Review

Multidrug-resistant (MDR-TB); resistant to at least isoniazid [INH] and rifampin [RMP]) strains of *Mycobacterium tuberculosis* are man-made problems mainly related to poor case management and lack of quality drugs. *M. tuberculosis* complex use several strategies to resist the action of antimicrobial agents [11].

2.1. Burden of Tuberculosis

Tuberculosis (TB) is a major cause of morbidity and mortality worldwide. In 2015, there were an estimated 10.4 million new (incident) TB cases worldwide, of which 5.9 million (56%) were among men, 3.5 million (34%) among women and 1.0 million (10%) among children. People living with HIV accounted for 1.2 million (11%) of all new TB cases. There were an estimated 1.4 million TB deaths and an additional 0.4 million deaths resulting from TB disease among people living with HIV. Although the number of TB deaths fell by 22% between 2000 and 2015, TB remained one of the top 10 causes of death worldwide [12].

One-third of the world's population is thought to be infected with TB. In 2014, there were 9.6 million cases of active TB which resulted in 1.5 million deaths. More than 95% of deaths occurred in developing countries. The number of new cases each year has decreased since 2000 [13]. About 80% of people in many Asian and African countries test positive while 5–10% of people in the United States population tests positive by the tuberculin test [14].

There were an estimated 9.0 million incident cases of TB and 1.5 million people died from the disease (1.1 million deaths among people who were HIV-negative and 360 000 people who were HIV-positive). Among these deaths there were an estimated 210 000 from MDR-TB, a relatively high total compared with 480 000 incident cases of MDR-TB. An estimated 13% of new TB cases were HIV-positive in 2013 [15].

TB is one of the major causes of morbidity and mortality in the horn of Africa, and Ethiopia ranks 7th with highest TB burden in the world [16]. According to the Ethiopian Federal Ministry of Health (MOH) data, tuberculosis is the 3rd cause of hospital admission and the 2nd cause of death after malaria [17, 18].

Although TB has the potential to affect all people regardless of sex and age, those in the age range 15 – 54years and with poor socio-economic status were found to be at higher risk [19, 20]. Various factors including poverty, malnutrition, overcrowded living condition, multidrug resistant (MDR) TB and HIV/AIDS have been known to increase the risk of developing the disease and for the continued threat of TB in the world [17, 21].

Early diagnosis of the disease and prompt treatment is essential for an effective and efficient TB control program. Delay in diagnosis may worsen the disease, increase the risk of death, and increase the chance to transmit the agent to community. Studies in Africa shows that patients and health care delays are the major problem in the control of TB [22].

2.2. Burden of MDR TB

Globally, 4.1% of new cases and 19% of previously treated TB cases were estimated to have had multidrug-resistant TB in 2016. In the same year, there were an estimated 600,000 incident cases of MDR/RR-TB with cases of MDR-TB accounting for 82% of the total and there were an estimated 350,000 MDR/RR-TB cases among notified TB patients. However only 153,119 cases were confirmed which is much lower than the estimated cases because only 41% of TB cases have been tested for resistance. There were about 240,000 deaths from MDR/RR-TB in 2016 [23].

In 2016, the 30 high MDR-TB burden countries accounted for 89.7% of the global incident cases of MDR-TB. While India, China and the Russian Federation alone accounted 47% of the global burden. In Africa, where little data is available, an estimated 93,000 cases were emerged in 2016 with estimated incidence of 2.7% among new and 14% among previously treated cases, but the vast majority of them went un-diagnosed. Ethiopia is one of the 30 MDR-TB high-burden countries, with an estimated 5800 cases reported in 2016 with the prevalence rate of 2.7% among new cases and 14% among previously treated patients [23].

Globally, 129,689 of the 153,119 notified cases of multidrug-resistant TB and rifampicin resistant TB (MDR/RR-TB) in 2016 were enrolled in treatment. It means 85% of diagnosed cases or only 22% of the estimated incident MDR/RR-TB cases initiated treatment by the year. Which shows improvement in coverage and access to MDR TB treatment; however the cure rate is low and on the other hand mortality, default and failure are high. Only 50% of the MDR-TB patients in the 2012 cohort of detected cases were successfully treated, 16% died, and 10% failed [23]. Similarly, 54% of MDR/RR-TB cases in the 2014 cohort have successful outcome by 2016 [23].

2.3. Trend Analysis of MDR TB

Eighty five percent of MDR-TB occurs in 27 countries [13, 14]. Globally, 3.7% of new cases and 20% of previously treated cases are estimated to have MDR-TB [5]. Ethiopian national drug resistance survey of 2005 estimated the prevalence of MDR-TB among new and retreatment cases was 1.6% and 12% respectively [10, 24, 25, 26, 27].

Africa is home to over 1 billion people and is disproportionately affected by tuberculosis with 2.6 million of the 10.4 million global tuberculosis cases, making the continent a key geographical area for health interventions. Sub-Saharan Africa, in particular, saw rates rapidly escalate in the early 1990s due to a delayed response to the emergent HIV epidemic at the time. These failures resulted in incidence rates that are the highest in the world and have made the task to end tuberculosis even more challenging. Nonetheless, the tide has changed with the rapid expansion of anti-retroviral therapy resulting in sharp declines in HIV-associated tuberculosis incidence in countries in sub-Saharan Africa, thus offering a window of hope [27].

Several factors threaten the potential to realise these targets, and key among these is drug resistant tuberculosis. Unfortunately, much like the global situation, drug resistant tuberculosis in Africa is largely missed with 93 000 cases estimated in 2016, while only 27 828 (30%) were diagnosed. Even when the diagnosis is made, only 59% achieve a successful treatment outcome [28].

According to Prevalence of Multi-drug Resistant Mycobacterium Tuberculosis among Tuberculosis patients admitted to Adama Hospital Medical College, out of 2332 TB suspected

cases from 2014 to 2018, 175 (7.5%) were confirmed MDR-TB cases or confirmed Rifampicin resistant cases. In particular, 97 (4.2%) presented presumptive MDR-TB alone and 78 (3.3%) showed confirmed Rifampicin resistance alone. Comparison among age groups showed the highest prevalence for 24 - 44 years with 1.9% and 1.5% confirmed MDR-TB and Rifampicin resistance. Detail data is shown for age category (<15, 15 - 24, 25 - 44 and >45) of 2014-2018 years. Comparatively, higher proportion of MDR-TB or Rifampicin resistance of 3.4% and 2.9% were registered in 2014 and 2015, respectively while a sharp decline was observed from 2015 to 2018. The admission of MDR-TB patients was compared for the past five years. The proportion of MDR-TB among new cases was 41 (1.8%) while among previously admitted cases were 159 (6.8%). The highest and lowest admission for previous MDR-TB cases was registered in 2018 and 2017, respectively. Similarly, relatively higher and lower new MDR cases were recorded in 2014 and 2017, respectively. Relative proportion of HIV/AIDS positive MDR-TB cases was higher for 2018 whereas least cases were detected in 2017 [29].

Across sectional study was done in Amhara National Regional State from May 2012 to May 2013 on prevalence of Multi Drug Resistant Tuberculosis among presumptive Multi Drug Resistant Tuberculosis cases show that, Samples processed using 2% N-acetyl-L-cysteine-sodium hydroxide for Lowenstein Jensen culture and ZiehlNeelsen staining. Resistance to rifampicin and isoniazid was made using molecular line probe assay. A total of 606 Presumptive MDR-TB cases were took part in the study and screened for MDR-TB status. The overall prevalence of MDR-TB was 93(15.3%). Rifampicin (RMP) and isoniazid (INH) mono resistance were 17(2.8%) and 15(2.5%) respectively. Considering RMP mono resistance as surrogate marker for MDR TB, prevalence of MDR TB/RMP resistance was 110(18.2%). Moreover, the rate of MDR TB among smear and/or culture positive samples were 42.9% and together with RMP mono resistance, it increased to 50.7%. Age at a range of 21-30 years old, being female and TB history of defaulters were significantly associated with having MDR-TB [30].

A cross-sectional study was conducted between May 2011 and January 2012 on prevalence and drug resistance profile of mycobacterium tuberculosis isolated from pulmonary tuberculosis patients attending two public hospitals in East Gojjam zone, northwest Ethiopia show that using region of difference-9 (RD9) typing for the identification of species mycobacterium. Drug

susceptibility testing (DST) of *M. tuberculosis* isolates to the first-line drugs: isoniazid, rifampicin, ethambutol and streptomycin was performed by the indirect proportion method on Middlebrook 7H10 Agar media. Out of 385 pulmonary TB suspects studied, 124 (32.2 %) were culture positive among which 120 were *M. tuberculosis* strains. Susceptibility testing was performed for 89 isolates. Resistance to at least one drug was 15.58 % among newly diagnosed and 50.0 % among previously treated cases. Resistance among newly diagnosed patients was most common for streptomycin 5.19 % (4/77) and ethambutol 5.19 % (4/77) followed by rifampicin 3.89 % (3/77). Among retreatment cases, isoniazid resistance was most frequent in which 33.33 % (4/12) of the isolates were resistant. MDR prevalence was 1.29 % (1/77) for newly diagnosed and 16.67 % (2/12) for retreatment cases. In a multivariate logistic regression analysis, age group of 25–34 years and previous history of treatment were independently associated with anti-TB drug resistance [31].

A cross-sectional study was conducted in West Armachiho and Metema districts between February 01 and June 25, 2014 on prevalence of Multi-drug resistant tuberculosis with risk factors in districts of Metema and West Armachiho, Northwest Ethiopia. A total of 124 consecutive smear positive pulmonary tuberculosis patients were included in the study. Socio-demographic and possible risk factor data were collected using a semi-structured questionnaire. Drug susceptibility testing was first performed for rifampicin using GeneXpert MTB/RIF. For those rifampicin resistant strains, drug susceptibility testing was performed for both isoniazid and rifampicin to identify MDR-TB using the proportional method on LJ media. Data were analyzed using statistical Package SPSS version 20; binary logistic regression was used to assess the association. Of 124 smear-positive pulmonary TB patients, 117 (94.4 %) were susceptible to Rifampicin, while 7 (5.7 %) were confirmed to be resistant to Rifampicin and Isoniazid. The overall prevalence of MDR-TB was 5.7 % (2.3 % among new cases and 13.9 % among previously treated cases). History of previous treatment was significantly associated risk factor for MDR-TB [32].

CHAPTER THREE

3. OBJECTIVES

3.1 General Objective

- To assess the three year prevalence trend analysis of rifampicin resistant Pulmonary Tuberculosis (MDR PTB) from 2019 - 2022 in Butajira General Hospital, Eastern Ethiopia.

3.2 Specific Objectives

- To describe the three year prevalence trend analysis of rifampicin resistant Tuberculosis among patients visited Butajira General Hospital
- To determine the distribution of TB and RR TB among socio-demographic groups.
- To determine prevalence of TB and RR TB among study subjects.

CHAPTER FOUR

4. Methodology

4.1 Study Design

A retrospective cross sectional study on prevalence of multi-drug resistance pulmonary tuberculosis was conducted among patients visited Butajira General Hospital.

4.2 Study Area

The study was conducted at Butajira General Hospital which is found in Butajira Town, the city of Gurage Zone which is located in South central of the Ethiopia. The Town is found 130km from Addis Ababa. Based on the 2007 Census conducted by the CSA, this town has a total population of 33,406, of whom 16,923 are men and 16,483 women. The majority of the inhabitants were reported as Muslim, with 51.27% of the population reporting that belief, while 39.58% practice Ethiopian Orthodox Christianity, and 8.72% were Protestants. The town geographical coordinates are approximately 8°7'15"N attitude and 38°22'45"E longitude. This town has an elevation of 2131 meters above sea level. Generally, the town is characterized by warm climate with a mean annual maximum temperature 30 °c and a mean annual minimum temperature of 140 °c. And annual rainfall of 600-1600mm.

Butajira General Hospital is one of the General Hospital found in Gurage Zone giving a better service and has a better set up relatively. It' have 15 general practitioner, 2 general surgeon, 2 emergency surgeon, 2 internist, 9 outpatient department, 5 impatient department and TB and MGR center.

4.3 Study Period

The study was conducted from April - May 2022 GC. By reviewing laboratory logbook of Butajira General Hospital.

4.4 Population

4.4.1 Source population:

All patients visited Butajira General Hospital from February 2019 - February 2022 GC.

4.4.2 Study population

All individuals who visited Butajira General Hospital laboratory TB clinic and recorded on laboratory logbook.

4.4.3 Study Subject

All patients, who have GeneXpert examination at Butajira General Hospital recorded on laboratory logbook from February 2019 - February 2022 GC.

4.5 Sample size and sampling technique

A total of 4196 presumptive TB/MDR clients recorded during the specified time were examined for X-pert MTB/Rif assay from different areas in Butajira General Hospital. Socio-demographic data and laboratory data was extracted from registration log book by data extraction sheet.

4.6 Study Variable

4.6.1 Dependent variable

- Prevalence of rifampicin resistant Pulmonary Tuberculosis (MDR PTB)

4.6.2. Independent variable

- Socio demographic factors: Age, Sex,
- year of Examination
- Patient registration group
- Presumptive TB/MDR-TB diagnosis

- HIV Status

4.7 Inclusion and exclusion criteria

4.7.1 Inclusion criteria

Presumptive MDR-TB patients with complete data registration in the last three years were included.

4.7.2 Exclusion criteria

Laboratory records which was lacked the necessary information; illegible lab records, lab records without age, sex and date.

4.8 Method of data Collection and Processing

4.8.1 Data Collection

Socio-demographic, clinical and laboratory data were collected by reviewing three years MDR-TB results from Butajira General hospital Laboratory log book.

Data was collected by well-prepared checklist format containing negative or positive results of TB, MDR and Rifampicin Resistance and by sub dividing the positive results in to age, sex, year, type of registration group, presumptive TB/MDR, HIV result, and then, those all recorded information were collected from the record/registration log.

4.8.2 Sample Processing and testing

The Laboratory was utilized Cartridge based nucleic acid amplification test (CB-NAAT, GeneXpert,) which is an automated cartridge-based molecular technique which not only detects Mycobacterium Tuberculosis but also rifampicin resistance within two hours. GeneXpert test is a highly sensitive and specific test for tuberculosis(TB) diagnosis that detects DNA sequences specific for Mycobacterium tuberculosis and rifampicin resistance i.e. rpoB gene.

4.8.3 Data Analysis

The recorded data was checked whether all the necessary information is properly fulfilled or not. Data was entered, coded and checked for its completeness and consistency analysis. It was processed and analyzed using SPSS. The data was presented using tables and graphs. Descriptive summary values such as frequency and percentage was calculated. Binary and Multinomial logistic regression were used to describe the association between positivity and independent variables such as age, sex, year of examination. P-value > 0.05 was considered as significant association.

4.9 Data quality control

To ensure the reliability and validity of the data, clearly stated and seasonally classified separated check list was used for each year. All necessary precautions was taken not to miss or add mistakenly any data. The findings was cross checked with the corresponding monthly report available.

4.10 Data Management

The data was collected using a check list from Butajira General Hospital laboratories, patient's registration logbook. Data were collected by all the group members.

4.11 Ethical Consideration

The study was cleared ethically by college of health sciences and medicine, institutional research ethical committee, Wolkite University. Then formal letter of cooperation was written to Butajira town General Hospital administration. The objective of the study was explained to the general hospital. The letter of agreement was attached to ensure confidentiality of data. The information taken from patients' recorded data were kept confidential. Only codes were used to identify the study groups.

4.12. Dissemination study finding plan

The result obtained from this study was disseminated to relevant bodies such as Wolkite University College of Health and Medical Sciences. This was done through submission of reports and presenting findings at appropriate seminars and workshops.

4.13 Operational Definitions

New case (N): a patient who never had treatment for TB or has been on previous anti TB treatment for less than four weeks.

Relapse(R): are previously treated for TB, were declared cured or treatments completed at the end of their most recent treatment episode and are now diagnosed with a recurrent episode of TB.

Treatment Failure (F): are previously treated for TB and whose treatment failed at the end of their most recent treatment episode.

Return after default (D): patient whose treatment was interrupted for two or more consecutive months for any non-medically approved reason and returns to health facility with smear positive sputum.

RR TB: a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs.

CHAPTER FIVE

5. Results

5.1 Socio-demographic and clinical data of Study Subject

A total of 4297 clinically TB suspected patients were submitted their samples for TB and MDR-TB diagnosis in three year, among 4196 had complete data in the registration log books. Of total 4196 examined study participants, 2237(53.3%) were male and the rest 1959 (46.7%) was female. Regarding age group, 15 – 34 age groups (1354, 32.3%) and 45 – 65 age groups (1267, 30.2%) were dominating respectively. And also HIV status was reported total are About 52(1.2%), N (Negative)'s are 520(12.1%) and 3725(86.7%) was Unknown status.

Among total study participants patient registration groups N (New case) are 3796 (88.3%), R (Relapse) are 477 (11.1%), TA (Treatment after lost to follow up) are 9(0.2%) and AF (After failure of first treatment) are 15(0.3) (figure 1).

Table 1: Socio-demographic and clinical data of Study Subject

Variables	Frequency	Percent	
Sex	M (Male)	2237	53.3
	F (Female)	1959	46.7
	Total	4196	100.0
Age	<15	501	12.0
	15 – 34	1354	32.3
	35 – 44	693	16.5
	45 – 65	1267	30.2
	>65	381	9.1
	Total	4196	100.0
HIV Status	P (Positive)	50	1.2
	N (Negative)	511	12.2
	Un (Unknown)	3635	86.6
	Total	4196	100.0
Patient Registration Group	N (New case)	3706	88.3
	R (Relapse)	467	11.1
	TA (Treatment after lost to follow up)	9	0.2
	AF (After failure of first treatment)	14	0.3
	Total	4196	100.0

5.2 Prevalence and association of tuberculosis with study subject characteristics

Of 4197 study subjects diagnosed within the 3-year, 526(12.5%) was contracted by Mycobacterium tuberculosis infection. Significantly high prevalence of TB was observed among male accounted 328(62.4%) (AOR= 1.628, 95%CL=1.342-1.974, p=< 0.001) and the rest 198(37.6%) was in female. TB was reported in all age groups but the infection rate was also significantly higher in the age group 15-34 years, with a prevalence rate of 244(46.4%)(AOR= 2.533,95% CL =1.720-3.732,P<0.001)followed by 45-65 age group with a prevalence rate of 121(23.0%), least in the age groups of <15 with a prevalence rate of 40(7.6%) and followed by age group >65 years 33(6.3%). Among the positive 5(1.0%) was HIV positive, with a prevalence rate of 55(10.5%) was negative and 466(88.6%) was unknown HIV status test. Among 526 patients who are positively examined in the past three years, new cases 457(86.9%), relapse 53(10.1%), treatment after lost to follow up 6(1.1%) and after failure of first treatment 10(1.9%).

Table 2: Association of TB with Socio-demographic and Clinical Characteristics (n=4196)

Variables		TB Status		COR(95%CI)	P	AOR(95%CI)	P
		N (%)	P (%)				
Sex	M	1909 (52.0)	328 (62.4)	1.528 (1.27-1.84)	0.000	1.628 (1.342-1.974)	0.000**
	F	1761 (48.0)	198 (37.6)				
	Total	3670 (100)	526 (100)	-	-	-	-
Age(years)	<15	461 (12.6)	40 (7.6)	0.915 (0.565-1.481)	0.718	0.926 (0.569-1.507)	0.756
	15 – 34	1106 (30.2)	244 (46.4)	2.326 (1.586-3.412)	0.000	2.533 (1.720-3.732)	0.000**
	35 – 44	605 (16.5)	88 (16.7)	1.534 (1.007-2.337)	0.047	1.631 (1.064-2.499)	0.025**
	45 – 65	1146 (31.3)	121 (23.0)	1.113 (0.744-1.666)	0.601	1.106 (0.736-1.662)	0.626
	>65	348 (9.5)	33 (6.3)				
	Total	3666 (100)	526 (100)	-	-	-	-
HIV Status	P	45 (1.2)	5 (1.0)				
	N	456 (12.4)	55 (10.5)	0.756 (0.298-1.913)	0.554	0.807 (0.315-2.063)	0.654
	Un	3169 (86.3)	466 (88.6)	0.820 (0.610-1.103)	0.190	0.762 (0.562-1.033)	0.080
	Total	3670 (100)	526 (100)	-	-	-	-
Patient Registration Group	NC	3249 (88.5)	457 (86.9)	0.056 (0.018-0.180)	0.000	0.104 (0.031-0.353)	0.000
	R	414 (11.3)	53 (10.1)	0.051 (0.016-0.169)	0.000	0.065 (0.019-0.222)	0.000
	TA	3 (0.1)	6 (1.1)		-		
	AF	4 (0.1)	10 (1.9)	0.800 (0.131-4.874)	0.809	1.300(0.200-8.469)	0.784
	Total	3670 (100)	526 (100)	-	-	-	-

Key words: M – Male, F – Female, Un (Unknown), N – Negative, P – Positive, NC – New Case, R – Relapse, TA – Treatment after lost to follow up, AF – After failure of first treatment

5.3 Prevalence and association of Rifampicin resistant Tuberculosis with study subject characteristics

Of total study participants, 46(8.9%) were positively examined for Rifampin resistant tuberculosis from those 32(69.6%) was male and the rest 14(30.4%) was female. MDR-TB was reported in all age groups but the infection rate was higher in the age groups 15-34 years, with a prevalence rate of 19(41.3%) followed by 45-65 age group with a prevalence rate of 14(30.4%), least in the age groups of <15 with a prevalence rate of 2(4.3%) and followed by age group >65 years 1(2.2%). Among the positive 1(2.2%) was HIV positive, with a prevalence rate of 8(17.4%) was negative and 37(80.4%) was unknown HIV status test. Among 46 patients who are positively examined in the past three years the patient registration group was new cases 29(63.0%), relapse 12(26.1%), treatment after lost to follow up 2(4.3%) and after failure of first treatment 6(1.3%).

Table 3: Association of Rifampicin resistant TB with Socio-Demographic and Clinical Characteristics Patient

Variables		RR Status		COR(95%CI)	P	AOR(95%CI)	P
		Sen (%)	P (%)				
Sex	M	292 (61.7)	32 (69.6)	1.417 (0.736-2.727)	0.297	-	-
	F	181 (38.3)	14 (30.4)				
	Total	473 (100)	46 (100)	-	-	-	-
Age	<15	37 (7.8)	2 (4.3)	1.730 (0.150-19.978)	0.661	2.180 (0.163-29.142)	0.556
	15 – 34	225 (47.6)	19 (41.3)	2.702 (0.350-20.879)	0.341	2.108 (0.247-17.955)	0.495
	35 – 44	72 (15.2)	14 (30.4)	6.222 (0.784-49.362)	0.084	4.692 (0.525-41.917)	0.167
	45 – 65	107 (22.6)	10 (21.7)	2.991 (0.369-24.257)	0.305	2.006 (0.221-18.227)	0.536
	>65	32 (6.8)	1 (2.2)				
	Total	473 (100)	46 (100)	-	-	-	-
HIV Status	P	3 (0.6)	1 (2.2)				
	N	46 (9.7)	8 (17.4)	3.820 (0.388-37.644)	0.251	3.546 (0.229-54.928)	0.365
	Un	424 (89.6)	37 (80.4)	1.993 (0.876-4.537)	0.100	2.577 (0.940-7.065)	0.066
	Total	473 (100)	46 (100)	-	-	-	-
Patient Registr ation Group	NC	423 (89.4)	29 (63.0)	0.137 (0.033-0.576)	0.007	0.961 (0.185-4.987)	0.963
	R	40 (8.5)	12 (26.1)	0.600 (0.130-2.767)	0.513	0.714 (0.133-3.837)	0.695
	TA	4 (0.8)	2 (4.3)				
	AF	6 (1.3)	3 (6.5)	1.000 (0.112-8.947)	1.000	1.081 (0.088-13.226)	0.951
	Total	473 (100)	46 (100)	-	-	-	-

Key words: M – Male, F – Female, Un (Unknown), Sen – Sensitive, N – Negative, P – Positive, NC – New Case, R – Relapse, TA – Treatment after lost to follow up, AF – After failure of first treatment

5.4 Three years trend of Tuberculosis and multidrug resistant tuberculosis

In the years 2019–2022, the prevalence of pulmonary TB was 98(18.6%), 220(41.8%) and 208(39.5%) respectively [Figure 2]. And also MDR-TB (Rifampicin Resistance) was 7(15.2%), 23(50.0%) and 16(34.8%) respectively [Figure 3]. The overall prevalence of TB prevalence over the 3 years had a declining trend but with inconsistencies [Figure 2].

Table 4: Trend of Tuberculosis and Rifampicin resistant Tuberculosis

Variables		TB Status		Total	Rif. Resistance		Total
		N (%)	P (%)		Sen (%)	Res (%)	
Years	1st Year (Feb,2011 - Feb,2012)	921 (25.1)	98 (18.6)	1019(24.3)	92 (19.5)	7 (15.2)	99 (19.1)
	2nd Year (Mar,2012 - Feb,2013)	1613 (44.0)	220 (41.8)	1833 (43.7)	195 (41.2)	23(50.0)	218 (42.0)
	3rd Year (Mar,2013 - Feb,2014)	1136 (31.0)	208 (39.5)	1344 (32.0)	186 (39.3)	16 (34.8)	202 (38.9)
	Total	3670 (100)	526 (100)	4196 (100)	473 (100)	46 (100)	519 (100)

Keywords: N- Negative, P- Positive, Sen- Sensitive,

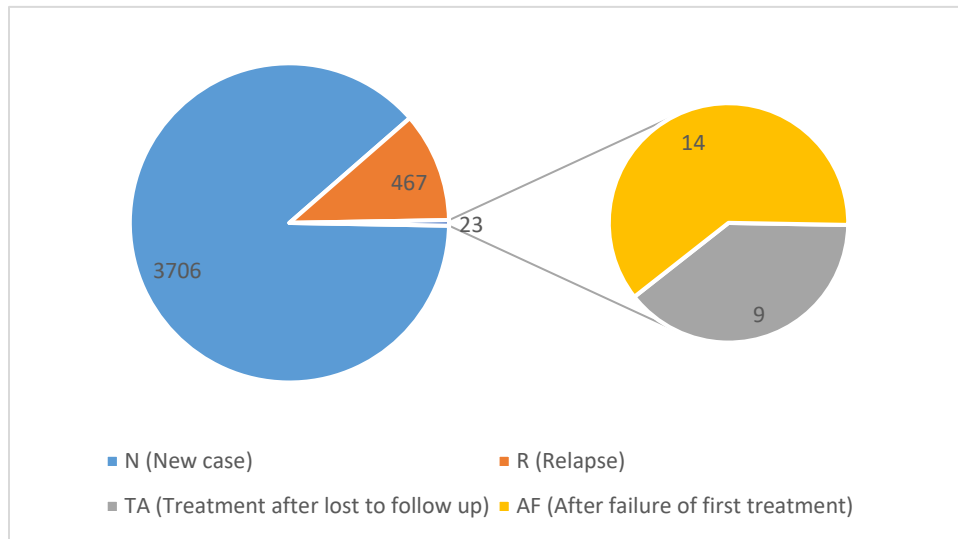


Figure 1: Patient registration status of study population

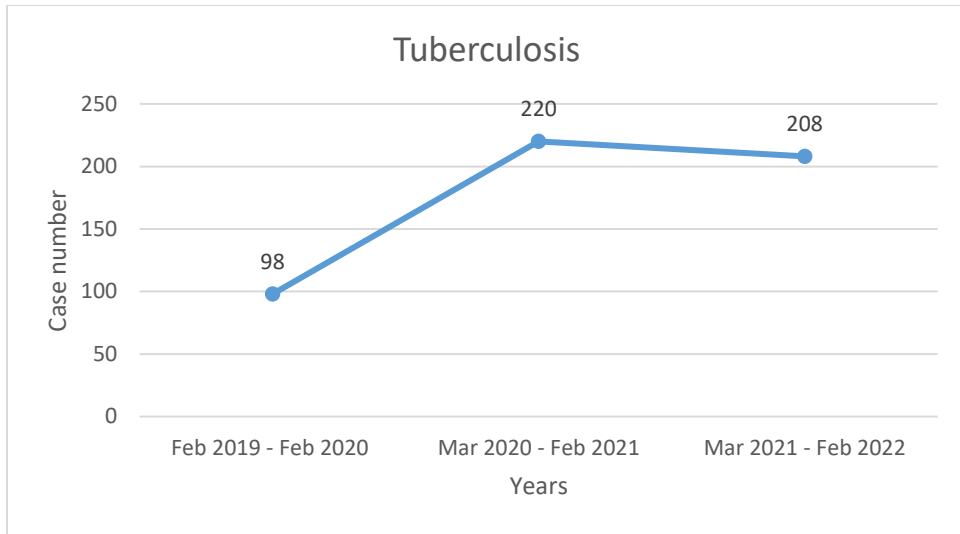


Figure 2: Line graph of three year trend of Tuberculosis

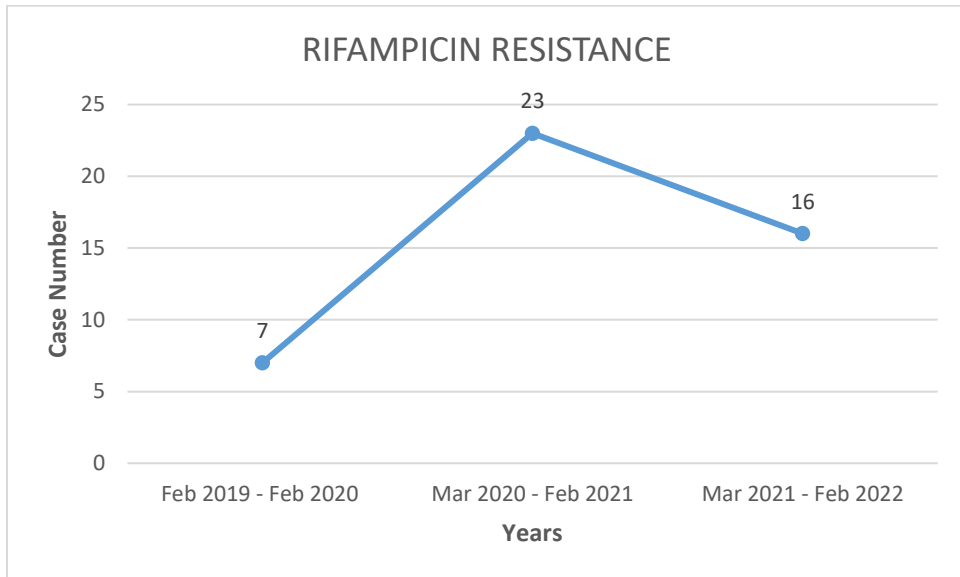


Figure 3: Three years trend of Rifampicin resistant Tuberculosis

CHAPTER SIX

6. Discussion

In this study, 3 year data were collected to analyze the trends of MDR-TB in Butajira General Hospital, Eastern Ethiopia. A total of 4196 patient records were collected. The overall detection rate of TB in study was 12.5% and MDR-TB was 8.9%. The prevalence of TB burden was higher among people of productive age groups (15–34 years). In the years from 2019 to 2022, the prevalence of TB were 98 (18.6%), 220 (41.8%) and 208 (39.5%) respectively.

Previous TB trend analysis held in the Tigray Region [33, 34], Bale Zone of Oromia Region [35], East Gojjam Zone of Amhara Region [36], Addis Ababa [37], Harari Region [38], and Awi Zone of Northwest Amhara Region [39] reported a decreasing trend of TB over time. Our finding also shows a decreasing trend of the disease though it lacks consistency. Previous reports in the Harari Region [38] and some parts of the Amhara and Oromia [40] Regions reported seasonal variations in TB incidence. Differences in comorbid diseases, the population's knowledge about TB, institutional capacity for diagnosis of TB, and strategic approaches in the prevention of TB may contribute to variations in TB patterns and disease burden among these settings [41].

HIV incidence is decreasing in Ethiopia, and this may contribute to the reduction in TB as well. Our findings showed a significant association between male and the incidence of TB, and this is already a well understood phenomenon. And also there is significant association between age group of 15 – 34 and incidence of TB, also age group of 35 – 44 and incidence of TB. Higher prevalence of TB was reported among the productive age group of 15–34 years and the lowest among the age groups 65 and above, which was in line with the national report. Ethiopia is estimated to miss 35% of incident TB cases annually, and management of TB and drug resistant TB face multiple challenges that would affect the attainment of the global End TB Strategy [33].

The overall prevalence of drug-resistant TB among all TB cases in the Butajira was 8.9% (46/516). This finding was lower compared to a similar study conducted in China . This may be due to differences in the structure of the healthcare systems and methods for detecting drug resistance TB, as well as socioeconomic differences between the countries. Our findings are also

lower as compared to the 2017 WHO TB report, which showed that 4.1% of new and 19% of previously treated TB cases involved MDR or RR TB[41]. Our prevalence rates were also lower as compared to a systematic review study conducted in Ethiopia. There is no associated factor with sex, age and HIV status [42].

The existence of RR-TB is a serious health problem in the study population. The prevalence of RR-TB in this study is in line with previous studies in Ethiopia (9– 10.3%) [43, 45] and Nigeria (12.1%) [46]. However, other studies in the country reported a lower (5.7–7.5%) [47, 48] and a higher (15.8–33.3%) [44, 49, 50] level of RR-TB. In the years from 2019 to 2022, the prevalence of RR-TB were 7(15.2%), 23(50.0%) and 16(34.8%) respectively.

The variation of RR-TB across the country might be related to differences in patient selection, sample size (small sampling could generate higher resistance rate).

6.1 Limitation of the Study

This study has limitation. Since this is retrospective data, we encountered missed and incomplete data. Despite this, the study enabled a comprehensive insight into the trends of TB burden in Butajira that could guide potential intervention strategies.

6.2 Conclusion and Recommendation

The trend of MDR-TB proportion in Butajira, Eastern Ethiopia, is fluctuating in the past three years (2019 - 2022) it increase slightly in the first past three years and decreased slightly in the last three years. Productive age (15 – 34 and 35 – 45)) groups and males were at the greater prevalence of TB and MDR-TB, highlighting the importance of strengthening sustainable TB care and prevention interventions toward these groups of people.

Generally there is high prevalence of TB and MDR-TB so the government should give attention to this need to make intervention. Attention should be given to strengthen the laboratory services for TB and MDR-TB investigation and diagnosis in Butajira General Hospital in particular and in the city in general. Health education about TB transmissions and prevention should be given and large scale study on the prevalence on TB infection.

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ANNEX- ONE

WOLKITE UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCE

DEPARTMENT OF MEDICAL LABORATORY SCIENCES

Checklist for data collection for the prevalence of rifampicin resistant pulmonary tuberculosis was conducted among patients visited Butajira General Hospital in the past three years.

Code town number

1. Id N° _____

2. Time of examined:

Year _____ Month: _____ Day _____

3. Sex: Male

Female

4. Age: _____

5. Case

New Case Relapse Case

6. Genexpert Results

T

RR

TI

N

NR

I

E

7. Type of registration group

1. New

3. Treatment after lost to follow up

2. Relapse

4. After failure of first treatment

8. Defaulted HIV status

1. Positive

2. Negative

3. Unknown

9. Reason for examination 1. Diagnosis 2, presumptive T

ANNEX-TWO

Declaration

We the undersigned declare that this research proposal is our own original work and has not been presented for a degree in any other university and all sources of materials used for the research have been duly acknowledged.

Investigators:

1. Kidane Daniel: Signature _____ Date: _____
2. Mideksa Haji: Signature _____ Date: _____
3. Robera Deresa: Signature _____ Date: _____
4. Sherefa Awel: Signature _____ Date: _____

Supervisor/s

1. Mr. Daniel Kahase (BSc, MSc, Assistant Professor)

Signature _____ Date _____

2. Mr. Rabie Kedir (BSc, MSc)

Signature _____ Date _____

ANNEX-THREE

3. GeneXpert

What is usually referred to as the Genexpert test, has now been developed into a series of molecular tests. Depending on the cartridge/assay used, the Genexpert can test for a number of infectious diseases including TB & COVID. The Genexpert diagnoses TB by detecting the presence of TB bacteria. The test is a molecular TB test which detects the DNA in TB bacteria. It uses a sputum sample and can give a result in less than 2 hours. The Genexpert can also detect the genetic mutations associated with resistance to the drug Rifampicin.

The Genexpert has been developed by the Foundation for Innovative New Diagnostics (FIND), who have partnered with the Cepheid Corporation and the University of Medicine and Dentistry of New Jersey.

3.1 Principle of Genexpert Test

Cartridge based nucleic acid amplification test (CB-NAAT, GeneXpert,) is an automated cartridge-based molecular technique which not only detects Mycobacterium Tuberculosis but also rifampicin resistance within two hours. GeneXpert test is a highly sensitive and specific test for tuberculosis(TB) diagnosis that detects DNA sequences specific for Mycobacterium tuberculosis and rifampicin resistance i.e. rpoB gene. It is also called Gene Xpert because it works as its name.

3.2 Requirements for GeneXpert Test

1. Kit contains-

- Cartridge
- Dropper
- and reagent

2. Gene Xpert machine

3. Desktop

4. Bar code reader/ bar code scanner

5. Specimen: sputum, CSF, urine, and other body fluids like pleural fluid, synovial fluid, ascitic fluid, and so on

3.3 Procedure of GeneXpert Test

1. Mix specimen (sputum) and reagent in equal volume.
2. Wait for 15 minutes.
3. Transfer reagent treated specimen into cartridge sample well by using a dropper. (Volume up to mark in dropper)
4. Go to the desktop and click create test.
5. Scan cartridge bar code by the scanner and fill the form mainly patient name and specimen type.
6. Click the Start test button and finally load the cartridge on the holder as shown by default (A1/A2/A3/A4) also notice clicking orange signal.
7. After that push the door and wait for the result (1 hour 51 minutes)

3.4 Result Interpretation of Test

- MTB not detected
- MTB detected with grading either
 1. very low
 2. low
 3. medium
 4. or high with
- Rif Resistance NOT DETECTED or
- Rif Resistance DETECTED

3.5 Advantages of GeneXpert Test

1. GeneXpert test is highly sensitive comparatively AFB stain and culture of Mycobacterium tuberculosis. (to be AFB positive load should be in sample 10000 bacteria/ml, in culture 10-100 whereas in gene Xpert only 1-10).
2. Very little technical training is required to operate.
3. Minimized bio hazard comparatively AFB stain and culture. (reagent having 10% sodium hypochlorite not only dissolve the specimen but also minimizes contamination)
4. Time is taken to Mycobacterium culture 2-6 weeks and needs 3 weeks extra for drug resistance test that is minimized in this test within hours. We can dispatch the report within 2 half an hour.

3.6 Disadvantages of GeneXpert Test

1. The shelf life of the cartridge is only 18 months.
2. A very stable electricity supply is required.
3. Calibrations need annually.
4. Test cost is high.