Prevalence and Treatment Outcome of Tuberculosis and TB/ HIV Co-infection *Among Patients Visiting Boru Meda Hospital, Dessie Town, Northeast* Ethiopia

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Acronyms and Abbreviations

AFB_ Acid Fast Bacilli

AIDS_ Acquired Immunodeficiency Syndrome

BAL_ Bronchoscopy Samples

BMH_ Boru Meda Hospital

CDR_ Case Detection Rate

DOTS_ Directly Observed Treatment Short Course

DSM_ Direct Sputum Microscopy

DST _Drug Sensitive Testing

EPTB _Extra Pulmonary Tuberculosis

FMoH _Federal Ministry of Health

MDGs_ Millennium Development Goals

MDR-TB_ Multi Drug Resistant Tuberculosis

MTB_ Mycobacterium Tuberculosis

NTLCP_ National Tuberculosis and Leprosy Control Program

OIs _ Opportunistic Infections

PCR_ Polymerase Chain Reaction

PPD_ Pure Protein Derivative

PTB_ Pulmonary Tuberculosis

SNPTB_ Sputum Negative Pulmonary Tuberculosis

SPPTB_ Sputum Positive Pulmonary Tuberculosis

SSA_ Sub-Sahara Africa

TB_ Tuberculosis

TSR_ Treatment success rate

TST_ Tuberculin skin test

WHO_ World Health Organization

ZN_ Ziehl-Neelsen

Abstract

Tuberculosis (TB) is a highly infectious air born bacterial disease that is caused by Mycobacterium tuberculosis. It is the major cause of death in developing countries. There were an estimated 9.0 million incident cases of TB which is equivalent to 126 cases per 100,000 populations in 2013.The study on TB indicates that the average TB prevalence and mortality rates in Ethiopia are estimated to be 623 and 42 per 82,950 individuals respectively. The present study was conducted at Boru Meda Hospital one of the areas which is affected by this disease. The main objective of this study was to determine the prevalence and treatment outcomes of TB and TB/HIV co- infections in six consecutive years from 2012 to 2017. Retrospective cross-sectional design of the study was used from documents of patients. In this study, among 958 TB patients registered, 57.8% cases were PTB, 29.6% EPTB and 12.6% were MDR-TB patients. The prevalence of MDR-TB was almost equivalent to MDR-TB cases of Africa and Ethiopia in 2016. The highest prevalence rate of TB was registered in the year 2012 and the lowest was in 2017 which showed a declined trend. New cases were 85.5% and 14.5% were previously treated TB patients. Among PTB cases 55.8% were SPPTB and 44.2% were SNPTB. Out of the total TB cases, 32.2% were SPPTB and 25.6% were SNPTB. The Case Detection Rate (CDR), 32.2% was much lower than the data obtained from Global TB report 2015. All TB patients were tested for HIV infection and 16.7% were co-infected. The trend in prevalence of TB decreased; and in TB-HIV co-infection it was increased from year to year. The prevalence of TB-HIV co-infection in MDR-TB cases was higher than the prevalence in Pulmonary and Extra pulmonary TB cases. The study indicated that males suffered from TB, TB-HIV co-infection and MDR-TB and the highest frequency of these diseases were showed in the age group of 16-45 years. A successful treatment outcome of TB was achieved about 88.0%. Improvement of treatment success rate (TSR) was shown. TB-HIV co-infection and drug resistant TB have been proposed as factors contributing to unsuccessful treatment and limited evaluation of treatment outcomes. The treatment success of TB-HIV coinfection and MDR-TB were 83.1% and 86% respectively. Finally, further research on associated factors and other issues concerning these diseases were recommended to be investigated.

***Keywords / Phrases**: Tuberculosis, TB-HIV co-infection, Pulmonary tuberculosis, Extra Pulmonary Tuberculosis, Multidrug Resistant tuberculosis*

1. INTRODUCTION

1.1 Back Ground of the study

Tuberculosis (TB) is a highly infectious air born bacterial disease that is caused by *Mycobacterium tuberculosis* (MTB) and occasionally by other species of MTB complex such as *M. bovis*, *M. africanum* and recent addition of *M. canetti* and *M. microti*, which are genetically closely related (Raviglione *et al*., 2001). According to Jenkins (1998), these organisms are also known as tubercle bacilli. They are classified in the family of Mycobacteriaceae and in the order of Actinomycetales. MTB is a rod- shape; non-spore forming thin aerobic bacterium measuring about 0.5µm by 3µm.

Tuberculosis is known to be the most important threats to human and animal health causing mortality, morbidity and economic losses in the world, particularly in developing countries (Pal *et al*., 2014). TB is a major global health problem and ranks the second leading cause of death from infectious diseases next to HIV (WHO, 2014). In developing countries, the annual infection rate of TB was reached 2% or more and declined to 0.5% in developed countries (Haileyesus Getahun *et al.*, 2010).

About one-third of the 34 million HIV-infected people globally are infected with latent TB and patients with TB-HIV co-infection are 21–34 times more likely to develop active TB disease than HIV-negative individuals (WHO, 2013). Over the past decades, in many countries of SSA and in parts of South East Asia increasing in TB case rates were highly related to the HIV epidemics (Global TB report, 2014). This infectious disease mostly appears before the occurrence of other opportunistic infections in HIV infected persons (Aliso *et al*., 2001). Before 1990, the number of TB cases was increased from 5% to 10% per year which results to an increase in the transmission of TB within the community; and in HIV infected people the risk of developing active TB disease was 60% (WHO, 2003). The treatment outcomes of TB were highly affected by HIV status in co-infected patients. Therefore, HIV positive individuals were at high risk of developing drug resistant TB (MDR-TB) (Garrait *et al*., 1997).

The main target of United Nations Millennium Development Goals (MDGs) in 2000 was to ensure the decline of the incidence rate of TB by 2015 (Wikipedia, https://en.wikipedia. org/wiki /Millennium_Development_Goals). This was also aimed to halve the prevalence and mortality rates of TB by 2015 as compared to 1990. As indicated by WHO (2006), the final goal is to eliminate TB by 2050. The same report indicated that the global TB mortality rate has declined by 45%, and TB incidence rates were decreased in most parts of the world since 1990. An estimated 37 million lives were saved through effective diagnosis and treatment between 2000 and 2003 and the global TB strategy developed by WHO for the period between 2006 to 2015 was to stop TB (Global TB report, 2014). The goal of this strategy is to achieve 2015 global targets for reductions of the burden of TB. Therefore, the same report indicated that the global absolute number of TB incident cases was declined slowly at an average rate of 1.5% from 2000 - 2013 and 0.6% between 2012 and 2013 due to high awareness on detection, treatment and funding gaps as well as the development of new tools.

A recent report showed that there was a trend in declining of prevalence, incidence and mortality rate of TB (FMoH, 2014). Accordingly, the prevalence of TB that was recorded 425/100000 in 1990 has decreased to 211/100000 in the year 2013. Similarly, the incidence which was 367/100000 in 1990 was reduced to 224/100000 in the same year. According to global TB report (2014), only 71% of TB patients in Ethiopia knew their HIV status by 2013. Available data in the country also suggests wide variations in the prevalence, treatment success rate and case detection rate of TB, TB/HIV co-infection and MDR-TB in different areas including Amhara Region. In Dessie Town, there is also high scarce of investigations and lack of awareness on this among the society.

1.2. Statement of the problem

Tuberculosis is one of the most widely spread infections next to HIV/ADIS. It is major cause of death particularly in low-income countries. According to FMoH in 2016, TB is clinically diagnosed as pulmonary tuberculosis (PTB) and extra-pulmonary tuberculosis (EPTB) that constitutes 80% and 20% of the TB infections respectively. PTB is also any bacteriologically confirmed or clinically diagnosed TB case which involves the lung parenchyma or trachea, bronchial tree. The same report indicated that once a person develops the disease, there will be

several suggestive clinical features, especially a persistent and progressive cough with non-specific systemic symptoms such as fever, night sweats, loss of weight and some patients may present with chest pains, breathlessness, coughing up sputum or blood and/or localized wheeze due to local TB bronchitis**.** The PTB is also categorized into smear positive and smear negative TB that account for 75-80% and 20-25% of all PTB cases respectively. EPTB can be military, lymph nodes, abdominal, urinary tract, skin, bone and joints and pleurisy (Sharma and Mohan, 2004). According to Alemu Fanosie *et al*. (2016), among the total TB cases, the proportion of EPTB infection in Africa and Ethiopia were reported as 17.7% and 32.5 by the year 2013 and 2012 respectively.

WHO TB report (2014) shows that Globally, there were an estimated 9.0 million incident cases of TB which is equivalent to 126 cases per 100,000 populations in 2013. Among the incident cases of TB occurred in 2013, most of them were in Asia (56%) and the African Region (29%); while, the smaller proportions of cases occurred in the Eastern Mediterranean Region (8%), the European Region (4%) and the Region of the Americas (3%). According to the same report, there were 22 the TB "high burden" countries, and they have been prioritized at a global level since 2000. And, India, China, Nigeria, Pakistan, Indonesia and South Africa were the six countries with the largest incident cases in 2013; but, India and China alone accounted for 24% and 11% of global cases, respectively. From which, Ethiopia is among the 22 TB high burden countries in the world having the 7^{th} rank in the world and the 2^{nd} rank in Africa. Another study on TB indicates that the average TB prevalence and mortality rates in Ethiopia are estimated to be 623 and 42 per 82,950 individuals respectively (Fantahun Biadglegne *et al*., 2014).

Tuberculosis is among the leading causes of morbidity and mortality in Amara Regional State of Ethiopia as it is in other parts of the country. However, there are lack of studies on the prevalence, treatment success rate and case detection rate of TB, TB/HIV co-infection and MDR-TB in some areas of the Region such as Dessie town, south Wollo. And, there is a knowledge gap on associated factors, ways of transmission and prevention of the disease in the society. Therefore, this study was conducted at Boru Meda Hospital (BMH) in Dessie Town to assess the trends in prevalence and treatment outcomes of TB and TB/HIV co-infection in the last six-years (20122017).

1.3. Objectives of the Study

1.3.1. General Objective:

The main objective of this study was to estimate the prevalence and treatment outcomes of TB and TB/HIV co- infection among patients who visited BMH in Dessie Town from 2012-2017.

1.3.2 Specific Objectives

1. To assess the prevalence of TB, TB/HIV co-infection and MDR-TB in different age groups and sex of TB patients at the study area.
2. To determine the pattern of the disease (pulmonary, extra pulmonary and MDR-TB) with different age groups and sex of TB patients.
3. To determine the proportions of HIV seropositive and HIV seronegative TB among pulmonary (smear-positive and smear-negative), extra pulmonary and MDR TB patients.
4. To determine the extent by which the case detection rate and treatment success rate are achieved among patients according to DOTS strategy.

1.4. Significance of the Study

It is obvious that there have been different studies carried out in Ethiopia on TB and TB/HIV coinfections, but there is a scars information on the prevalence of these infections and no studies were conducted in the study area. Hence, the researcher aimed to study the trends in prevalence and treatment outcomes of TB and TB/HIV co-infections at BMH in Dessie Town. The study is used to provide accurate estimates of the prevalence of TB and TB/HIV co-infection, which are crucial to provide important findings as recommendation for the improvement of services in the Hospital. And, this is also used to provide some information for further study to be carried out by other investigators in this area.

1.5. Scope of the Study

Geographically the study was delimited to be carried out at BMH in Dessie Town, South Wollo, and Amara Regional State, Ethiopia. It was also delimited to estimate the prevalence and treatment outcomes of TB and TB/HIV co-infection with consideration of different socio-demographic characteristics of TB patients in the study area.

2. REVIEW OF RELATED LITRATURE

2.1. Pathogenesis and Transmission of TB

Tuberculosis is highly transmitted from person to person via inhalation of droplets from air borne nuclei during coughing and sneezing by infected people with active TB. These droplets are passed in to the air when persons infected with TB cough, sneeze or speak (Bass *et al.*,1990). When a healthy individual inhale the bacilli, the first implant is in the lungs at bronchiole or alveolar level. The bacilli multiply and produce the primary lesion there. Some bacilli pass in to the Hilary lymph nodes causing lymph node enlargement. Then, the bacilli from alveolar lesion and enlarged lymph nodes can be disseminated via lymphatic system or blood stream, leading to serious complications such as meningitis, joint and renal TB (Fostensteien and Grange, 1991).

Hypersensitivity to the organism appears at 8 to 10 weeks and the infected individual becomes tuberculin-test positive. It is estimated that 10% of infected individuals develop clinical TB during their life time. Around 50% of them will develop TB during the first years of infection and the rest many years later (Bass *et al*., 1990).

2.2. Risk Factors of TB

Different studies indicated that various risk factors affect the influence of TB and spread of the disease to ensure the proper public healthcare and to prioritize targets for TB control. Among the factors, the most significant independent risk factor in association with active pulmonary or extra-pulmonary TB is HIV infection contributing to high transmission among individuals (Reid *et al*., 2006). According to Cailhol *et al*. (2005), age has also been shown as a risk factor in increasing TB incidence; while women have been found to be more susceptible to TB than men probably due to the effect of female hormones or underreporting of TB cases. And, according to Patel *et al*. (2007), past history of TB in the family, smoking, place of residence, place of origin, malnutrition and alcoholism are also other risk factors. In countries with low TB incidence, immigrants from countries with high TB prevalence constitute potential increased risk for recent transmission of infection to local populations (Dale *et al*., 2005). Another study indicated that in some industrialized countries, TB has been associated with certain risk factors, such as overcrowding, reduced funding, poverty, homelessness, improper TB management and negligence in

implementing TB control program (Dye *et al*., 2009). Consumption of unpasteurized milk was also considered as a risk factor for TB caused by *M. bovis* in different parts of the world (Coker *et al*., 2006).

2.3. TB-HIV co-infection

Tuberculosis is the most common opportunistic infection (OI) in HIV/AIDS patients in developing countries. In SSA including Ethiopia, the HIV/AIDS has contributed to the rising levels of TB incidence. HIV/AIDS is the most important risk factor for the development of TB. The risk of TB disease is very high in HIV co-infected patients than non-infected TB patients; which is proved by the study as TB patients who are co-infected with HIV have a higher risk of developing TB disease in their lives than TB infected person without HIV infection (Antonucci *et al*., 2004). HIV lowers the host's immune response to TB. Another study indicated that the lifetime risk of developing active TB in HIV infected individuals is 10% per year compared with lifetime risk of 5-8% in individuals without HIV (Korenromp *et al*., 2003).

Globally in different regions including Ethiopia, TB/HIV co-infection is an additional problem in the control of TB. Therefore, 10-15% of TB patients in Ethiopia were HIV co-infected every year (FMoH, 2016). The same source showed as the WHO Global TB Report (2008) estimates that in Ethiopia 40% of TB patients tested for HIV are HIV positive and the most common manifestation of TB in adults infected with HIV is PTB, which occurs at various stages of HIV infection.

2.4. MDR-TB

The main barrier that affects the control of TB is high burden of multidrug-resistant TB (MDRTB). The major contributing factor identified for the spread of MDR-TB is poor infection control (WHO Report, 2013). A report of FMoH showed that about half million new cases of MDRTB emerged yearly and kills an estimate of 110,000 individuals every year. Among the newly emerging MDR-TB cases, only 3% get serious treatment globally (FMoH, 2009). According to the Ethiopian national TB drug resistance surveillance report, 2.3% of new TB cases and 17.8% of previously treated TB cases were estimated to have MDR-TB (Dereje Abate *et al*., 2012). While in Africa, there was a report of 69,000 MDR-TB cases (Gemeda Abebe *et al*., 2012). Ethiopia ranked 15th with new cases of MDR-TB each year and is one of the 27 countries

with high MDR-TB burden (FMoH, 2009). Even if MDR-TB is highly prevalent in retreated TB cases, the prevalence of MDR-TB in newly diagnosed TB patients has been reported to be 2.8% (WHO TB report, 2013). Globally in 2016, an estimated 4.1% of new cases and 19% of previously treated cases had MDR-TB (Global TB report, 2017). There are a number of published studies on MDR-TB available worldwide. However, accurate data on MDR-TB in Ethiopia is scarce.

2.5. Burden of TB

2.5.1. International Burden of TB

Tuberculosis is the second most frequent cause of deaths among infectious diseases particularly in least developing countries. And also, the studies regarding the global trend of TB during the period 1982 to 1992 showed an increase of cases which estimated at 8 million new cases in 1990 (Sinder,1997). For example, in United States the yearly incidence of TB cases increased slightly from 9.4 per 100,000 in 1985 to 1990. In this period, the annual number of cases was increased by 51,500 compared with 1984 and earlier. The HIV epidemic and emigration from high prevalence countries was considered to be the reasons for the increase. During the same period an increase of TB notifications in other WHO regions of the world was observed. The international prevalence of TB infections is estimated to be 1.8 billion and the number of new cases was 8.8 million in 2002 (WHO, 2004).

Each year, 8 million cases of active TB with over 2 million deaths were estimated to occur globally. Although, the majority of the deaths were occurred in Africa with annual death rates of 75 per 100,000 people per year (Corbett *et al.*, 2003). The age group mostly affected by TB in the developing countries is 15-59 years and over (Christopher *et al*., 1999). The same report showed that the annual risk of infection has fallen in the developed countries to 0.1% or less, while in SSA the estimated was 1.0-2.5%, indicating high rates of TB transmission.

The estimated number of new cases were 8.9 million in 2004, 8.8 million in 2005 and 9.2 million in 2006 (WHO, 2006; 2007; 2008). Where as in 2014, 6 million new cases of TB were reported to WHO, fewer than two-thirds (63%) of the 9.6 million people estimated to have fallen sick with the disease. Among that, 12% of the 9.6 million new TB cases were HIV-positive (WHO, 2015).

According to this study, there were also 1.5 million TB deaths from both HIV negative and positive people worldwide. This shows, the reduction of this burden is due to high awareness on detection, treatment and funding gaps as well as the development of new tools.

Each person with active TB if left untreated will infect an average between 10 and 15 people each year (Blumberg *et al*., 2005). The global targets for reductions in TB disease burden by 2015 were set within the context of the United Nations‟ Millennium Development Goals (MDGs) (WHO, 2015). This indicates that the special emphasis and critical topic of the 2015 global TB report is on assessment of whether the 2015 targets have been achieved or not. This assessment is made for the world, for the six WHO regions and for the 22 high-burden countries that collectively account for 80% of TB cases. The WHO ranks countries by number of cases and 22 developing countries account for 80% of TB cases (WHO, 2003).

2.5.2. Burden of TB in Ethiopia

The burden of TB in Ethiopia is estimated at 168 new smear-positive cases per 100,000 populations according to the WHO global TB report 2008. Ethiopia is among the 22 TB high burden countries in the world; and the country ranks 8th out of the 22 high burden countries based on estimated number of incident cases of all forms of TB in 2004 and the country has an estimated TB incidence rate of 353, prevalence of 533 and mortality rate of 79 per 100,000 populations per year (WHO, 2006). WHO (2014), showed that Ethiopia is the seventh ranked country in the world and the second ranked country in Africa among the 22 high burden countries in the world. According this report, the average prevalence and mortality rates of TB in Ethiopia were 623 and 42 per 82,950 individuals respectively.

2.6. Clinical Manifestation of TB

A person infected with PTB will have several suggestive clinical features, especially 2 weeks‟ or above duration of cough, sputum production and weight loss which are important for the diagnosis of PTB. Others respiratory symptoms like chest pain, hemoptysis, breathlessness and constitutional symptoms like fever, night sweats, tiredness, loss of appetite can also occur (WHO, 2004).

People with EPTB initially may have similar symptoms to people with pulmonary TB: fever, night sweats and weight loss. Then, they often develop complaints that are specific to the body site that has been infected with TB.

2.7. Diagnosis of TB and HIV/AIDS

2.7.1. Diagnosis of TB

Diagnosis of TB is commonly based on the finding of acid-fast bacillus (AFB) on microscopic examination of a diagnostic specimen such as a smear of expectorated sputum or of tissue (for example, a lymph node biopsy or fine needle aspiration) (Johnson and Ellner ,2006). Microscopic examination of sputum smears for acid-fast bacilli is used throughout the World as a diagnostic test for suspected PTB. Bacilli of *Mycobacteria* can be demonstrated by Ziehl-Neelsen (ZN) or fluorochrome staining methods (Gothi *et al*., 2004). The standard WHO recommendations for TB diagnosis in the DOTS program are the use of direct sputum microscopy (DSM) on three stained sputum specimens. First and third are on spot while the second is the early morning sample (Steingart *et al*., 2006).

According to Katoch (2004), the gene probes can help in rapid identification of isolates, gene amplification methods (E.g. PCR) developed for diagnosis of TB is demonstrably highly sensitive and detection can be done within hours. Alternative specimens for diagnosis of TB can be aspirated effusions, blood for cultures, early morning urine for TB culture and bone marrow biopsy (Johnson and Ellner, 2006). This finding also showed that the skin testing with pure protein derivative (PPD) is most widely used in screening for MTB infection. The test has a limited value in the diagnosis of active TB because of its low sensitivity and specificity.

The following are the criteria to diagnose the various clinical forms of TB: 1) SPPTB: at least 2 sputum smear examinations positive for AFB, or one sputum positive for AFB and radiographic abnormalities consistent with active PTB, or one sputum specimen positive for AFB and culture positive for *M tuberculosis. 2)* SNPTB: at least three sputum examinations negative for AFB, radiographic abnormalities consistent with active PTB and not responding to a course of general antibiotics, or diagnosis based on positive culture but negative AFB sputum examinations. Others consider the patient is SNPTB when three sputum smear examination is negative and bronchoscopy samples (BAL) show „scanty" to 1^+ positivity or if two of any samples were

positive after concentration (Harries *et al*., 2001). 3) EPTB: one culture-positive specimen from an extra pulmonary site, or histological evidence, or strong clinical evidence consistent with active extrapulmonary TB (WHO, 2005). Although, diagnosing EPTB remains challenging because clinical samples obtained from relatively inaccessible sites.

DRTB is caused by organisms that are resistant to the most effective anti TB drugs (JCDR, 2015). It is resulted from either infection with organisms which are already drug-resistant or may develop in the course of patient's treatment (WHO, 2013). Late diagnosis of DR-TB results in lower treatment success and failure rates (Mukherjee *et al.*, 2004). DRTB is a laboratory diagnosis which is made only by reference laboratories performing culture of TB strains, with additional testing of anti TB drug sensitivity (DST: Drug Sensitivity Test) (FMoH, 2008).

2.7.2. Diagnosis of HIV/AIDS

Different testing methods can be used for the diagnosis of HIV/AIDS. These methods indicate the presence of infection by detecting one of the following: HIV antibody, HIV antigen, combined HIV Ab/Ag, HIV viral nucleic acid and HIV virus by viral culture method. The detection of viral nucleic acid may be achieved by different laboratory techniques (Priester and Korsman, 2006). HIV antibody detection can be done using Enzyme-linked Immunosorbent Assay methods, rapid tests and western blot assay methods. For surveillance as well as diagnostic purpose in developing countries, WHO recommends alternative testing strategies using combination of Enzyme-linked Immunosorbent Assay or rapid tests (WHO, 2001).

2.8. Treatment of TB

Active TB disease can be cured with combinations of antibiotics. As reported by WHO (2009), effective treatments quickly make a person with non-contagious to prevent further spread of TB. To achieve a cure treatment about eight months of daily treatment is needed (Volmink *et al*., 2000); and it is often recommended that the patient takes his/ her pills in the presence of someone who can supervise the therapy. Such type of approach is called DOTs (Direct Observed Treatment, short course). This approach has been predicted to cure 95% of TB cases (Wandwalo *et al*., 2005). WHO (2016) TB report recommended that the standard treatment of active TB begins with four medicines given for 2 months, continuing treatment for 4 to 9 months or longer if needed, using DOTs and using different treatment programs for people infected with HIV,

MDR-TB, pregnant women and children. Globally, the treatment success rate for the 5.9 million new and relapse cases that were treated in the 2015 cohort was 83%, as in 2014.

2.9. Strategies for TB control

2.9.1. DOTS strategy

It is internationally accepted measure in TB control and it is a short stand for directly observed short course treatment strategy, which combines five elements:1) political commitment from governments and authorities 2) case detection by microscopy and through mainly passive case finding 3) establishment of DOTS 4) regular logistic supplies of essential anti-TB drugs (isonized, rifampicin, pyrazinamide, streptomycin and ethambutol); and 5)strong and sustainable reporting and recording system and follow up and monitoring of individual treatment (Harries *et al.*, 2002).

WHO TB report (2015) indicated that this strategy aimed to end the global TB epidemic, with targets to reduce TB deaths by 95% and to cut new cases by 90% between 2015 and 2035, and to ensure that no family is burdened with catastrophic expenses due to TB. Ethiopia claimed to have achieved the MDGs for TB in 2015 and now adopted new post Global TB strategy called “end TB strategy”.

2.9.2. Stop Strategy (2006-2015)

The STOP TB partnership was established in 2000 as a global and political measure to stop the spread of TB around the world. The partnership’s goal is to eliminate TB as a public health problem, and to secure a world free of TB (Stop TB partnership, 2000). This strategy was developed by WHO, designed to guide tuberculosis control efforts during 2006 to 2015. It built on DOTS strategy. Nearly 92% of Hospitals and 95% of health centers implemented DOTS based-services in 2011 (FMoH, 2011).

2.9.3. The End TB strategy (2016-2035)

It was established to reduce number of TB death compared with 2015; in 2020 by 35%, in 2025 by 75%, in 2030 by 90% and in 2035 by 95% and also to reduce TB incidence rate in 2020 by 20%, in 2025 by 50%, in 2030 by 80% and in 2035 by 90% and finally, to stop 100% the effect of TB on families facing catastrophic costs (WHO, 2015).

3. MATERIALS AND METHODS

3.1. Description of the Study Area

This study was carried out in Dessie Town which is located in the northern part of Ethiopia about 411km from Addis Ababa (fig. 1). Specifically, the study was conducted at BMH which is about 10km from Dessie and was established by Sudanese interior mission in 1955. BMH is located at 11007'21.33"N, 39038'05.87" E with an elevation of 2706 meters above sea level. The hospital provides services in different departments; one of which is the TB clinic. The clinic registers and treats patients diagnosed with TB using DOT strategy designed by the National Tuberculosis and Leprosy Control Program (NTLCP) of Ethiopia. The DOT strategy is implemented to enhance medication adherence and reduce subsequent drug resistance; hence, patients administer their medication under direct supervision of a health care provider. As per the state policy, the TB clinic provides the recommended medications for registered TB cases, screening for HIV serostatus, and referrals to ART clinic for HIV positive TB patients.

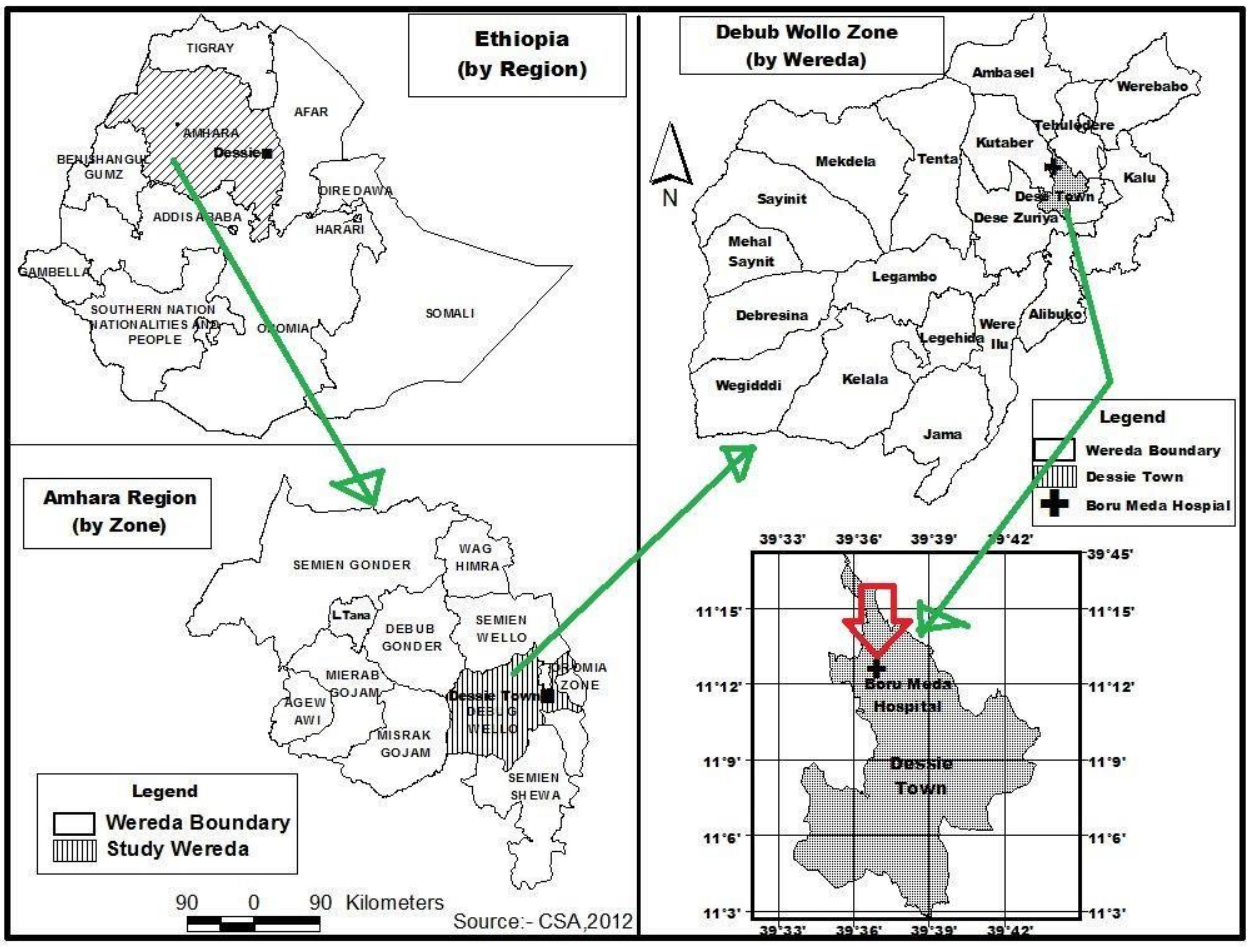

Figure 1: Map of the study area

3.2. Design of the study

A cross-sectional retrospective study was used by reviewing a 6-year period (2012-2017) of medical records of TB and TB/HIV co-infected patients from TB Registry Unit of the TB clinic at BMH. The data were collected from September to December, 2017. Patients with all age groups who had started and completed a course of anti-TB therapy or transferred during the study period were included in the study. All TB and TB/HIV co-infected patients‟ medical records were reviewed to extract socio-demographic data of patients, TB type and treatment outcomes. Finally, the investigator used a descriptive statistic in percentages and ratios to determine the prevalence of TB, TB/HIV co-infections and MDR-TB among patients who have been visiting the BMH from the years 2012-2017.

3.3. The study population and sample size

The population and sample size for this study were the medical records of all confirmed TB patients in the Registry Unit of the hospital between 2012 and 2017. The selection of the study site was due to high inflow of TB patients.

3.4. Methods of data collection and data analysis

Some data collection checklists that contain socio-demographic characteristics, disease-related factors and treatment outcomes were prepared to extract the data from patients‟ medical records. Relevant data were collected by analyzing individuals‟ card using formats developed by student researcher. Accordingly, the selected TB, TB/HIV co-infected and MDR-TB patients‟ cards which are available in the hospital were inspected and appropriate information were collected, analyzed and discussed.

4. RESULTS AND DESCUSSIONS

4.1 Prevalence of TB by sex, age, TB form and patient types at BMH (2012-2017)

Among 958 TB patients registered in the last six years at Boru Meda Hospital between 2012 and 2017, 554(57.8) cases were PTB, 283(29.6) were EPTB and 121(12.6) were MDR-TB patients. From the total TB patients registered, 578(60.3%) were males and 380(39.7%) of them were females with ratio of 1.5:1 which showed slightly a great difference when compared with 2014 national TB prevalence among males and female with ratio of 1.2:1 and slightly lowered from 2014 global TB prevalence with 1.7:1 male to female ratio (Global TB report, 2015). The majority of the patients, 695(72.5) with 1.5:1 male to female ratio, belonged to the age group of 16-45 and followed by 143(14.0) with 1.5:1, 80(8.4) with 1.2:1 and 40(4.2) with 7:1 male to female ratios belonged to age group of 46-64, ≤15 and ≥65 years respectively (Table 1).

The highest prevalence rate of TB was registered in the year 2012 which was 22.2% and followed by 2013, 2014, 2015, 2016 and 2017 with 19.9%, 17.4%, 14.9%, 14.1% and 11.5% respectively with declining rate from earlier to recent years. This showed that the annual trends of TB for both sexes and for new cases were gradually declined in the last six years**.** The reason for the overall fall of annual prevalence of all forms of TB registered cases in this study agreed with other studies (Jemberu Alemu *et al*., 2017) and the countries profile (WHO, 2014). The probable reasons of falling down might be due to continuous implementation of DOTS, increased availability of health facilities and health service delivery increment and increased awareness by the public about the disease in the study area.

Of the total 958 TB cases, 819(85.5) were new cases among which 489(59.7%) were males and 330(40.3%) females with the ratio of 1.5:1, whereas 139(14.5) were previously treated and of which 89(64.0) were males and 50(36.0) were females in the ratio of 1.8:1. The ratio between new TB cases and previously treated was 85.5: 14.5 or 5.9 :1.

Table 1: Distribution of TB by sex, age, TB forms and TB types at BMH(2012-2017)

Year	Sex	Total	Age category (year)				TB form			patient type	
			≤15 no (%)	16-45 no (%)	46-64 no (%)	≥65 n(%)	PTB no (%)	EPTB no (%)	MDR-TB no (%)	New no (%)	Previously treated no (%)
2012	Male	**131**(22.7)	14(56)	93(61.6)	19(59.4)	5(100)	87(62.1)	28(66)	16(69.6)	111(60.3)	20(69)
	Female	**82**(2.6)	11(44)	58(38.4)	13(40.6)	0(0.0)	53(37.9)	22(34)	7(30.4)	73(39.7)	9(31)
	Total	**213**(22.2)	25(11.7)	151(70.9)	32(15.0)	5(2.3)	140(65.7)	50(23.4)	23(10.8)	184(86.4)	29(13.6)
2013	Male	**112**(19.4)	12(57.1)	78(60.5)	14(43.8)	8(88.9)	57(52.3)	42(73.7)	13(52)	100(57.8)	12(66.7)
	Female	**79**(20.3)	9(42.9)	51(39.5)	18(56.2)	1(11.1)	52(47.7)	15(26.3)	12(48)	73(42.2)	6(33.3)
	Total	**191**(19.9)	21(11)	129(67.5)	32(3.3)	9(4.7)	109(57)	57(29.8)	25(13)	173(90.6)	18(9.4)
2014	Male	**97(**6.8)	8(53.3)	73(55.7)	14(82.3)	2(50)	54(55.1)	30(62.5)	13(62.0)	83(57.2)	14(63.6)
	Female	**70(**18.4)	7(46.7)	58(44.3)	3(17.7)	2(50)	44(44.9)	18(37.5)	8(38.0)	62(42.8)	8 (36.4)
	Total	**167(**17.4)	15(9.0)	131(78.4)	17(10.2)	4(2.4)	98(58.7)	48(28.7)	21(12.6)	145(86.8)	22(13.2)
2015	Male	**91(**5.7)	5(55.6)	65(63.1)	15(60)	6(100)	42(59.2)	38(73)	11(55.0)	73(64.0)	18(62.1)
	Female	**52(**13.7)	4(44.4)	38 (36.9)	10(40)	0 (0.0)	29(40.8)	14(27)	9(45.0)	41(36.0)	11(37.9)
	Total	**143(**14.9)	9(6.3)	103(72.0)	25(17.5)	6(4.2)	71(49.7)	52(36.4)	20(14.0)	114(79.7)	29(20.3)
2016	Male	**80(**13.8)	3(42.9)	54(57.4)	16(61.5)	7(87.5)	41(59.4)	26(53.1)	13(76.5)	67(60.9)	13(52.0)
	Female	**55(**14.5)	4(57.1)	40 (42.6)	10(38.5)	1(12.5)	28(40.6)	23(46.9)	4 (23.5)	43 (39.1)	12(48.0)
	Total	**135(**14.1)	7(5.2)	94 (69.6)	26(19.3)	8(5.9)	69(51.1)	49(36.3)	17(12.6)	110(81.5)	25(18.5)
2017	Male	**67(**11.6)	2(66.7)	49(56.3)	9(82.0)	7(88.0)	43(64.1)	15(55.6)	9(60.0)	55(59.1)	12(75.0)
	Female	**42(**11.1)	1(33.3)	38 (43.7)	2 (18)	1(12)	24 (35.8)	12(44.4)	6(40.0)	38(40.9)	4(25.0)
	Total	**109(**11.5)	3(2.3)	87(80.0)	11(10.1)	8(7.3)	67(61.5)	27(24.8)	15(13.8)	93(85.3)	16(14.7)
Total	Male	**578(**60.3)	44(55.0)	412(59.3)	87(60.8)	35(87.5	324(58.5)	179(63.3)	75(62.0)	489(59.7)	89(64.0)
	Female	**380 (**39.7)	36(45.0)	283(40.7)	56(39.2)	5(12.5)	230(41.5)	104(36.7)	46(38.0)	330(40.3)	50(36.0)
	Total	**958(**100)	80(**8.4**)	695(**72.5**)	143(**14.9**	40(**4.2**)	554(**57.8**	283(**29.6)**	121(**12.6**	819(**85.5**)	139(**14.5)**
M:F ratio		**1.5:1**	**1.2:1**	**1.5:1**	**1.5:1**	**7:1**	**1.4:1**	**1.7:1**	**1.6:1**	**1.5:1**	**1.8:1**
Ratio of each category			**2.0:17.4:3.6:1** respectively				**4.6:2.3:1** respectively			**5.9:1**	

Note: PTB=pulmonary TB, EPTB=Extra Pulmonary TB, MDR-TB=Multidrug Resistance tuberculosis, F: M

Of 554 PTB cases 309(55.8%) were SPPTB with male to female ratio 63.1%: 36.9% or (1.7: 1) and 245(44.2%) were SNPTB with 52.7: 47.3 or (1.1:1) ratios of males to females. The proportion of SPPTB disease among males was 33.7% and 30.0 among females. Correspondingly, the proportion of SNPTB, EPTB and MDR-TB among males and females were 22.3% and 30.5%, 31.0% and 27.4, and 13.0% and 12.1% respectively. The proportion of SPPTB cases, 32.2% (Table 3) was almost equal when compared to the national average reported by the WHO between 2011 and 2015, of 32.4%. Tuberculosis most frequently affected the age group between 16- 45 years in both sexes and in both forms of TB (PTB and EPTB) 446(53.3%) and of which 163(54.2) were SPPTB and 138(45.8) were SNPTB and followed by 46-64 years of age 216(25.8) with 81(56.6) SPPTB and 62(43.4) SNPTB. The ratio of SNPTB, SPPTB and EPTB diseases in the age group 16-45 and 46-64 years were consistent 1:1.2:1.1 and 1:1.3:1.2

respectively, but the ratios in the age group ≤15 and ≥65 were1:1.4:1.4 and 1:1.5:1.5 indicating variations in the infection of the different forms of TB by these age groups (Table 2).

Table 2: Prevalence of different forms of TB by age and gender distribution of patients

Age	Forms of TB		Total PTB and EPTB Patients (2012-2017)				Ratio of SNPTB: SPPTB: EPTB
			Male n (%)	Female n (%)	Total n (%)		
≤15	PTB	SPPTB	23(65.7)	12(34.3)	35(58.3)	60(62.5)	1:1.4:1.4
		SNPTB	16(64.0)	9(36)	25(41.7)		
	EPTB		25(69.4)	11(30.6)	36(37.5)		
	Total		64(66.7)	32(33.3)	96(11.5)		
16-45	PTB	SPPTB	106(65.0)	57(35.0)	163(54.2)	301 (67.5)	1:1.2:1.1
		SNPTB	71(51.4)	67(48.6)	138(45.8)		
	EPTB		89(61.4)	56(38.6)	145(32.5)		
	Total		266(59.6)	180(40.4)	446(53.3)		
46-64	PTB	SPPTB	48(59.3)	33(40.7)	81(56.6)	143 (66.2)	1:1.3:1.2
		SNPTB	31(50.0)	31(50.0)	62(43.4)		
	EPTB		43(58.9)	30(41.1)	73(33.8)		
	Total		122(56.5)	94(43.5)	216(25.8)		
≥65	PTB	SPPTB	18(60.0)	12(31)	30(60.0)	50 (63.3)	1:1.5:1.5
		SNPTB	11(55.0)	9(45.0)	20(40.0)		
	EPTB		22(75.9)	7(24.1)	29(36.7)		
	Total		51(64.6)	28(35.4)	79(9.4)		
Total N(%)	PTB	SPPTB	195(33.7)	114(30.0)	309(55.8)	554 (57.8)	1:1.3:1.2
		SNPTB	129(22.3)	116(30.5)	245(44.2)		
	EPTB		179(31)	104(27.4)	283(29.6)		
	Total		503(87.0)	334(87.9)	837(87.4)		

Note: PTB=pulmonary TB, PPTB=smear positive pulmonary TB, SNPTB=smear-negative pulmonary TB, EPTB=Extra Pulmonary TB, MDR-TB=Multidrug Resistance tuberculosis.

4.2 Case Detection Rate of PTB Cases

For the year 2012-2017 at BMH, the detection rate (SPPTB diagnosed) and clinical diagnosis of TB (SNPTB diagnosed) among the total of 958 TB cases were investigated. Out of the total 958 TB cases, 309(32.2) comprising 195(63.1) males and 114(36.9) females were smear positive and 245(25.6) consisting of 129(52.7) males and 116(47.3) females were smear negative PTB cases. In addition, the rest 283(29.5) and 121(12.6) were EPTB and MDR-TB respectively (Table 3). The Case Detection Rate (CDR) of the study site (32.2) was much lower than the data obtained from Global TB report 2015, which released a report for 2014 showing high CDR in Global (58%), Kenya(53%), Brazil(70%), India(66%), Nigeria(64%), and Ethiopia(49%), and comparable to the CDR registered in China(33%), Myanmar(39%), and Philippines(41%). In

2013, 64% CDR was registered at a global level whereas Ethiopia, Nigeria and Kenya achieved CDR of 62%, 16% and 75% respectively (Global TB report, 2014). According to the Global Stop TB partnership, 70% CDR was projected as a reference point for its achievement during 2015 (Global TB Report, 2010); but, Ethiopia including the site of this study seems very late to achieve the goal of the partnership. This might be due to poor quality of diagnosis, co-existence of TB/HIV co-infection, etc. Therefore, some measures should be taken in the study area to increase the CDR of TB to reach at the next reference point (82.3%) in 20120.

Table 3: CDR and clinical diagnosis of TB patients(2012-2017)

Forms of TB		Total TB Patients (2012-2017)			
		Male N (%)	Female N (%)	Total N (%)	
PMTB	SPPTB	195(63.1)	114(36.9)	**309(32.2**)	554 **(57.8)**
	SNPTB	129(52.7)	116(47.3)	245(25.6)	
EPTB		179(63.3)	104(36.7)	283(29.5)	
MDRTB		75(62.0)	46(38.0)	121(12.6)	
Total		578(60.3)	380(39.6)	958(100)	

4.3 Prevalence of TB-HIV co-infection

Among the 958 medical reviews of TB patients, all of them (100%) were tested for HIV infection, among them 160(16.7%) were HIV co-infected cases with male, 97(**60.6**), to female, 63(**39.4**) proportions, indicated that males in the study site were 1.5 times much more affected by TB-HIV co-infection than females. Whereas, 798(83.3%) were HIV sero-negative TB patients comprised 451(58.7) males and 317(41.3) females (Table 4). From this 97(60.6) were males and 63(39.4) were females with the proportion of 1.5 to 1. According to Global TB report of 2015, an estimated 1.2 million (12%) of the 9.6 million people who developed TB worldwide were HIV positive in 2014. In this study, the majority, 120(22.6), of the HIV infected TB patients were belonged to the age group of 16–45 years with male to female ratio of 2.6:1 and followed by 28(11.8%), 11(10.6%) and 1(1.2%) with the age groups of 45-64, ≤15 and ≥65 years and male to female ratios of 1.5:1, 2.6:1 and 1:0 respectively (Table 4). This also indicated that males suffered more from HIV co-infection than females (**1.5:1**) and age group of 16-45 years showed the highest frequency of HIV co-infection with prevalence of 22.6% and again particularly males with prevalence of 60.6%. This indicated that age group from ≤15 ,16-45 and 46-64 years old

were 8.8, 18.8 and 9.8 times likely to be risk of TB-HIV co-infection, respectively, as compare to ≥65 age groups years old (Table 4).

The prevalence (16.7%) in the study area indicates a declining trend when compared with some high prevalence sub-Saharan countries such as Tanzania, Zimbabwe, Zambia, Malawi, Kenya and Ivory Coast with 32%, 60%, 64%, 28-50% and 38% with high prevalence respectively (Glynn *et al.*, 2004). The prevalence in Ethiopia was also 42% (WHO, 2003).

Table 4: Pravalence of TB-HIV co-infection by age and gender distribution

Age Category	HIV status	Total TB patients tested for HIV (2012-2017)				
		Male N (%)	Female N (%)	Total N (%)	M: F ratio	Seropositive ratios
≤15	Positive	8(72.7)	3(27.3)	11(10.6)	2.6:1	For the ratio of ≥65**:** 4664**:**16-45**:** ≤15 years of age (1:9.8:18.8:8.8)
	Negative	71(69.6)	31(30.4)	102(98.1)	2.2:1	
	Total	79(69.9)	34(30.1)	113(11.8)	2:1	
16-45	Positive	71(59.2)	49(40.8)	120(22.6)	1.4:1	
	Negative	243(59.1)	168(40.9)	411(77.4)	1.4:1	
	Total	314(59.1)	217(40.9)	531(55.4)	1.4:1	
46-64	Positive	17(60.7)	11(39.3)	28(11.8)	1.5:1	
	Negative	122(58.1)	88(41.9)	210(88.2)	1.3:1	
	Total	139(24.0)	99(26.1)	238(24.8)	1.4:1	
≥65	Positive	1(100.0)	0(0.0)	1(1.2)	1:0	
	Negative	54(64.3)	30(35.7)	84(98.8)	1.8:1	
	Total	55(9.5)	30(7.9)	85(8.9)	1.8:1	
Total N (%)	Positive	97(60.6)	63(39.4)	160(16.7)	1.5:1	
	Negative	451(58.7)	317(41.3)	768(80.2)	1.5:1	
	Total	578(60.3)	380(39.7)	958(100)	1.5:1	

N=number M: F= male to female ratio

The prevalence of sero-positive and sero-negative TB in 2012, 2013, 2014 and 2015 were almost consistent; but, co-infection in the years 2016 (17.8%) and 2017 (19.3%), showed an increasing trend by 1.7% and 3.2% respectively when compared to co-infected patients of 2015 (16.1). (Table 5). SSA had a prevalence of TB-HIV co-infection of approximately 41.2% (Pennap *et al.*, 2010) which was 2.4 times greater than the result of this study.

Table 5: Prevalence of TB-HIV co-infection from 2012-2017

HIV status	TB patients of each Year											
	2012		2013		2014		2015		2016		2017	
	Males N(%)	Females N(%)	Males N(%)	Females N(%)	Males N(%)	Females N(%)	Males N(%)	Females N(%)	Males	Females	Males	Females
Positive	23 (67.6)	11 (32.4)	18 (58.1)	13 (41.9)	16 (59.3)	11 (40.7)	12 (52.2)	11 (47.8)	15 (62.5)	9 (37.5)	13 (61.9)	8 (38.1)
	34(16.0)		**31(16.2)**		**27(16.2)**		**23(16.1)**		**24(17.8)**		**21(19.3)**	
Negative	108 (60.3)	71 (39.7)	94 (58.8)	66 (41.2)	81 (57.9)	59 (42.1)	79 (65.8)	41 (34.2)	65 (58.6)	46 (41.4)	54 (61.4)	34 (38.6)
	179(84.0)		**160(83.8)**		**140(83.8)**		**120(83.9)**		**110(82.2)**		**88(80.7)**	
Total	131 (61.5)	82 (38.5)	112 (58.6)	79 (41.4)	97 (58.1)	70 (41.9)	91 (63.6)	52 (36.4)	80 (59.3)	55 (40.7)	67 (61.5)	42 (38.5)

Out of the TB-HIV co-infected patients 160(**16.7**, 36(22.5%) with proportion of males 20(20.6%) to females16(25.4%), were PTB and 20**(12.5%)** with 12(12.4%) to 8(12.7) male to female proportion were EPTB, respectively. Whereas, 518(64.9%) and 263(33.0%) were seronegative PTB and Extra-PTB with 304(63.2%) to 214(67.5%) and 167(34.7%) to 96(30.3%) male to female ratios respectively (Table 6). The results were much lower than 77.3% for PTB and 22.7% for EPTB (Sebsibe and Takele, 2013).

Table 6: Distribution of PTB and EPTB among HIV seropositive and seronegative patients

HIV	Total TB patients			Pulmonary TB			Extra-pulmonary TB		
	Males N (%)	Females N (%)	Total	Males N (%)	Females N (%)	Total	Males N (%)	Females N (%)	Total
Positive	97	63	160	20	16	36	12	8	20
	60.6	39.4	16.7	20.6	25.4	**22.5**	12.4	12.7	**12.5**
Negative	481	317	798	304	214	518	167	96	263
	60.3	39.7	83.3	63.2	67.5	67.4	34.7	30.3	34.2
Total	578	380	958	324	230	554	179	104	283
	60.4	39.6	100	58.5	41.5	57.8	63.3	36.7	29.6

4.4. Smear result of pulmonary TB by HIV status

The high differences observed in the proportion of both smear-negative and smear-positive pulmonary TB by HIV-status. Out of the PTB cases 554(57.8%), 255(32.0%) and 263(33.0%) were sero-negative pulmonary smear-positive and smear-negative TB respectively. Of TB-HIV co-infected PTB patients 36(22.5%), 22(14.0%), with proportion of males 13(13.4%) to females 9 (14.3%), had Smear positive TB and followed by 14(9.0%), with males 7(7.2%) and females

7(11.1%) having 1:1 ratio, who had Smear negative TB (Table 7). The patients with SPPTB were more likely to be HIV positive than those with SNPTB. But, according to Sebsibe and Takele (2013), the greater prevalence of SNPTB (49.5%) were reported than SPPTB (27.8%).

Table 7: Prevalence of SPPTB and SNPTB among HIV seropositive and seronegative TB patients

HIV status	PTB					
	Smear positive			Smear negative		
	Males N (%)	Females N (%)	Total N (%)	Males N (%)	Females N (%)	Total N (%)
Seronegative	162(33.7)	93(29.3)	255(32.0)	142(38.2)	121(38.2)	263(33.0)
Seropositive	13(13.4)	9(14.3)	22(14.0)	7(7.2)	7(11.1)	14(9.0)
Total	175(30.3)	102(26.8)	277(28.9)	149(25.8)	128(33.7)	277(28.9)

4.5. Prevalence of MDR-TB in The Study Area from 2012-2017

In this study, 12.6% of all TB cases were MDR-TB and it was almost equivalent to MDR-TB cases of Africa and Ethiopia 16.7% for each, Kenya and South Africa 10.5% for each; but it was slightly lower than MDR-TB cases of Global 23.1%, DR Congo 19.2%, Pakistan 20.2% and far from Nigeria 29.3%, Bangladesh 30.6%, China 31.1%, Myanmar 32.1% and Somalia 55.7% in 2016 (Global TB report, 2017). 80(66.1%) of the MDR-TB cases were from the age category of 16-45 years old and followed by age groups of 46-64 with 27(22.3%), ≤15 with 8(6.6%) and ≥65 with 5.0%; and their male to female ratios of MDR-TB cases were 1.5:1, 1.7:1, 3:1 and 2:1 respectively (Table 8). This indicated that males were more affected by MDR-TB than females in each age group and the highest frequency of MDR-TB was showed in the age group of 16-45 years of TB cases.

Table 8: Prevalence of MDR-TB by age and gender distribution

Age Category	Total TB patients			MDR-TB Patients (2012-2017)			
	Male N (%)	Female N (%)	Total N (%)	Male N (%)	Female N (%)	Total N (%)	M: F ratio
≤15	70(67.3)	34(32.7)	104(10.9)	6(75.0)	2(25.0)	8(6.6)	3:1
16-45	314(59.1)	217(40.9)	531(55.4)	48(60.0)	32(40.0)	80(66.1)	1.5:1
46-64	139(58.4)	99(41.6)	238(24.8)	17(63.0)	10(37.0)	27(22.3)	1.7:1
≥65	55(64.7)	30(35.3)	85(8.9)	4(66.7)	2(33.3)	6(5.0)	2:1
Total	578(60.3)	380(39.7)	958(100)	75(13.0)	46(12.1)	121(12.6)	1.6:1

In this study, the majority of MDR-TB cases 104(65.0%) with 1.6:1 a male to female ratio were HIV seropositive and the rest 17(2.2%) were HIV seronegative TB cases with 1.4:1 a male to female ratio. The prevalence of TB-HIV co-infection in MDR-TB cases (38%) (Table 9) was higher than the prevalence in PTB (22.5%) and EPTB cases (12.5%).

Table 9: Prevalence of MDR-TB among the HIV positive and negative TB patients

HIV status	Total TB Patients			MDR-TB		
	Males N (%)	Females N (%)	Total M: F	Males N (%)	Females N (%)	Total M: F ratio
Positive	97(60.6)	63(39.4)	160(1.5:1)	65(62.5)	39(37.5)	104(65.0),1.6:1
Negative	481(60.3)	317(39.7)	798(1.5:1)	10(58.8)	7(41.2)	17(2.1),1.4:1
Total	578(60.4)	380(39.6)	958(1.5:1)	75(62.0)	46(38.0)	121(12.6),1.6:1

4.6. Treatment outcomes of TB at the study area from 2012-2017

The treatment outcomes of 958 tuberculosis cases are shown in Table 10. A successful treatment outcome (treatment completed plus cured) was achieved in 843(88.0%) of the cases in this study. Out of these, 510(60.5%), of which 308(60.4%) males and 202(39.6%) females were cured and 333(39.5%) consisting of 199(59.8%) males and 134(40.2%) females were treatment completed. Whereas, only 33 treatment defaulters (28.7%), 16 deaths (4.9%),18 treatment failures (15.7%), and 48 transferred out (41.7%) (to other clinics and health facilities) totally, 115 (12.0%) were recorded from unsuccessful treated patients.

Among the six WHO Regions, the highest TSRs in 2015 were in the 92(91%) in Western Pacific and Eastern Mediterranean Regions respectively. The lowest rates (76%) was in the Americas probably due to high levels of loss to follow-up and missing data, and the European Region (due to high rates of treatment failure and death, influenced by the high frequency of MDR-TB). Only seven of the 30 high-TB burden countries reached or exceeded a 90% treatment success rate, although the validity of treatment outcome data was not always ascertained. According to the report on TB by Setegn Eshetie *et al.*, 2018, the global TB treatment success in 2000 was 36%, but significant improvement has been reported in 2015; nearly 60%; whereas, the WHO report in 2015 claims that Ethiopia has achieved 90%, but the report indicates the validity of treatment outcome data remains in question and might not be the reflection of the reality and the report for

2016 was 83.7%. These are also the best indicators of significant improvement of the coverage and treatment success rate shown in this study; 88%.

In this study, the highest death rate 5(31.3%), failure rate 5(27.8%), and defaulter rate 9(27.3%) were recorded in the year 2012, 2013 and 2014 respectively. TB-HIV co-infection and drug resistant TB have been proposed as factors contributing to unsuccessful treatment and limited evaluation of treatment outcomes in resource-limited countries like Ethiopia were shown (Setegn Eshetie *et al*., 2018). The treatment success rates of cured and treatment completed ones among the years were within the lower range of 64(6.7%) in 2016 and 41(12.3%) in 2017 respectively; whereas, the higher ranges were 131(25.7%) in 2012 for cured and 64(19.2%) in 2014 for completed treatment (Table 10).

Table 10: Treatment outcomes of TB patients

Years		TB patients	Treatment successful		Treatment unsuccessful			
			Treatment completed	Cured	Transferred out	Defaulted	Died	Failure
2012	Male	131 (61.5)	38 (64.4)	80 (61.1)	5 (55.6)	4 (57.1)	3 (60.0)	1 (50.0)
	Female	82 (38.5)	21 (35.6)	51 (38.9)	4 (44.4)	3 (42.9)	2 (40.0)	1 (50.0)
	Total	213 (22.2)	59 (17.7)	131 (25.7)	9 (18.8)	7 (21.2)	5 (31.3)	2 (11.1)
2013	Male	112 (58.6)	36 (57.1)	61 (59.2)	7 (63.6)	3 (50.0)	2 (66.7)	3 (60.0)
	Female	79 (41.4)	27 (42.9)	42 (40.8)	4 (36.4)	3 (50.0)	1 (33.3)	2 (40.0)
	Total	191 (19.9)	63 (18.9)	103 (20.2)	11 (22.9)	6 (18.2)	3 (18.8)	5 (27.8)
2014	Male	97 (58.1)	44 (68.8)	41 (53.9)	5 (50.0)	3 (33.3)	2 (50)	2 (50)
	Female	70 (41.9)	20 (31.2)	35 (46.1)	5 (50.0)	6 (66.7)	2 (50)	2 (50)
	Total	167 (17.4)	64 (19.2)	76 (14.9)	10 (20.8)	9 (27.3)	4 (25.0)	4 (22.2)
2015	Male	91 (63.6)	31 (58.5)	52 (65.8)	5 (83.3)	2 (100.0)	0 (0.0)	1 (50)
	Female	52 (36.4)	22 (41.5)	27 (34.2)	1 (16.7)	0 (0.0)	1 (100)	1 (50)
	Total	143 (14.9)	53 (15.9)	79 (15.5)	6 (12.5)	2 (6.1)	1 (6.3)	2 (11.1)
2016	Male	80 (59.2)	28 (52.8)	39 (60.9)	6 (66.7)	3 (75.0)	2 (100)	2 (66.7)
	Female	55 (40.7)	25 (47.2)	25 (39.1)	3 (33.3)	1 (25.0)	0 (0.0)	1 (33.3)
	Total	135 (14.1)	53 (15.9)	64 (6.7)	9 (18.8)	4 (12.1)	2 (12.5)	3 (16.7)
2017	Male	67 (61.5)	22 (53.7)	35 (61.4)	3 (100)	3 (60.0)	1 (100)	2 (50)
	Female	42 (38.5)	19 (46.3)	22 (38.6)	0 (0.0)	2 (40.0)	0 (0.0)	2 (50)
	Total	109 (11.5)	41 (12.3)	57 (11.2)	3 (6.3)	5 (15.2)	1 (6.3)	2 (11.1)
Total	Male	578 (60.3)	199 (59.8)	308 (60.4)	31 (64.6)	18 (54.5)	10 (62.5)	11 (61.1)
	Female	380 (39.7)	134 (40.2)	202 (39.6)	17 (35.4)	15 (45.5)	6 (37.5)	7 (38.9)
	Total	958 (100)	333 (39.5)	510 (60.5)	48 (41.7)	33 (28.7)	16 (3.9)	18 (15.7)
		Successful =843 (88.0)			Unsuccessful =115 (12.0)			

The TSR of TB cases at BMH was evaluated in terms of the national and global target (Table 11). Accordingly, the treatment success was 88% which was similar to 82-92 success that included Oromo(83%), Benshangul and S. Region(88%), Gambella(89%), Amara(84%), Afar(92%) in 2011(FMOH, 2014) and South-East Asia Region(88%), Ethiopia(89%), Rwanda and Somalia(85%), Sudan(82%), Eastern Mediterranean Region(91%), Western Pacific Region(92%) and Global(86%) in 2013 (Global TB report, 2015), but slightly greater than the 72%79% success recorded at some sampling sites in various regions like Addis Ababa(72%), Tigray(79%) in 2011 and South Africa(78%), Region of the Americas(75%), European Region(76%) and African Region(79%) in 2013 (Table 11).

Table 11: Trends of TSR of TB from the study area to national and global levels

Study area	Study period	TSR (%)	Sources
Boru Meda	2017	88	**This study**
Benshangul	2011	88	FMoH, 2014
S. Region	2011	88	
Gambella	2011	89	
Addis Ababa	2011	72	
Afar	2011	92	
Amhara	2011	84	
Oromia	2011	83	
Tigray	2011	79	
Somalia	2011	85	
Ethiopia	2013	89	Global TB report, 2015
Ethiopia	2003-2016	83.7	Setegn Eshetie *et al*., 2018
Rwanda	2013	85	Global TB report, 2015
Sudan	2013	82	
South Africa	2013	78	
Eastern Mediterranean Region	2013	91	
Region of the Americas	2013	75	
European Region	2013	76	
African Region	2013	79	
Western Pacific Region	2013	92	
South-East Asia Region	2013	88	
Global	2013	86	

The average national treatment success of TB from 2003-2016 was 83.7% (Setegn Eshetie *et al*.,2018) and it was improved to 91% in 2017 (Daniel Gemechu Datiko *et al*., 2017). But, the Global TB report estimated the Ethiopian treatment success at 87%, in comparison to the global success of 83% in 2015 (Global TB report, 2017). This showed that the TSR among patients in this study was in better improvement. This might be due to the measures being taken in the implementation of DOTS and increasing efforts made in the screening of TB patients for HIV

and imitation of antiretroviral therapy. But, the achievement of TSR should be further improved by accelerated monitoring and close follow up against defaulter patients from the site and transfer out.

4.7. Treatment outcome by HIV status

The TSR of TB-HIV co-infection at BMH was shown in Table 12. Treatment result were obtained from 798(83.3) HIV seronegative and 160(16.7) seropositive TB patients. Among all HIV seropositive cases, 83.1% were successfully treated, of which 78(48.8) were cured and 55(34.4) were treatment completed; 16.9% were unsuccessfully treated, of which 5(3.1) were failed, 9(5.6) were transferred out, 8(5.0) were defaulted and 11(1.5) were died. Whereas, among HIV seronegative cases, 89% were successfully treated, of which 432(54.1) were cured and 278(34.8) were treatment completed; 11% were unsuccessfully treated, of which 13(1.6) were failed, 39(4.9) were transferred out, 25(3.1) were defaulted and 5(3.1) were died. This showed that the HIV seropositive status was associated with a higher frequency of default, failure, transfer out and die cases; i.e., the higher treatment failure rate 16.9% from HIV-seropositive patients was shown than treatment failure rate of seronegative TB patients (11%) (Table 12). The TSR of TB/HIV co-infection in this study (83.1%) was much higher and improved than the 2013 treatment successes of different countries and WHO regions like Ethiopia %, Rwanda 76%, South Sudan 62%, South Africa 76%, Eastern Mediterranean Region 60%, Region of the Americans 53%, European Region 47%, African Region 70%, Western Pacific Region 73%, South-East Asia Region 74% and Global 69% (Global TB report, 2015).

Table 12: Treatment outcomes of HIV seronegtive and seropositive

Treatment Responses	Total TB patients					
	HIV$^+$			**HIV-**		
	Male N (%)	Female N (%)	Total (M: F)	Male N (%)	Female N (%)	Total (M: F)
Treatment completed	37(67.3)	18(32.7)	55(34.4),**2.1:1**	162(58.3)	116(41.7)	278(34.8),**1.4:1**
Cured	47(60.3)	31(39.7)	78(48.8),1.5:1	261(60.4)	171(39.6)	432(54.1),1.5:1
Failed	4(80.0)	1(20.0)	5(3.1),4:1	11(84.6)	2(15.4)	13(1.6),5.5:1
Transferred out	3(33.3)	6(66.7)	9(5.6),1:2	28(71.8)	11(28.2)	39(4.9),2.5:1
Defaulted	4(50.0)	4(50.0)	8(5.0),1:1	13(52.0)	12(48)	25(3.1),1.1:1
Died	2(40.0)	3(60.0)	5(3.1),1:1.5	6(54.5)	5(45.5)	11(1.5),1.2:1
Total	97(60.6)	63(39.4)	160(16.7),1.5:1	481(60.3)	317(39.7)	798(83.3),1.5:1
Treatment Success			83.1%	Treatment Success		89%
Unsuccessful Treatment			16.9%	Unsuccessful Treatment		11%

Note: N=number M: F=male to female ratio HIV$^+$ =HIV seropositive HIV$^-$ =HIV seronegative

The TSR of seropositive PTB in this study was three forth (75%) of unsuccessful treatment of seropositive PTB (25%); whereas, TSR of seronegative PTB was (89%) and (11%) was unsuccessful treatment of seronegative PTB. The treatment success and unsuccessful treatment of seronegative and seropositive PTB and EPTB were almost proportional with 1:1 ratio respectively; i.e. the ratio of treatment success of seropositive PTB to seropositive EPTB is 75%:75% or (1:1) and the same is true for the ratio of seronegative PTB seronegative EPTB 89%:89.7% or 1:1. Whereas, the ratio of unsuccessful treatment of seropositive PTB to seropositive EPTB was 25%:25% or (1:1) and the same was true for the ratio of unsuccessful treatment of seronegative PTB to seronegative EPTB 11%:10.3% or 1:1 (Table 14).

Table 13: Treatment outcomes of seronegative and seropositive TB among PTB and EPTB patients

Treatment Responses	PTB				EPTB			
	HIV^+ N (%)		HIV^- N (%)		HIV^+ N (%)		HIV^- N (%)	
	Male	Female	Male	Female	Male	Female	Male	Female
Treatment completed	5(62.5)	3(37.5)	92(56.8)	70(43.2)	3(60.0)	2(40.0)	67(60.4)	44(39.6)
Cured	11(57.9)	8(42.1)	170(56.9)	129(43.1)	6(60.0)	4(40.0)	86(68.8)	39(31.2)
Failed	1(100)	0(0.0)	9(100)	0(0.0)	1(100)	0(0.0)	2(66.7)	1(33.3)
Transferred out	1(75.0)	3(25.0)	17(63.0)	10(37.0)	0(0.0)	2(100)	9(90.0)	1(10.0)
Defaulted	1(33.3)	2(66.7)	10(90.9)	1(9.1)	2(100)	0(0.0)	3(21.4)	11(78.6)
Died	19(100)	0(0.0)	6(60.0)	4(40.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Total TB patients	20(6.2)	16(44.4)	304(58.7)	214(41.3)	12(60.0)	8(40.0)	167(63.5)	96(36.5)
Total	36(6.5%)		518(93.5%)		20(7.1%)		263(92.9%)	
T/Success	27=75%		461=89%		15=75%		236=89.7%	
T/Unsuccessful	9=25%		51=11%		5=25%		27=10.3%	

Note: HIV^+ =HIV seropositive HIV^- =HIV seronegative PTB= pulmonary tuberculosis EPTB =extra-pulmonary tuberculosis

The successful treatment among smear-negative HIV seropositive patients was 11(78.6) and 16(72.7) among smear-positive HIV seropositive TB patients. In this study, sputum smear positive HIV seropositive TB patients (27.3%) had a higher probability of unsuccessful treatment than smear-negative HIV seropositive TB patients (21.4%). The successful treatment among smear-negative HIV seronegative patients was also 229(87.1) and 232(91.0) among smear positive HIV seronegative TB patients. Sputum smear-negative seronegative TB patients (12.9%) had a high probability of unsuccessful treatment than smear-positive HIV seronegative TB patients (9.0%) (Table 15).

Table 14: Treatment success by HIV serostatus and sputum smearstatus

Smear	HIV **serostatus**	Treatment outcome		Total, N (%)
		Unsuccessful, N (%)	Successful, N (%)	
Negative	Negative	34(12.9)	229(87.1)	263(94.9)
	Positive	3(21.4)	11(78.6)	14(5.1)
	Total	37(13.4)	240(86.6)	277(50.0)
Positive	Negative	23(9.0)	232(91.0)	255(92.1)
	Positive	6(27.3)	16(72.7)	22(7.9)
	Total	29(10.5)	248(89.5)	277(50.0)

As the data indicated in Table 16, the treatment success of MDR-TB with seropositive TB patients was 87.5% with 47.1% cured and 40.4% treatment completed patients. Unsuccessful treatment 12.5% also was due to 3.8% deaths, 2.9% treatment failures, defaulters and transfer outs for each. Among MDR-TB seronegative TB patients, 76.5% was successfully treated with 47.1% cured and 29.4% completed treatment; and unsuccessful treatment was 23.5% with 5.9% deaths and treatment failures for each, 0% defaulters and 11.8% transfer outs. The total treatment success of MDR-TB was 86% and 14% unsuccessfully treated. In the 2014 cohort, the treatment success rate was highest in the WHO Eastern Mediterranean Region (65%) and lowest in the WHO Region of the Americas (46%) (Global TB report, 2017) and still, the treatment success of MDR-TB in this study remained very high 86%. In contrast, this report showed that the treatment failure was highest in the WHO European Region (13%), and the death rate was highest in the WHO African and South-East Asia regions (20%) and Loss to defaulters was highest in the WHO Region of the Americas (21%) (Global TB report, 2017) and relatively these items were lowered in this study (Table 16). This might be due to the presence of high effort.

Table 15: Treatment outcomes of MDR-TB patients

Treatment Responses	MDR-TB					
	HIV^+ N (%)			HIV^- N (%)		
	Male	Female	Total	Male	Female	Total
Treatment completed	29(69.0)	13(31.0)	42(40.4)	3(60.0)	2(40.0)	5(29.4)
Cured	30(61.2)	19(38.8)	49(47.1)	5(62.5)	3(37.5)	8(47.1)
Failed	2(66.7)	1(33.3)	3(2.9)	0(0.0)	1(100)	1(5.9)
Transferred out	2(66.7)	1(33.3)	3(2.9)	2(100)	0(0.0)	2(11.8)
Defaulted	1(33.3)	2(66.7)	3(2.9)	0(0.0)	0(0.0)	0(0.0)
Died	1(25.0)	3(75.0)	4(3.8)	0(0.0)	1(100)	1(5.9)
Total TB patients	65(62.5)	39(37.5)	104(86.0)	10(58.8)	7(41.2)	17(14.0)
Successful Treatment			87.5%	Successful Treatment		76.5%
Unsuccessful Treatment			12.5%	Unsuccessful Treatment		23.5%
Total treatment success (104) =86% and unsuccessful treatment (17) =14%						

Note: HIV^+ = HIV seropositive, HIV^- =HIV seronegative, MDR-TB=Multidrug resistance TB

The TSR of MDR-TB case at BMH (86%) was shown comparatively with the 2013 national and global targets. Accordingly, the treatment success was 86% which was nearly similar to Ethiopia 83% and Rwanda 98% success and highly greater than the 48%-62% success recorded at some sampling countries including Sudan 62%, South Africa 49%, South-East Asia Region 48%, Eastern Mediterranean Region 65%, Region of the Americas 57%, European Region 49%, African Region 53%, Western Pacific Region 51% and Global 50% (Global TB report 2015). Treatment success in 2014 was also less than 50% in China, India, Peru, the Philippines and Ukraine, due to high death rates 21% in India and Ukraine (17%), high rates of treatment failure in Ukraine (18%) and loss to follow-up or missing data (Global TB report, 2017). From the same report, by 2016, 35 countries, mostly in Africa and Asia, reported having used shorter MDR-TB regimens and achieved high treatment success rates (87–90%) in selected MDR-TB patients and a standardized shorter MDR-TB regimen is recommended by WHO subject to eligibility criteria (Global TB report, 2017).

4.8. Limitation of the study

The study was limited to secondary data from recorded documents in the hospital between 20122017 about trends in prevalence of TB and TB/HIV co-infections. Also, some demographic characteristics were not being completely filled on the registration books while it is filling by technicians; shortage of related studies in the area and there was shortage of time encountered by investigator.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion

In this study, among 958 TB patients registered in the last six years at Boru Meda Hospital between January 2012 and December 2017, 57.8% cases were PTB, 29.6% EPTB and 12.6% were MDR-TB patients. The highest prevalence rate of TB was registered in the year 2012 and the lowest was in 2017 which showed a declined trend. New cases were 85.5% and 14.5% were previously treated TB patients. The (CDR), 32.2% was much lower than the data obtained from Global TB report 2015.

All TB patients were tested for HIV infection and 16.7% were seropositive patients. The trend in prevalence of TB-HIV co-infection increased from year to year. The prevalence of MDR-TB was 12.6%, almost equivalent to MDR-TB cases of Africa and Ethiopia in 2016; but, slightly lower than international MDR-TB cases. The study indicated that males were more affected TB, TBHIV co-infection and MDR-TB in each age group and the highest frequency of these diseases were showed in the age group of 16-45 years.

Improvement of treatment success was shown in this study (88.0%). TB-HIV co-infection and drug resistant TB have been proposed as factors contributing to unsuccessful treatment and limited evaluation of treatment outcomes. The treatment success of MDR-TB was 86%.

5.2 Recommendation

Based on the findings of this study the researcher suggests the following recommendations:

1. The case detection rate (32.2%) was much lower. Hence, some measures on poor quality of diagnosis and co-existence of TB-HIV co-infection should be taken to reach at the next reference point of CDR (82.3%) in 2020.
2. So, the student researcher recommended the hospital to have modern documentation system with full history of patients.
3. Residence, marital status, educational back grounds, CD4 of patients and others factors associated with TB, TB-HIV co-infection and MDR-TB were not identified in this study. Therefore, they need further investigation.
4. Prevalence of TB-HIV coinfection showed an increasing trend from year to year and it is recommended that high attention and collaborative activities could be taken to create awareness on associated factors, ways of transmission and prevention of the disease in the study area.

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7. Declaration

I, the undersigned, declare that this Thesis is my original work and all source materials used are duly acknowledged.

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8. Statement of supervisor(s)

This Thesis has been approved for submission to the Department of Zoological Sciences for public defense.

Name Hassen Mamo (PhD)

Signature_____ Date_____