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MADDA WALABU UNIVERSITY

COLLEGE OF NATURAL AND

COMPUTATIONAL SCIENCES

DEPARTMENT OF BIOLOGY

RETROSPECTIVE ANALYSIS OF TRENDS OF TB AND TB-HIV COINFECTIONS AMONG PATIENTS AT BATU SHER HOSPITAL AND HEALTH CENTER FROM 2014-2019

BY

TESFAYE DABI

June 2021

Bale Robe, Ethiopia

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A THESIS SUBMITTED TO THE DEPARTMENT OF BIOLOGY, COLLEGE OF NATURAL AND COMPUTATIONAL SCIENCES, MADDA WALABU UNIVERSITY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN BIOLOGY.

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APPROVED BY EXAMINING BOARD:

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Internal-Examiner	_____	_____

Declaration

I declared that this thesis is a result of my research investigation and findings. Source of information other than my own have been acknowledged and reference list has been appended. This work has not been previously submitted to other university for award of academic degree. I have followed all ethical principles of scholarship in the preparation, data collection, data analysis and completion of this thesis.

Name: Tesfaye dabi Edeo

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Date of Submission: _____

Advisor approval sheet

This is to certify that the thesis entitled "RETROSPECTIVE ANALYSIS TRENDS OF TB AND TB-HIVCOINFECTED AMONG PATIENTS DIAGNOSED AT BATU SHER HOSPITAL AND HEALTH CENTER FROM 2014-2019" submitted in partial fulfillment for the Degree of Master of science in Biology has been carried out by Tesfaye Dabi Edao under my supervision.I recommended that the student has fulfilled the requirments and hence there by can submit to the thesis to the department for defence .

Name of Advisor: Diriba Temesgen (PhD)

Signature _____

Date_____

Examiner approval sheet of the thesis

As members of the board of examiners of the final master's degree open defense, we certify that we read and evaluated the thesis prepared by Tesfaye Dabi Edao entitled "RETROSPECTIVE ANALYSIS TRENDS OF TB AND TB-HIVCOINFECTED AMONG PATIENTS DIAGNOSED AT BATU SHER HOSPITAL AND HEALTH CENTER FROM 2014-2019" and I recommended that the thesis has been accepted in partial fullfilment of the requirements for the Degree of Master of science in Biology.

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List of Abbreviations and Acronyms

ACSM Advocacy Communication and Social Mobilization.

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AFB Acid-fast bacilli.

ART Anti-retroviral treatment.

ARV Anti-retroviral.

CSA Central Statistics Authority.

CDCP Centres for Disease Control and Prevention

CD4 Cluster differentiation-4

CPT Cotrimoxazole prophylactic therapy

DST Drug sensitivity testing.

DOTs Directly observed therapy

EHNRI Ethiopian Health and Nutrition Research Institute.

FMOH Federal Ministry of Health.

FDRE Federal democratic and republic of Ethiopia.

HMIS Health Management Information System

HAART Highly active antiretroviral treatment.

HIV Human immunodeficiency virus.

IPT Isoniazid Preventive Therapy.

ISDI International Site Development Initiative

ISN Individual Survey Number.

IGAD Intergovernmental authority on development

IUATLD International Union against TB and Lung Disease.

MDR Multi drug resistance

PLHIV People living with HIV.

PTB+ Smear-positive pulmonary TB.

NTLCP National Tuberculosis and leprosy control programme.

TB Tuberculosis.

UNAIDS United Nations Programme on HIV/ AIDS.

USAID United States Agency for International Development

WHO World Health Organization.

Abstract

Tuberculosis (TB) is an illness that is caused by a bacterium known as *Mycobacterium Tuberclosis* and mainly affects the lungs, but sometimes can affect other parts of the body . An alarming epidemic is far-reaching across the developing world aggravated by coinfection with HIV. This study was based on a health retrospective analysis of TB, and TB/HIV co-infection cases and TB treatment outcome from outpatients at Batu Sher hospital and Health Center, Oromia Regional State, Southern Ethiopia from 2014 until 2019, a total of 808 TB cases were recorded over the study period: 51.36% males and most affected age group were 25-34 years. TB infection and TB/HIV co-infection had shown slight falls and rises over the study period and recorded cases in 2019 were higher or equal to that of 2014 that necessitate to much effort to reduce infection. The overall treatment success was found to be 74.4% for TB patients during treatment and 66.4% for TB/HIV co infection during treatment which was closer to target set by WHO (2015). ART coverage of the study was 52.57%, which is lower than 100% targeted by WHO, (2015). More attention should be given and appropriate measures should be taken to reduce the infection of TB and TB/HIV co-infection, to further improve treatment success and ART coverage.

Key words: ART coverage, *Mycobacterium tuberculosis* treatment outcome, trend.

1. INTRODUCTION

1.1 Background of the study

Tuberculosis (TB) is an ancient infectious disease caused primarily by *Mycobacterium tuberculosis,* Van Soolomgen (2001).Despite that TB burden has been declined in the past 20 years in the globe, currently TB is the leading cause of death from single infectious agent above HIV/AIDS. Globally in 2018, there were an estimated 10 million incident TB cases, 1.5 million deaths from TB, and 0.5 million people with drug resistant TB. In addition, 8.6% of TB cases in the world were living with HIV, of whom 72% were in Africa, WHO (2019).

TB and HIV co-infections are associated with special diagnostic and therapeutic challenges and constitute a huge burden on the healthcare systems of developing countries such as Ethiopia.(FMOH, 2021). A person infected with M. Tuberculosis has a 10% risk of developing TB disease during their lifetime, but for people co-infected with both M. tuberculosis and HIV, the annual risk of developing active TB disease exceeds 10%(Macperson et al, 2020). The complication of treatment outcomes of both diseases due to the TB/HIV co-infection results particularly from the concomitant use of anti-retroviral treatment (ART) and the intensive phase of TB treatment; in addition, it leads to drug–drug interactions, side effects of multiple drugs, increased pill burden, decreased adherence, and the development of higher rates of drug-resistant organisms because of the combination of these factors.

Ethiopia, a country with population size of 109 millionsis among the 30 high burden countries for TB, TB/HIV and MDR-TB. By 2018, the estimated total TB incident, notified TB cases and TB mortality in Ethiopia was 165,000, 114,233 and 24,000, respectively (CSA and ICF, 2018) Ethiopia is one of the developing countries with a high burden of TB/HIV co-infections. An Ethiopia National TB/HIV Sentinel Surveillance report showed that the prevalence of HIV among TB patients was 20%.(FMOH, 2011-2012)Although both TB and HIV infections are preventable, the global burden of TB has increased since the epidemic of HIV/AIDS as it increases both new TB infections and latent TB, causing active TB as a result of compromised immunity in HIV/AIDS patients(Corbett EL, 2011-2012). The mortality and morbidity of patients with this co-infection is also high compared to isolated infections with TB or HIV.(Merce, 2018).

Among the main indicators for TB program performance are TB case finding, notification, and treatment outcome (FMOH, 2017). There, this study was designed to analyze trends of TB and Tb-HIV coinfections among patients at Sher Hospital and Batu Health Center from 2014-2019" so that can provide important information to design and take appropriate measures against the spread of the infections.

1.2. Statement of the Problem

The problem of HIV and TB has greatly affected the whole world economically, as the government has to develop many programs to fight the spread of the disease. The impact of HIV on TB differs according to different countries, depending on the total population of HIV/AIDS has greatly uplifted the TB statistics. Though anti-retroviral therapy is used in certain cases, the use of condoms and education continues – this problem still exists and appears to be increasing gradually.

Tuberculosis (TB) is a leading killer among people living with human immunodeficiency virus (HIV). At least one in four deaths among people living with HIV can be attributed to TB, and many of these deaths occur in resource-limited settings, WHO (2014).

Ethiopia has adopted the WHO Stop TB strategy, which is reflected in Ethiopia's various policy documents and many implementation guidelines, for example: HSDP IV, the National TB and Leprosy Strategic Plan 2011-2015 and the TB/Leprosy, MDR TB(Multi Drug Resistant Tuberculosis) MTB(*Mycobacterium Tuberculosis*),TB/HIV, DOTS(Directly Observed Therapy, Short-course) Community-based TB Care implementation, and TB infection control guidelines, WHO (2015).

TB treatment has different outcomes TB and HIV confection can have different trends in different countries or regions in a country which should be elucidated via scientific research. Such studies have been carried out in different countries and some regions of Ethiopia. Accordingly, Getahun et al (2013) reported 18.1% cure and 64.4% completed treatment for TB patients in enrolled in DOTS program in government owned health centres over the course of five consecutive years in Addis Ababa. Endris et al (2014) indicated 417 TB patients were registered at DOTS clinic of Enfraz Health Center (Northwest Ethiopia) of which 17 were transferred and 379 (94.8%) of the remaining 400 TB patients had successful treatment outcome (302 treatment completed and 77 cured).

The authors also added that the TB-HIV confection was 24/206 (11.7%). Ayele and Nenko (2015) investigated the treatment outcomes of 3722 patients at four selected health facilities of Gedeo Zone, Southern Ethiopia from September 2009 to August 2014 and reported 1042 (28%) cured, 1431(38.45%), treatment completed, 197 treatment defaulters (5.29%), 161 deaths (4.33%), 12 treatment failures (0.32%) and 879 cases transferred out (23.62%) to other health facilities. Wondale et al (2017) reported increase in some years and decreases in other years in number of TB patients with over all 154 (13.1) cured and 714 (60.9) treatment completed patients from 1172 TB patients registered at at Jinka General Hospital, southern Ethiopia, from July 2004– June 2014. Alemu and Gutema (2019) reported a decline in the magnitude of TB from 2012 to 2014, a rise in 2015 but again a decline in 2016 in Awi Zone,

Northwest Ethiopia based on data obtained from Awi Zonal Health Department Health Management Information System (HMIS) database and TB program unit. Fentie et al (2020) reported 11.9% HIV positive, 238(67.6%) complete treatment, and 95(27%) cure among 352 patients with tuberculosis registered at public primary healthcare facility in Addis Ababa (central Ethiopia) from July 2014 to July 2018.

The studies showed irregularities in the number of TB patients registered at the health facilities in most cases with various treatment outcomes that could be associated with some factors that need to be carefully investigated.

As no study was conducted in retrospective analysis of trends of TB and Tb-HIV coinfections among patients at Batu Sher Hospital and Health Center, these study was initiated to analyze these from 2014-2019 at the study area

1.3. Objectives of the study

1.3.1. General objective of the study

- ✓ To investigate the trends of TB infection, TB/HIV co-infection and treatment outcomes among patients diagnosed at Batu Hospital and health centre from 2014 - 2019

1.3.2. Specific objectives of the study

- ✓ To determine the yearly TB infection, TB/HIV co-infection with respect to age and sex and TB treatment outcomes among TB patients registered at Batu Sher Hospital and Health center from 2014 - 2019
- ✓ To determine the trends of TB and TB/HIV co-infections among patients diagnosed at Batu Sher Hospital and Health center from 2014 - 2019

1.4. The scope of the study

The research focused only on retrospective analysis of prevalence HIV and TB among patients diagnosed at Batu Town Administration Sher Hospital and Health centre, which is found in East Shewa Zone, Oromia Regional State from 2014 - 2019.

1.5. Limitation of the study

Time constraint, uncooperativeness of some office members during collecting the recorded data from source documents, Due COVID-19 prevalence it was difficult to get hard copy and soft copy of recorded documents and identify clearly the patient's profile, member of Batu Hospital and health centre officers were always too busy. Even though different efforts were made, there were faced some challenges while doing this study. Furthermore, some were not as such willing to give or to explain the patients' document.

1.6. Significance of the study

The significance of this study laid in its ability to show the actual representation of retrospective level of TB and HIV patients in the year of 2014-2019 in East Shewa Zone

specifically, Batu Town Administration Sher Hospital and Health centres. It may provide important information to the national and local policy makers and program designers so that they would further revise and develop appropriate programs. Furthermore, this study would also enhance in motivating different researchers to conduct similar studies serving as baseline.

2. LITERATURE REVIEW

2.1 The Global TB situation

Of the 10 million people estimated to have developed TB in 2019, 7.1 million (71%) were identified and reported to national TB programs around the world, leaving a gap of 2.9 million people (29%). These missing people with TB include those who were diagnosed with TB, but were not reported to public health authorities, (including those not reported from the private sector) and those who were not diagnosed and therefore not treated. This pool also includes patients with drug -susceptible or drug-resistant TB, using current definitions. However, a greater proportion of people with drug resistant TB are missing: of the estimated 500,000 people with rifampicin resistant/multidrug-resistant TB (RR/MDR-TB), only 206, 030 (41%) were identified, as a result of inadequate testing for drug susceptibility especially among new people with TB. In 2019, only 57% of people identified to have pulmonary TB were bacteriologically confirmed, and of those who were bacteriologically confirmed, only 61% were tested for RR/MDR-TB, comprising 59% of people not previously treated for TB and 81% of those who had previously been treated for the disease. Whilst 206, 030 people with MDR/RR-TB were detected and notified in 2019, (a 10% increase from 186, 883 in 2018), only 177,099 people were enrolled in treatment, comprising only 38% of the estimated number of people who developed RR/MDR-TB in 2019.

Another important sub-group of the missing people with TB are children under 15 years of age. Tuberculosis diagnosis and treatment gaps are wider among children than adults.

There needs to be a sustained, concerted effort and universal focus on identifying and treating missing people with TB., WHO (2020) reported that a 50% drop in the number of people with TB detection could result in up to 400,000 additional TB deaths in a year. Governments of high TB endemic countries need to ensure there are rapid TB diagnostic services available in every health facility, so all people with TB can be reached. With COVID-19 causing disruption of health services, many countries have been reported to be using Gene expert machines for COVID-19 testing, and others have reassigned TB programme staff to COVID-19, causing further shortages of the already meagre TB diagnostic and treatment resources. Innovative plans are needed to maintain TB diagnostic services in the wake of the COVID-19 pandemic, Zumla et al (2020). Innovations to adapt TB diagnostic platforms to screen for both TB and COVID-19, rolling out additional machines, and investing in development of low-cost rapid diagnostic tests for both infections are important and urgently needed.

The methods used by the WHO to estimate the global burden of TB includes the use of data from national prevalence surveys; notification data adjusted by a standard factor to account for under -reporting, over - and under diagnosis; inventory studies that measure under-reporting;

and expert opinion on TB detection gaps. Prevalence surveys, more commonly than not, have shown that country estimates of prevalence have been lower than what was observed, consequently, the incidence estimates upon which the global estimates are based may be lower than what actually exists. While the methods used to estimate the burden of TB are continuously being improved, imperfections remain which may explain the relatively wide uncertainty intervals especially with country level estimates. Differences in methodological approaches for the estimation of the burden of TB have in the past led to significant differences in the estimates of the global burden of TB provided by the WHO and the Institute for Health Metrics and Evaluation that undertakes the Global Burden of Disease project, Garcıa-Basteiro et al (2018). These methodological challenges in the estimates of the global burden of TB may have significant consequences at the programmatic level in countries. National TB programs may set unrealistically high targets or appear to be setting unambitious targets if national targets are basedo n trends of TB notifications as has been proposed by some experts, Trebucq and Schoebel (2016)

To continue to address this challenge and to harmonize approaches for the estimation of the burden of TB so that disease burden estimates become more robust with a more precise estimate of the size of the TB incidence -detection gapWHO (2019).

It is also equally important to develop robust approaches and tools for the estimation of the burden of TB at sub-national level where efforts to identify people with TB are focused as has been proposed by some countries e.g., Indonesia, Parwati et al (2020).

Several interventions, many of which have been implemented to a variable degree in various settings are in place to narrow the TB incidence-detection gap and excellent reviews have been published on this subject, Reid et al (2019).

Some of the major steps that need to be taken to address the challenge of missing people with TB at the national and sub-national level in countries include the identification of TB at risk populations to be targeted to actively find people with TB, the use of highly sensitive methods for TB screening and specific TB diagnostic tests (e.g. Expert MTB/RIF), linkage to care and treatment of all people identified to have active TB, measures to ensure retention in care and adherence to treatment, engagement with communities, development of strong partnerships with the non-state health sector and ensuring that TB is an integral component of evolving universal health care programs. Cascade analysis at all levels of the national TB program is an effective way of identifying bottlenecks in the pathway to care, treatment and cure of TB, Subbaraman et al (2019).

The misalignment of TB services with the places where people seek health care may be a significant impediment to detection of people with TB. Alignment of health services would be

useful, not only for TB but for more efficient provision of health care services in general. Ensuring that a large proportion of the targeted population is reached with TB screening and diagnostic test services that is sustained over time has been documented to reduce the incidence of TB in diverse settings, Marks et al (2019). Such approaches need to be adopted and scaled up in each country to ramp up TB detection efforts and to narrow the TB incidence-notification gap

2.2 The challenge of TB treatment outcomes

The 2020 WHO global TB report contains data on the treatment outcomes of people treated for drug susceptible TB in 2018 and those initiated on treatment for drug resistant TB in 2017. Globally 85%, 76% and 57% of people with new and relapse TB, HIV-associated TB and MDR-TB, respectively, were treated successfully. These figures represent a sub-optimal performance. The poor treatment outcomes are driven mainly by lack of evaluation, poor linkage to treatment, death and high loss to follow-up. The underlying causes of poor treatment outcomes include un-identified or additional drug resistance, Cegielski et al (2014), inadequate support provided to people with TB to ensure high level of adherence, weak recording and reporting systems and inadequate prevention and management of advanced HIV disease including the provision of anti-retroviral treatment. Furthermore, attempts have been made in the recent past to reduce the duration of treatment in drug susceptible TB focused on the use of fluoroquinolones, however, the large clinical trials that were undertaken for this purpose failed to demonstrate efficacy for relapse free cure, Grace et al (2019).

To ensure that TB treatment is taken as prescribed, directly observed of treatment (DOT), has been a pillar of TB care and prevention athough its efficacy compared with self-administered treatment has been questioned , Volmink and Garner (2007).

However, direct observation of TB treatment ingestion may be disempowering to the person being treated in addition to imposing demands on that person and the health care system that can be difficult to cope with. An approach that is based on providing comprehensive and individualized support to people being treated for TB is more likely to be acceptable to people with TB and their families and has been associated with better treatment completion rates, Alipanah et al (2018).

Furthermore, in current digital world, new ways of supporting people on treatment, including interactive two-way mobile phone text message reminders and video assisted DOT have also been associated with good levels of treatment adherence while providing psychological support through remote counselling, Ngwatu et al (2018)

2.3 TB prevention

Recent estimates of the global burden of latently infected persons with *Mycobacterium tuberculosis* suggests that 23% (95% uncertainty interval 20-4%-26.4%) of the global population or about 1.7 billion people harbor this infection. This large pool of latently infected persons is the seedbed of future TB. It has been estimated that by 2030 and 2050, this pool of latently infected persons will generate 16.3 and 8.3 people with active TB per 100,000 populations respectively, Houben and Dodd (2016). However, with current and hopefully future diagnostic and treatment tools most if not all these episodes of TB can be prevented. A major challenge for TB prevention currently is that there are no easily deployable tools that can identify the subset of latently infected persons who are likely to progress to active TB. While some bio-signatures offer this potential, Sumner et al (2019) none has been developed to a state that can be used to support programs intended to deliver targeted TB preventive therapy.

The development of new regimens that are shorter and equally effective such as a weekly dose of rifapentine and isoniazid for 3 months (3HP), a daily dose of rifampicin plus isoniazid for 3 months (3HR), a daily dose of rifapentine plus isoniazid for 1 month (1HP), a daily dose of rifampicin for 4 months (4R), Swindells et al (2019) and WHO (2020) appeared to have helped to advance implementation of TB preventive therapy at the country level.

Preventing future TB must not just be focused on finding and treating people with TB but should also include efforts to address social and other determinants of the disease. While efforts are being made to actively find people with TB and to provide TB preventive therapy, governments must ensure that the expansion of economies continues in this COVID-19 era, WHO (2020) and percolate to all segments of the populations in every nation. The major drivers of TB – undernutrition, poverty, diabetes, tobacco smoking, and household air pollution, must be addressed if the world is to expect to end TB as a public health threat by 2035, Lee et al, (2020) and Noubiap et al (2019).

Moreover, Since the year 2000, WHO has projected that 54 million people have survived tuberculosis (including a large proportion of children and adolescents), Allwood et al (2020), however, these people are more likely to develop residual lung damage and recurrent tuberculosis, Allwood et al (2019) and Allwood et al (2020) and are at increased risk for all cause-mortality (standardized mortality ratios: 2.91 (95% CI 2.21-3.84), Romanowski et al (2019) compared with the general population or matched controls.

It is advisable national TB programs to incorporate post-tuberculosis health and wellbeing interventions in the package of services provided to people with TB, Chakaya et al (2016) and encourage the research community to undertake research intended to unravel the biomedical

and social determinants impacting TB survivals' long-term prognosis, Romanowski et al (2019).

The world's TB control programs were already failing to meet the ambitious goals during the past 2-3 years, largely because of systemic weaknesses. The COVID-19 pandemic and its rapid global spread, highlights the intrinsic weaknesses of health care systems. The ultimate generic issue for all communicable diseases of public health importance is that of creating a systemically strong healthcare base upon which to build disease-specific programs such as for TB

2. 4. Co existence of HIV/TB

Mycobacterium tuberculosis is an important pathogen associated with human immunodeficiency virus infection and its resulting immune suppression. (HIV) It has been estimated that persons with the acquired immunodeficiency syndrome (AIDS) have more than a 100 fold risk of developing TB compared to the general population, Corbett (2006).

HIV- infection results in an impairment of the immune system and entails a substantial risk of further contracting TB in those individuals who are or become infected with the tubercle bacillus. The association between HIV and TB was first recognized in Haitians and intravenous drug abusers. Based on available information, it is difficult to reach any conclusion on the relative infectiousness of HIV associated TB. However there is a fear that the increasing numbers of HIV-positive patients with TB will lead to increases in the transmission of TB in the rest of the population and, thereby, increase the size of the population infected with tubercle in the future. Although the transmissibility may depend on the stage of HIV-infection, it is possible that the rises in the number of TB cases in many countries will increase TB transmission both to the HIV-positive and HIV- negative populations, Maher (1999).

Tuberculosis is the single most important opportunistic disease in HIV positive individuals and presents a great challenge to clinical and preventive medicine. The HIV pandemic will be worsen the TB situation in developing countries in three ways over and above the existing situation, Sinshaw et al (2017).

a. By reactivation of a latent TB infection among dually infected persons

b. By new infection with tubercle bacilli and rapid progression to active disease in HIV infected persons; and

c. By increasing the number of cases in the general population whose infection and disease is the result of transmission from HIV positive individuals developing TB by either reactivation or recent infection. The impact of HIV-infection on the epidemiological situation of tuberculosis depends on several factors Perriens et al (1991).

-The prevalence of HIV infection in the community and its trend

-The prevalence of tuberculosis infection in the general population aged 15-49 years.

The rate of development from tuberculosis infection to active tuberculosis the level of and the trend in the annual average risk o f tuberculosis infection. The detection rate of new and relapse cases of TB and the cure rate of smear positive cases. In comparison with other types of infections associated with HIV-infection, TB appears to develop at a somewhat earlier stage in the progression from HIV infection to AIDS, Cruciani et al (2001).

2.5. Reciprocal influence of HIV and TB

2.5.1. Influence of HIV on the development of active TB

HIV promotes the progression of infection with Mycobacterium tuberculosis to active TB, both in people with recently acquired infections and those with latent infections. Undeniably, HIV is the most powerful risk factor known for activation of latent M. tuberculosis infection. For an HIV-infected person-co-infected with M. tuberculosis, the risk of developing active TB reaches 5–10% annually, instead of the 5–10% lifetime risk for an individual not infected with HIV. This discrepancy is clearly linked to the immunodeficiency caused by HIV. Furthermore, HIV infection increases the rate of recurrent TB, which can be due to either endogenous reactivation or exogenous reinfection, Lienhardt and Rodriques (1997*)*.

2.5.2. Influence of HIV on the transmission of TB

TB is one of the most common infections in HIV-infected people, especially in high TB prevalence areas. HIV greatly increases the number of TB patients, which in turn increases TB transmission from family members (the highest TB transmission risk is from household contacts, such as children and HIV-positive partners) and community members (through contact in work-places, schools and hospitals) where there is a risk of nosocomial infections from both patients (whether HIV-positive or -negative) and health care workers. Moreover, the risk of MDR-TB transmission may be increased if effective and uninterrupted TB treatment is not ensured, Girardi et al (2000*)*.

2.5.3 Influence of HIV on the clinical presentation of TB

As HIV infection progresses, CD4 lymphocytes decline by about 50–80 cells/mm3/year, and the immune system becomes less able to prevent the growth and local spread of M. tuberculosis.

Pulmonary TB (PTB) remains, especially in adults, the commonest form of TB, but its presentation depends on the degree of immune suppression. The clinical pictures, sputum-smear results and chest X-rays are often different in the early stage of HIV infection (CD4 >350 cells/mm3) and the late stage (CD4 <200 cells/mm3). The clinical presentation of TB cases in early HIV infection is similar to that of individuals without HIV infection, resembling post-primary PTB, that is, with positive sputum smears (defined as two or more initial smear

examinations that are positive for acid-fast bacilli (AFB), or one plus consistent radiographic abnormalities) and often with cavities in the chest X-ray. In contrast, the clinical presentation in late HIV cases resembles primary PTB: the sputum smear is often negative and radiological infiltrates are present instead of cavities, Ackah et al (1995).

In case of severe immunodeficiency, the rate of extra pulmonary TB (EPTB) increases in both adults and children. Because of difficulties in diagnosis, disseminated TB may account for a high proportion of misattributed hospital deaths.

2.5.4 Influence of TB on HIV morbidity and mortality

Active TB itself is responsible for a mild immune deficiency. In countries with independent epidemics of TB and HIV/AIDS, TB does not always indicate severe deterioration of the immune system in HIV-infected people because it may occur before HIV infection or in its early stages, before the immune system has deteriorated. When active TB occurs in HIV patients, a worsening of the HIV-related deficiency is commonly observed, facilitating the progression of other opportunistic infections such as Candida albicans oesophagitis, Cryptococcus meningitis and, particularly, Pneumocystis jirovecii pneumonia. Any of these opportunistic infections may be lethal. If so, TB is indirectly responsible for the death, Badri et al (2001*)*.

In addition, TB has been found directly responsible for an average mortality rate of 30% among HIV/AIDS cases in many reports Harries et al (2001). These data emphasize the need of early diagnosis and specific treatment of TB in all HIV-infected patients, especially when the clinical pattern of CD4 cells count shows a severe degree of immune deficiency

2.6. Predictors of tuberculosis among HIV positive patients on care and ART

2.6.1. Baseline socio-demographic factors and ART

Despite people on ART, they have still high rate of tuberculosis infection when compare with HIV free people. Most of the peoples Tuberculosis infections were occurred in early periods after initiation of ART, Ayalew et al (2015).

A Systematic Review and Meta-analysis done on the incidence of opportunistic (OIs) and other infections in ART-naive and -exposed people shows that tuberculosis is the second most common infections next to bacterial pneumonia in Among HIV-infected patiens in Low- and Middle income Countries with the prevalence of combined TB 17(12.36%) in ART-naive patens and combined TB type 20(8.84%)ART-exposed patients, Drouin et al (2016). In different studies, age is the most common socio-demographic significant predictor associated with early tuberculosis after initiation of ART. Being age above 5 year, Edmonds et al (2009) , age 1-5 year, Ebonyil et al (2016), age 12–35month, Anigilaje et al (2016) were associated with tuberculosis infection after initiation of ART. A

retrospective study done in Nigeria shows that being male gender was significant predictors of incident of TB, Ebonyil et al (2016).

On Univariate analysis having more than one patient in the household has an Association for the development of tuberculosis, Li et al (2013). A retrospective study done in Tanzania and Nigeria shows on multivariate analysis being male has an association form the development of tuberculosis, Li et al (2013)respectively. A retrospective study done Nigeria living in urban area has an association for the occurrence of tuberculosis among HIV positive children, Anigilaje et al (2016).

2.6.2. Clinical and laboratory factors

Declining of CD4 level of the patient is considered as predictor of incidence of tuberculosis in different studies. A Systematic Review and Meta-analysis done worldwide in low and middle income countries, Drouin et al (2016) were important predictors of time to TB occurrence. Another retrospective studies done in Tanzania, Li et al (2013) and Nigeria, Ebonyi et al (2016) were important predictors of time to TB occurrence .Advanced WHO clinical stage (III and IV) of the child is considered as predictor of incidence of tuberculosis in different studies. A retrospective studies done in Tanzania , Li et al (2013). Democratic Republic of Congo, Auld et al (2014) were important predictors of TB occurrence. Similarly institution based retrospective cohort studies conducted in northern part Ethiopia also showed that ambulatory functional status and having base line anemia, Ayalew et al (2015) were important predictors of time to TB occurrence. Furthermore a retrospective study done in Nigeria, Anigilaje et al (2016) shows past history of TB in peoples was significantly associated of development of tuberculosis.

2.6.3. ART and other medication factors

A prospective cohort study done in four Latin American countries, shows The vast majority (87.0%) of TB cases were diagnosed prior to enrolment into International Site Development Initiative (ISDI); only nine cases of TB (13.0%) were diagnosed after study enrolment. Two (2.9%) cases did not have ART start dates available, 25 (36.2%) cases of TB were diagnosed prior to the start of ART, three (4.3%) had the diagnosis of TB and ART initiation occur within three days of each other, and 39 (56.5%) cases were on ART. Eleven of the 39 cases on ART prior to TB diagnosis had been on HAART for less than three months when TB manifested itself and another five cases were diagnosed between three and six months following initiation of HIV treatment, Krauss et al (2015).

Another prospective cohort study conducted in Kenya showed that recent ART initiation remained a significant predictor for incident TB, Abuogi et al (2013). Another an institutional based retrospective cohort study done in northern part of Ethiopia in Ahmara region show

that Absence of cotrimoxazole preventive therapy and absence of isoniazid preventive therapy were an independent predictor for increased incidence of TB respectively, Alemu et al (2016). Additionally a retrospective cohort study done in northern part of Ethiopia show that Inappropriate vaccination with was an important predictors of time to TB occurrence, Ayalew et al (2015).

2.6.4. Nutritional factors

A retrospective cohort studies done in Tanzania shows severe wasting was independently associated with a higher risk of TB, Li et al (2013). A retrospective cohort studies which have been conducted in northern part of Ethiopia showed that Nutritional status underweight was associated with increased incidence of TB after initiation of ART, Alemu et al (2016).

2 .7. Clinical overview HIV/TB

The influence of HIV-infection on the clinical picture of tuberculosis appears to relate to the extent of immunodeficiency due to the HIV-infection. In patients who are markedly immune compromised, haematogenous dissemination or progressive primary TB appears to be more common. Moreover, pulmonary cavities are uncommon and granulomas in lung tissue are poorly developed, Castro et al (1992).

The increased TB incidence is mainly due to the depression of cellular immunity caused by HIV infection in subjects previously infected with tubercle bacilli, and only to an extent due to recent infections in previously uninfected subjects, or re- infections in those previously infected. However, if the current risk of TB infection is high and the annual decrease in the risk of infections is low, an excess of infectious TB cases caused by HIV may gradually increase the risk of TB infect i on in the general population. In conclusion, the current level of the risk of TB and its trend are the most decisive factors in containing the deterioration of the epidemiological situation of tuberculosis caused by HIV- infection in the future, Johnston et al (2009).

It is unclear whether HIV- associated TB is usually, the primary, reactivated type, or secondary exogenous infection but whatever the source, people infected by both HIV and mycobacterium TB have an accelerated progression to over TB. Patients with both HIV infection and TB can present in various ways but while many have the typical clinical and radiographic features of TB, most studies in Africa have noticed a change in the pattern of the disease. Most patients seem to produce no sputum, or have negative sputum smear; chest radiography may show little change, or t here may be diffuse pulmonary infiltrates without cavitations.

Extra pulmonary disease also appears to be more common. This change in disease pattern has made diagnosis of TB more difficult. The common denominator of AIDS is a profound immune suppression, predominantly of cell-mediated immunity, that leads to a variety of

opportunistic diseases, particularly certain infections. The main cause of the immune defect in AIDS is a qualitative and quantitative deficiency in the subset of T- lymphocytes termed the T, population, Perriens et al (1991).

There are two distinct but overlapping clinical patterns of tuberculosis in HIV sero-positive persons depending on when the TB develops in relation to HIV induced Immune suppression. At the early stage of HIV-infection, the clinical presentation of TB is much more classical. Colebundersetal in Kinshasa found classical TB in HIV sero positive patients, who mainly appeared to be at an early stage of HIV infection. In immune competent individuals approximately 5-15% of those infected with Mycobacterium tuberculosis will develop active TB within their life time. Of those, roughly one-third will develop TB within one year of initial, Kefale and Angaw (2017).

At least 30% of persons with previous TB infection were capable of undergoing reactivation following HIV infection. The main strategy of TB control is cure rate by early diagnosis and to improve the treatment of tuberculosis cases with primary focus on open (smear positive) cases, Peou (2010)

The interaction of HIV and mycobacterium TB include difficulties in diagnosis because of the increased numbers of smear- negative pulmonary disease, increased congestion in those countries who administer the initial intensive phase of treatment in hospital, increased coetaneous hypersensitivity reactions from thiacetazone, increased HIV-related illness during treatment, increased mortality rates and increased relapse rates after completing anti TB therapy.

2.8. TB situation in Ethiopia

Ethiopia is located in the Horn of Africa and is bordered by Kenya, Somalia, Sudan, South Sudan, Eritrea, and Djibouti. Ethiopia, a country with population size of 109 million ,is among the 30 high burden countries for TB, TB/HIV and MDR-TB. By 2018, the estimated total TB incident, notified TB cases and TB mortality in Ethiopia was 165,000, 114,233 and 24,000, respectively, CSF and ICF (2018).

The government's commitment to providing health care for the entire population is a major strength of Ethiopia's NTLP. The most recent FMOH health development plans have focused on rapidly expanding access to services. Considerable progress has been achieved in numbers of health facilities providing TB services: 156 government hospitals, 3,335 public health centers, 48 private hospitals, 222 private health facilities, 7 primary clinics, and 10,013 health posts. The FMOH has also expanded the number of medical schools from 3 to 33 in order to address the shortage of physicians, Talha (2016).

The Ethiopian government overtly acknowledges the magnitude and complexity of the country's TB problem. In addition to the HSTP, the government has a revised National Tuberculosis and Leprosy Strategic Plan 2013–2020, which is more specific—and sets more concrete targets—for TB than the HSTP. The strategic plan outlines nine strategic objectives. The Standard of Care tool introduced by the USAID-funded HEAL TB project is being used to institute a quality improvement cycle on many of these issues.

The FMOH has also committed to global TB targets such as the three pillars of the currentglobal WHO/Stop TB Partnership's End TB Strategy:

1) Integrated, patient-cantered care and prevention;

2) Bold policies and supportive systems; and

3) Intensified research and innovation, WHO (2015)

The FMOH has recently accepted WHO's End TB Strategy goal for achieving 90 percent treatment success by 2020, WHO (2015), and has made major changes to the NTLP that guides the country's national and regional TB control efforts, FMOH (2013-2020)

2.8.1. TB burden in Ethiopia

According to the WHO Global TB Report 2009 (used as background document for the development of this study protocol), Ethiopia ranked seventh in the world for TB burden and third in Africa in 2008, with an estimated TB incidence (all forms) of 378 new cases per 100,000 persons, 163 new smear positive cases per 100,000 persons, and a prevalence (all forms) of 579 per 100,000 population, Ikushi and Sismandis (2011).

Following an update to estimates for TB cases and deaths in the African Region, the most recent WHO estimates for Ethiopia are: annual TB incidence (including HIV positive) of 261 per 100,000; prevalence (including HIV positive) of 394 per 100,000 and mortality (excluding HIV) of 35 per 100,000 people Ikushi (2008).

In the year 2009/10 Ethiopia registered 146,172 cases of TB. Among these, 139,261 were new cases; 46,132 new smear-positive (33.1%); 49,037 new smear-negative (35.2%); 44,092 new extra-pulmonary TB (31.6%), Ikushi (2011).

TB is affecting all sexes and age groups. Poverty is a risk factor for developing TB, which places Ethiopia as a high-risk environment. The country is one of the least developed in the world. Among the total smear positive TB cases reported in 2009/10, 55.5% were males, 7.5% were children <14 years old, and 2% were above the age of 65. The 15 to 34 age group was found to be the one most affected with TB, accounting for 62% of notified new smear positive TB cases, Marina and, Ikushi (2011).

2.8.2. TB/HIV collaborative activities

In Ethiopia the proportion of TB patients with known HIV status is 43% and 15% of those with known HIV status are positive. Sixty-nine percent of TB and HIV co-infected patients have started cotrimoxazole prophylaxis, while 39% are on ART, Ikushi (2008).

2.8.3. Multi-Drug Resistant TB

The first Drug Resistance Survey, conducted between 2003 and 2006 showed that multi-drug resistance to TB drugs (MDR-TB) is present in 11.8% of previously treated cases and 1.6% of newly diagnosed TB cases, with an estimated 5,200 cases annually, Marina et al (2011).

The program capacity to treat MDR-TB patients is limited to two referral hospitals in Addis Ababa (St Peter & ALERT) and one in Gondar (Gondar University Hospital). At the end of February 2012, a total of 424 cases of MDR-TB patients were enrolled on treatment. The routine MDR-TB surveillance system to detect MDR-TB suspects for early diagnosis and treatment is not yet fully formed.

2.8.4. TB control strategies in Ethiopia

Ethiopia has adopted the WHO Stop TB strategy, which is reflected in Ethiopia's various policy documents and many implementation guidelines, the National TB and Leprosy Strategic Plan 2011-2015 and the TB/Leprosy, MDR TB, TB/HIV, Community-based TB Care implementation, and TB infection control guidelines. The national TB control program has currently achieved 100 percent geographical coverage and 92% of public hospitals and health centres offer DOTS, Sismandis and Timimi (2011).

The TB program emphasizes the need to increase the access of quality DOTS by expanding TB diagnostic and treatment services in line with the increasing number of public and private health facilities. The program is scaling up the access to drug sensitivity testing (DST) and MDR treatment with quality-assured drugs supplied through the Green Light Committee. TB/HIV collaborative activities are being scaled-up in health centres and hospitals to provide TB patient's access to HIV testing and HIV care including ART, and reducing TB burden in people living with HIV (PLHIV) through TB screening and scale-up of IPT.

2.9. Treatment out comes definitions

According to the standard definitions of the National Tuberculosis and Leprosy Control Program guideline (NTLCP), FDRE MoE (2012) and the WHO Definitions and reporting framework for tuberculosis 2013 revision, WHO (2013), the following treatment outcome definitions were used:

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

Died: A TB patient who dies for any reason before starting or during the course of treatment.

Extra-pulmonary TB (EPTB): This included tuberculosis of organs other than the lungs, such as lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meanings, etc. Diagnosis of EPTB was based on fine-needle aspiration cytology or biochemical analyses of cerebrospinal/pleural/ascitic fluid or histopathological examination or strong clinical evidence consistent with active extra-pulmonary tuberculosis, followed by a decision of a clinician to treat with a full course of anti-tuberculosis chemotherapy. A patient in whom both pulmonary and extra-pulmonary TB has been diagnosed should be classified as a pulmonary case.

Lost to follow-up is a TB patient who has been got treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks.

Poor treatment outcome: The sum of treatment failed, died and loss to follow up.

Successful outcome: If TB patients were cured (negative smear microscopy at the end of treatment and on at least one previous follow-up test) or completed treatment with resolution of symptoms.

Treatment completed: A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least (Tola et al, 2019) one previous occasion were negative, either because tests were not done or because results are unavailable.

Treatment failure: A TB patient whose sputum smear or culture is positive at 5 months or later during treatment. Or Patients found to harbor a multi drug resistant (MDR) strain at any point of time during the treatment, whether they are smear-negative or -positive.

Transferred out to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit

Smear-positive pulmonary TB (PTB+): A patient with at least two sputum specimens which were positive for acid-fast bacilli (AFB) by direct microscopy, or a patient with only one sputum specimen which was positive for AFB by microscopy, and chest radiographic abnormalities consistent with active pulmonary TB as determined by a clinician.

Smear-negative pulmonary TB (PTB-): A patient with symptoms suggestive of TB, with at least three sputum specimens negative for AFB by microscopy, and with chest radiographic abnormalities consistent with active pulmonary TB, and lack of clinical response to one week of broad-spectrum antibiotic therapy, or a patient whose diagnosis is based on culture-positive Tuberculosis but with three initial smear examinations negative by direct microscopy diagnosis is based on culture-positive Tuberculosis but with three initial smear examinations negative by direct microscopy.

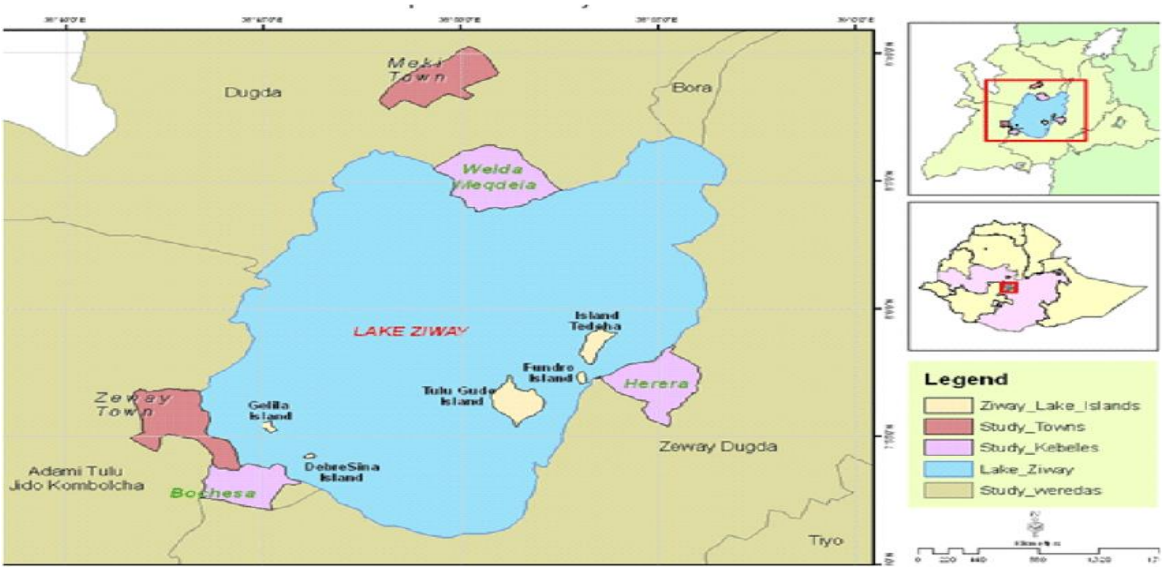
Unsuccessful treatment outcome: If treatment resulted in treatment failure (remaining smear-positive after 5 months of treatment), defaulted (patients who interrupted their treatment for two consecutive months or more after registration), or died

3. MATERIALS AND METHOD

3.1. Description of the study area

The study was conducted at Batu Sher hospital (private hospital) and health centre (Public government health centre) in the Oromia Region This study was conducted in Batu , a town found 165 kms along the main road from Addis-Ababa. Batu has a latitude and longitude of $7^0$56'N38^{0}43'E/7.933^{0}N38.717^{0}E with an elevation of 1643 meters above sea level. Based on the 2014 Census reported a total population for Batu of 43,660 of whom 22,956 were men and 20,704 were women. Batu Health centre and Sher Hospital was Institutions in Batu town that started providing ART services since 2003.

Fig: 1 Batu Town map



3.2. Study design

The study involved descriptive health institutional based retrospective study design using document analysis from TB Registry Unit of the TB to assess trend of TB and treatment outcomes at Batu health centre and Sher Ethiopia Hospital from 2014 to 2019

3.3. Study population

The population study was People those living with HIV and TB infected were enrolled to chronic HIV Care in Batu Sher Hospital and health centre from 2014 to 2019.

3.4. Data collection and tools

Data were collected from two health institutions namely Sher Hospital, and Batu Health centre; based on demographic and clinical data such as year, age, sex, type of TB and HIV status were extracted from the two institution document TB registry. The data were collected through reviewing all the necessary documents (TB treatment registry, monthly cohort form, and follow up form) of the TB patients using a pre-tested structured data extraction format which was

developed by considering the variables to be studied. The format contained all the important socio demographic, baseline clinical and laboratory, and follow up data.

3.5. Data analysis

All data were analyzed using Descriptive statistical analysis and then presented into tables and figures. Before analysis, data were entered and stored into Microsoft Excel 2007 spread sheet and was done each topic in its own sheet to minimize data entry errors. After that each data was converted to tables and figures to describe the real data that was documented from the source data General characteristics of the population were described by Number and percentages.

3.6. Ethical considerations

Ethical clearance was obtained from the School of graduate studies, Madda walabu University. Permission letter was obtained from head of Biology Department of Mada Walabu University. As this was a retrospective study, informed consent from individual patients was not requested. Since, the study was done through reviewing of medical records, the individual patients might not be subjected to harm as much as the confidentiality was kept. To keep the confidentiality all collected data were coded and locked in a separate room before entered into the computer.

4. RESULTS

4.1 Study variables among general population

4.1.1. New TB cases infection relating Ages and Gender

From 808 new TB patients documented at Batu Sher Hospital and Health centers from 2014 to 2019, males comprised of 415(51.36%) while females 393 (48.64%)(Table 1).Among these the highest New TB case group was age 15-44 which consists 382 (47.28%).The least TB patients were recorded among 0-14 years,which was 87/808 (10.77%). The highest number of infection of all new Tb cases was recorded during the study period was in 2014 and 2019 respectively.

Table 1: New TB cases infection relating Age and Gender

All new TB (PTB and EPTB) Infection		
Variables	Frequency	%
Sex		
M	415	51.36
F	393	48.64
Age		
0-14	87	10.77
15-44	382	47.28
45-64	232	28.71
>65	107	13.24
year of new PTB infection		
2014	140	17.33
2015	129	15.97
2016	136	16.83
2017	128	15.84
2018	135	16.71
2019	140	17.33

4.1.2. Pulmonary TB Positivity relating Age and Gender

Over the study period 448 patients were infected with Pulmonary TB .From these male comprised 226 (50.45%) and female comprised 222 (49.55%), from the total infection male infected more than females.Among these pulmonary TB infected patients the highest number were 223 (49.78%).These were the Age between 15-44. The TB infected groups were the age group between 0-14, which were 50 (11.6%). During these 6 study period the highest PTB infected was recorded in 2014 which were 80 (17.86%). The lowest number of TB infected was recorded in 2017 which were 71 (15.85%)

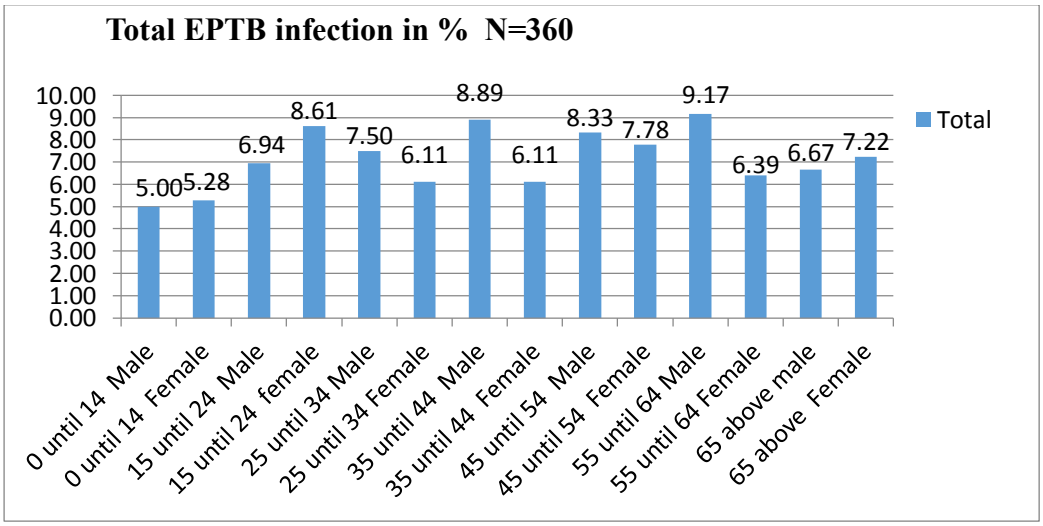
Table: 2 Pulmonary TB cases infection relating Age and Gender registered at Batu sher hospital and health center from 2014-2019

PTB infection in the study period		
Variables	Frequency	%
Sex		
M	226	50.45
F	222	49.55
Age		
0-14	50	11.16
15-44	223	49.78
45-64	118	26.34
>65	57	12.72
year of new TB infection		
2014	80	17.86
2015	74	16.52
2016	75	16.74
2017	71	15.85
2018	73	16.29
2019	75	16.74

4.1.3. Extra Pulmonary TB Positivity relating Age and gender

Three hundred sixty extra pulmonary TB (EPTB) patients documented over the study period (2014-2019) (Figure 2). EPTB male patients comprised 189/360(52.50%) compared to 171/360(47.50%) females among the overall EPTB cases registered over the study period, The highest number of EPTB (56) was recorded for 55-64 age range:33(9.17%) males . The lowest number of EPTB cases was attained by patients with in 0-14 year groups.

Fig: 2 Extra Pulmonary TB infection relating Age group and Gender



4.1.4. TB/HIV confected patients relating to Age and Gender

Total number of HIV positive TB patients registered in the reporting period were 447, male comprises 197(44.07%) and female 250(55.93%) respectively. From the table the more infected age group was the age between 15-44 which were 222 (49.66%). The lowest HIV+ group were the age between 0-14 ,which were 12 (2.68%). In the mean time the highest number of HIV + were registered in 2019 which were 82 (18.34 %.The lowest number of infection were registered in 2015 that were 64 (14.32%)

Table: 3 Number of HIV+/TB co infection patients registered in the reporting period

HIV + TB patients registered in the study period		
Variables	Frequency	%
Sex		
M	197	44.07
F	250	55.93
Age		
0-14	12	2.68
15-44	222	49.66
45-64	135	30.20
>65	78	17.45
years of new TB infection		
2014	78	17.45
2015	64	14.32
2016	74	16.55
2017	71	15.88
2018	78	17.45
2019	82	18.34

Among these total number of previously known TB patients, 235/447 (52.57%):104 (44.26%) males and 131(55.74%) were on ART during the study period. From this the highest number showed the male group. The age group 15-44 indicated the highest number on ART. The age >=65 showed the smallest number. In 2019 the more number of HIV + TB patients on ART, that were 54 (22.98%).I n 2017 low number of HIV + TB patients on ART durin the study period(Table 4)

Table 4: Number of previously known HIV positive TB (HIV/TB Co-infection) patients on ART during the reporting period

Number of previously known HIV + TB patients during on ART		
Variables	Frequency	%
Sex		
M	104	44.26
F	131	55.74
Age		
0-14	32	13.62
15-44	117	49.79
45-64	76	32.34
>65	10	4.26
years of new TB infection		
2014	39	16.60
2015	33	14.04
2016	42	17.87
2017	31	13.19
2018	36	15.32
2019	54	22.98

4.1.5. TB/HIV co-infected patient's treatment outcomes

Among the total of 447 TB/HIV co-infected patients 175(39.1%) were completed their treatment, 122(27.3%) were cured, 30(6.7%) were lost to follow up their treatment, 22(4.9%) transferred to other health institution, 39(8.7%) were got treatment failure and 59(13.2%) were died during the treatment.

The overall TB/HIV co-infection patient's successful treatments outcomes were 297/447 (66.4%). In 2018 the highest Successful treatment was recorded during the study time that was 67/91(82.7%). In 2016 the lowest treatment success outcome was scored during the study time, it was 36/61 (52.2%) (Table: 5)

Table: 5 TB/HIV co-infected patients' treatment outcomes during the study period (2014-2019).

TB/HIV Co-infected patients treatment outcomes	2014		2015		2016		2017		2018		2019		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Completed	24	38.7	27	35.1	24	34.8	30	42.9	40	49.4	30	39.0	175	39.1
Cured	14	22.6	23	39.7	12	17.4	21	30.0	27	33.3	25	32.5	122	27.3
Lost to follow-up	4	6.5	5	8.6	6	8.7	6	8.6	3	3.7	6	7.8	30	6.7
Transferred Out	2	3.2	3	5.2	4	5.8	5	7.1	4	4.9	4	5.2	22	4.9
Treatment Failure	7	11.3	6	10.3	7	10.1	8	11.4	6	7.4	5	6.5	39	8.7
Dead	10	16.1	12	20.7	8	11.6	9	12.9	11	13.6	9	11.7	59	13.2
Total	61		76		61		79		91		79		447	

4.2. PTB Treatment out comes

From 2014-2019 years The Total of PTB patients successful treatment outcome was achieved in 345 (77%) of PTB patients of which 208(46.4%) were completed treatment 137(30.6%) cured 38(8.5%) were treatment lost to follow up, 26(5.8%) were transferred to other health facilities ,12 (2.7%) were got treatment failure and 27 (6.0%) died .In 2017 and 2015 treatment outcomes that was 65 (78.31%) and 62 (73.81%) respectively was achieved higher from the rest other years (Table:6)

Table 6: Number and Average of PTB treatment outcomes

PTB treatment outcomes	2014		2015		2016		2017		2018		2019		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Completed	33	45.8	38	45.2	32	43.8	39	47.0	29	47.5	37	49.3	208	46.4
Cured	25	34.7	24	28.6	24	32.9	26	31.3	16	26.2	22	29.3	137	30.6
Lost to follow up	3	4.2	7	8.3	7	9.6	7	8.4	8	13.1	6	8.0	38	8.5
Transferred out	4	5.6	6	7.1	5	6.8	5	6.0	2	3.3	4	5.3	26	5.8
Treatment failure	2	2.8	4	4.8	1	1.4	2	2.4	2	3.3	1	1.3	12	2.7
Dead	5	6.9	5	6.0	4	5.5	4	4.8	4	6.6	5	6.7	27	6.0
Total	72		84		73		83		61		75		448	

4.3. EPTB treatment outcome

From 2014-2019 years Successful treatment outcome was achieved in 256(71.1%) Of TB patients treatment of which 159(44.2%) was completed their treatment successfully and 97(26.9%) was cured .From the total of 360 EPTB patients 104(28.9%) not achieved successfully their treatment. From these 27(7.5%) lost to follow up the treatment,32 (8.9%) transferred out to other health insititutes,20 (5.6%) were got treatment failure during the treatment and 25(6.9%) were died. (Table:7).

During these study period the highest successful EPTB treatment outcomes was recorded in 2019 that was 53/72 (76.61%) and in 2015 that was 36/58(62.06%) the lowest successful EPTB patients treatment outcomes was registered (Table:7).

Table:7 Extra Pulmonary TB cases infection treatment outcomes relating Age and Gender during the study period.

EPTB Treatment outcome	2014		2015		2016		2017		2018		2019		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Completed	27	43.5	22	37.9	24	40.7	26	48.1	27	49.1	33	45.8	159	44.2
Cured	16	25.8	14	24.1	18	30.5	15	27.8	14	25.5	20	27.8	97	26.9
Lost to follow-up	5	8.1	6	10.3	5	8.5	4	7.4	3	5.5	4	5.6	27	7.5
Transferred Out	7	11.3	7	12.1	5	8.5	4	7.4	4	7.3	5	6.9	32	8.9
Treatment Failure	3	4.8	4	6.9	3	5.1	2	3.7	4	7.3	4	5.6	20	5.6
Dead	4	6.5	5	8.6	4	6.8	3	5.6	3	5.5	6	8.3	25	6.9
Total	62		58		59		54		55		72		360	

4.4. Total treatment outcomes (PTB and EPTB)

This secondary study result showed the treatment outcomes of 808 TB patients as shown on table: 7 from consecutive 6 years. A successful treatment outcomes were seen in 601(74.4%) of the cases in the study. In the mean time 65 (8.0%) were transferred out to another health centre/hospital within or another region, 58(7.2%) were lost to follow up, 32 (4.0%) were got treatment failure and 52(6.4%) were dead.

From these 6 years in 2019 higher number of successful treatment outcomes was recorded that was 112/147 (76.2%) and the lowest EPTB treatment outcomes was recorded in 2018 that was 86/116 (74.1%)(Table:8) .

Table 8: Total treatment outcomes (PTB and EPTB) through in 6 years

Overall TB treatment out comes	2014		2015		2016		2017		2018		2019		Total	
	N	%	N	%	N	%	N	%	N	% i	N	%	N	%
Successfully treated	101	75.4	98	69.0	98	74.2	106	77.4	86	74.1	112	76.2	601	74.4
Transferred out	8	6.0	13	9.2	12	9.1	11	8.0	11	9.5	10	6.8	65	8.0
Lost to follow up	11	8.2	13	9.2	10	7.6	9	6.6	6	5.2	9	6.1	58	7.2
Treatment Failure	5	3.7	8	5.6	4	3.0	4	2.9	6	5.2	5	3.4	32	4.0
Dead	9	6.7	10	7.0	8	6.1	7	5.1	7	6.0	11	7.5	52	6.4
Total	134		142		132		137		116		147		808	

Table: 9 Associations of TB Treatment outcome and TB/HIV co-infected patients registered at Bat usher hospital and health center from 2014-2019.

From the table the female group showed more the unsuccessful than female and also the died Case also more registered in male groups.

Variables		Successful	Unsuccessful	p value	Cured	died	p value
Sex	M	216	22	0.271	94	12	0.157
	F	271	16		123	8	
Age	0-14	50	9	0.346	21	5	0.213
	15-44	287	6		126	3	
	45-64	123	6		58	2	
	≥65	27	17		12	10	
TB type	PTB	346	32	0.015	139	17	0.037
	EPTB	141	6		78	3	
HIV status	positive	10	14	0.96	3	6	0.157
	negative	477	24		214	14	
Year of treatment	2014	101	7	0.242	46	4	0.263
	2015	84	9		37	3	
	2016	71	9		29	5	
	2017	94	6		41	3	
	2018	62	4		30	2	
	2019	65	3		34	2	

5. DISCUSSION

TB is one of the chronic infections diseases which remained a significant cause of morbidity and mortality for poor nations, Davies (2003).Recently aggravated by the HIV/AIDS epidemic; this remained a major public health problem in developing countries including Ethiopia, FMOH (2009).

WHO 2012 reported treatment successes rate of TB among all new cases in 2010 from the 22 high burden countries, eight of them including Ethiopia reported lower than 85%.

Human immunodeficiency virus and Tuberculosis are a major challenge in public health in many countries. In this study the incidence of TB/HIV Co-infection among patients who were HIV positive result is 15.63%.

This result was lower than the study conducted in, Indai18.9%, Shastri et al (2013) Harar town 22.8%, Tola et al (2019) Felege Hiwot referral hospital 25%, Biadgelegn et al (2013) and Debre Tabor general hospital 24.2% , but higher than According to UNDP-S studied in Nigeria 7.8% and Tanzania 8.5% respectively, Ejeta et al (2014).

This variation may be due to the geographical and socio-demographic nature of the countries. It has been noted that tuberculosis is seen more in countries that are poor, Madan et al (2018).My finding may not be representative of the whole town because the data were collected from only two health institutions.

Among the 447 patients with HIV/TB Co-infection the proportion of co-infection according to sex was Male comprises 197(44.08%) and female 250(55.92%).. Among these total number of previously known HIV positive TB patients on ART during the reporting period were 235.

From these male 104 (44.26%) and female 131(55.74%).

From total number of HIV/TB Confection patients the more vulnerable Age groups were <25 years male and female took the higher rank. Moreover proportion of TB/HIV Co-infection was associated with women age groups of<=25 years and poor TB treatment outcomes.

The ART coverage was also very low compared with that targeted plan of WHO 100%, WHO (2013). Hence creation awareness should be given especially to females and sexually active age (<=25years) groups of the population. Moreover communication and social mobilization must further strengthen to achieve 100% of ART coverage.

From 2014-2019 years of PTB patients successful treatment outcome was achieved in 345/448 (77 %) of TB patients of which 208(46.4%) were completed treatment 137(30.6%) cured. 38(8.5%) were treatment lost to follow up,12 (2.7%) were got treatment failure , 27 (6.0%) died, and 26(5.8 %) transferred to other health facilities .In 2017 and 2015 a successful treatment outcome 65(78.3%%) and 62(73.8%) respectively was higher than others(Table:6).

From 2014-2019 years EPTB patients Successful treatment outcome was achieved in 256/360(71.1%) of treatment of which 159(44.2%) was completed their treatment successfully and 97(26.9%) was cured .From the total of 457 EPTB patients 104(28.9%) not achieved successfully their treatment outcomes. From these 27(7.%) were lost to follow up the treatment, 20(5.6%) were got treatment failure 25(6.9%) Dead and 32(8.9%) were transferred out to another health institution for better treatment.

In 2019 the highest EPTB patients successful treatment outcomes were achieved, that is 53/68(76.6%). The lowest EPTB patient successful treatment outcomes was recorded during the study period was in 2015, That is 36/54(62.06%)(Table:7).

The result showed the overall TB treatment outcomes of 808 TB patients' successful treatment outcomes were seen for 601(74.4%) cases in this study. According to WHO 2017 Global TB report, the global treatment success rate for TB cases the 2015 cohort was 78% and in the WHO Africa region it was 80%, WHO (2017).

In this study the overall TB treatment success rate result among TB patients was 74.4%,which is similar or approached with the study was conducted from Vietnam 73% , Huyyen et.al (2016),Yavatmal India 75%, Ambadekar et.al(2015), South India 75%, Vijay et al (2011), Negele 73% Gebremariam et al (2016) and free Arsi state of suth Africa 75%, Engelbrecht et.al (2017).

This result was lower than from the study conducted in Addis Ababa 82.7%, Getahun et al (2013), Nekemte referral Hospital 82.5%, Kassa et al (2018), Sodo town 81.5%, Yakob et al (2018), Eastern Ethiopia 81.8%, Zenebe and Tefera (2016), Central Ethiopia 83.6%, Hamusse et al (2014),New Delhi India 81%, Madam (2018).

The treatment outcome of this study lower than WHO target set for the millennium development Goal (MDG) of 85%, Ejeta et al (2014)) and also ≥90% End TB Strategy success rate of milestone target set globally for 2025,Uplekar and Raviglione (2015)..

The possible explanation for this variation might be associated with the difference in the study design, difference in the quality of service TB/HIV clinics, proper counselling, health education, appropriate follow up by the clinician, characteristics and in the handling of patients documentation of the study.

Besides of the substantial figures of death recorded and socioeconomic condition of the society in case may contribute to low treatment outcomes.

The treatment challenge for TB/HIV co-infection relate primarily to the rising cost of drugs along with the danger of developing drug resistance. The most common cause of drug

resistance was treatment interruption, but drug resistant strains of TB could also been passed on to the others, WHO (2013). The most common cause treatment interruptions a decision was made by person to stop taking the drugs. TB patients started to feel better long before their six month drug course is finished, WHO (2013).

Lost to follow up from TB patients program is a major public health problem that can be associated with adverse drug reactions, social stigma and lack of awareness of the disease Fiseha et al (2015).

In the current study lost for follow up found in this study was 7.2%.This result is higher than the report from Mizan Aman 1.3%, Fiseha et al (2015), Tigray 2%, Belayneh et al (2015), Gonder 2.2%, Cheru et al (2013).

The possible explanation might be lack of implementation of DOTs program efficiently, lack of awareness and service less sufficient accessibility might have contributed to this higher proportion of lost for follow up in my setting.

In the mean time 8.0% transferred out cases in another health centre/hospital within or another region. From these 6 years in 2018 (9.5%) and 2015 (9.2%) took the highest number of transferred out to another health institute with in the town or another better town or region for better treatment. .The lowest transferred out result was seen in 2014 (6%).

The highest number of transferred out cases might be explained due to shortage of giving sufficient treatment for patients, lack of implementation DOTs program in the health institute.

The presence of HIV infection increases the chance of tuberculosis reactivation and infection due to TB Rocha et al (2003)

Among the total of 447 TB/HIV co-infected patients 175(39.1%) were completed their treatment, 122(27.3%) were cured, 30(6.7%) were lost to follow up their treatment, 22(4.9%) transferred to other health institution, 39(8.7%) were got treatment failure and 59(13.2%) were died during the treatment. The overall TB/HIV co-infection patient's treatments were 297/447 (66.4%). In 2018 the highest Successful treatment was recorded during the study time that was 67/91(82.7%). In 2016 the lowest treatment success outcome was scored during the study time, it was 36/61 (52.2%) (Table: 5).

The TB/HIV co-infection rate of successful treatment of this study was 66.4 %. This result is higher than the study was conducted by, Kassu (2007), 52.1%, Biadgelegn (2013), 26%, Tesema et al (2009) 29%.

Furthermore, the more treatment outcomes of TB/HIV co-infection success rate observed in this study could be due to the initiation of ART for all co-infected patients. As it has been reported in previous studies, Belayneh et al (2015) patients who had ART initiated were found to have high success rate compared with their counterpart. For example study conducted in

Tigray Ethiopia, Belayneh et al (2015) and Malaysian, Ismail (2013) stated that TB/HIV co-infected patients who were not receiving ART were more likely to have unsuccessful TB treatment outcomes than those who received ART.

The TB/HIV co-infection successful treatment outcomes of this study was lower than the study result that was conducted by, Asebe et al (2015) 76%, Ejeta et al (2015) 70.8%. Several possible explanations could be proposed for the striking difference in treatment success between patients with TB only and those co-infected with HIV, this could be

Associated administration of anti-TB and ART drugs, which can lead to default from higher pill burden, poor patient compliance, and missing pills due to fear of side-effects, Azeez et al (2018). All of these factors can lead to treatment failure, drug interactions, overlapping toxic effects, immune reconstitution syndrome and ultimately death Azeez et al (2018).

In the current study, the death cases among the TB/HIV co-infected patients during TB treatment was 13.2%,.This result was higher death rate with TB/HIV co-infected death rate that were seen in study conducted in Mizan Aman 6%, Fiseha et al (2015), Aurangabad city, India 9%, Vijay et al (2011), Gonder 9.6%, Cheru et al (2013), WHO Africa region 9%, WHO (2017).

The death rate in my study was lower death rate reported in different parts of Ethiopia, which reported a death rate ranging from 12.8% to 20.2%, Belayneh et al (2015),Cameron 29.4%, Ako et al (2014), Karntaka, India 15.7%, Shastri (2013), Malaysia 21%, Ismail (2013), Ebony state, Nigeria 19%, Oshi et al (2014), Iran 18.9%, (Tabarsi et al (2012).

The lower death rate in my study could be explained by the fact that more than half of the recorded patients had been on ART. ART is a protective against mortality which was seen during treatment out comes. During TB treatment as demonstrated by study previously was conducted in Tigray, Belayneh et al (2015), karataka India Shastri et al (2015), south India, Vijay et al (2011) and North west Ethiopia, Sileshi et al (2013).

Immunological studies have also shown that the host responses to *Mycobacterium tuberculosis* enhance HIV replication. Thus, accelerating the natural progression of HIV and further decreasing cellular immunity, Beyene et al (2016)

When I compared from the total TB treatment death and TB/HIV co-infection death the highest death rate was the TB/HIV co-infection that was 13.2 %, double the death rate of TB treatment that was 6.4%. The possible explanation for this result could be showed less attention especially for patients TB/HIV co-infection and also less the quality of treatment of TB/HIV co-infection service delivery.

6. CONCLUSION AND RECOMMENDATION

Based on the outcome of the study, the following conclusion and recommendations were forwarded

6.1. Conclusion

TB infection and TB/HIV co-infection had shown slight falls and rises over the study period (2014-2019) and recorded cases in 2019 were higher or equal to that of 2014 that shows the requirement much effort to reduce it. The overall treatment success was found to be 75.5% which is closer to target set by WHO. The DOTs strategy improved TB treatment success. ART coverage of the study was 52.57%, which is lower than 100%btargetted by WHO.

6.2. Recommendation

More attention should be given and appropriate measures should be taken to reduce the infection of TB and TB/HIV co-infection as they have shown no much change over the study period. Public awareness creation should be encouraged to achieve treatment success target by WHO. HIV test and provision of ART should be strengthened to reduce deaths due to TB and TB/HIV co-infected patients.

The increased unsuccessful treatment outcome among TB/HIV patients requires urgent public health interventions and the strengthening of existing control programs to improve the evaluation policy and control framework among TB and HIV co-infected patients.

This integrated and coordinated TB control program that includes active case surveillance, effective care and treatment, and quality laboratory diagnosis services reduces morbidity and mortality. Optimal provision of quality care, early identification, and prompt initiation of treatment for both TB treatment and HIV patients will help in bringing down the morbidity and mortality associated with TB-HIV co-infection.

Hence, interventions should also direct at modifiable risks such as treatment of opportunistic infections and other concomitant illnesses or conditions. Frequent supportive supervision and health education should be given for the society on the mode of transmission of TB, prevention of infection, benefits medication adherence, the impact of TB-HIV co- infection on TB treatment outcomes. Additionally, actions targeting predictor factors like education for rural residents and good coverage of diagnostic agents as well as the quality of laboratory services for EPTB are necessary.

Furthermore, future prospective and qualitative studies are needed to identify other potential sociodemographic, medication, clinical, delivery of services, patient compliance, and behavioral factors that could affect the treatment outcomes of TB patients.

7. References

Abuogi LL, Mwachari C, Leslie HH, Shade SB, Otieno J, Yienya N. (2013). Impact of expanded antiretroviral use on incidence and prevalence of tuberculosis in children with HIV in Kenya. Int J Tuberc Lung Dis ;17(10):1291-7.

Ackah AN et a. (1995). Response to treatment, mortality and CD4 lymphocyte counts in HIV-infected persons

Acosta CD. (2014). Conflict and drug-resistant tuberculosis in Ukraine. Lancet.; 384:1500–1.

Ako A, Agbor J, Bigna JR, Billong SC, Tejiokem MC, Ekali GL, Plottel CS, et al.(2014). factors associated with death during tuberculosis treatment of patients coinfected with HIV at the Yaounde´ central hospital, Cameroon: an 8-year hospital-based retrospective cohort study (2006–2013). PLoS One ; 9(12)

Alipanah N , Jarlsberg L , Miller C , Linh N.N , Falzon D , Jaramillo E. (2018). Adherence interventions and outcomes of tuberculosis treatment: A systematic review and meta analysis of trials and observational studies PLoS Med, 15 (7) (2018), p. e1002595.

Allwood B , Zalm M , Makanda G , Mortimer K , Andre F.S.A , Uzochukwu E. (2019).The long shadow post-tuberculosis Lancet Infect Dis, 9 (11) (2019), pp. 1170-1171.

Allwood B.W, Van Der Zalm M.M , Amaral A.F.S , Byrne A , Datta S , Egere U.(2020).Post-tuberculosis lung health: Perspectives from the First International Symposium Int J Tuberc Lung Dis, 24 (8) (2020), pp. 820-828.

Alemu T. and Gutema,H. (2019).Trend in magnitude of tuberculosis in Awi Zone, Northwest Ethiopia: a five- year tuberculosis surveillance data analysisBMC Research Notes.12(:209): 1-5.

Alemu YM, Andargie G, Gebeye E.(2016). High Incidence of Tuberculosis in the Absence of Isoniazid and Cotrimoxazole Preventive Therapy in Children Living with HIV in Northern Ethiopia: A Retrospective Follow-Up Study. PLoS One ;11(4):e0152941.

Alimuddin Zumla, B.J. Marais, T.D. McHugh, M. Maeurer, Adam Zumla, N. Kapata. (2020). COVID-19 and tuberculosis-threats and opportunities Int J Tuberc Lung Dis, 24 (8) (2020), pp. 757-760.

Ambadekar NN, Zodpey SP, Soni RN, Lanjewar SP. (2015). Treatment outcome and its attributes in TB-HIV co-infected patients registered under the revised national TB control program: a retrospective cohort analysis. Public Health; 129:783–8.

Anigilaje EA, Aderibigbe SA, Adeoti AO, Nweke NO. (2016). Tuberculosis, before and after Antiretroviral Therapy among HIV-Infected Children in Nigeria: What Are the Risk Factors? PLoS One ;11(5):e0156177.

Asebe G, Dissasa H, Teklu T, Gebreegizeabhe G, Tafese K, Ameni G. (2015). Treatment outcome of tuberculosis patients at Gambella Hospital, Southwest Ethiopia: three- year retrospective study, Journal of Infectious Diseases & Therapy 3 , 2.

Auld AF, Tuho MZ, Ekra KA, Kouakou J, Shiraishi RW, Adjorlolo-Johnson G, et al.(2014). Tuberculosis in human immunodeficiency virus-infected children starting antiretroviral therapy in Cote d'Ivoire. Int J Tuberc Lung Dis ;18(4):381-7.

Ayalaw S, Alene K, Adane AA.(2015). Incidence and Predictors of Tuberculosis among HIV Positive Children at University of Gondar Referral Hospital, Northwest Ethiopia: A Retrospective Follow-Up Study.

Ayele, B and Nenko, G. (2015).Treatment Outcome of Tuberculosis in Selected HealthFacilities of Gedeo Zone, Southern Ethiopia: A Retrospective Study.Mycobacterial Diseases.5 (5): 1-9

Azeez A., Ndege J., Mutambayi R., Associated factors with unsuccessful tuberculosis treatment outcomes among tuberculosis/HIV coinfected patients with drug-resistant tuberculosis, International Journal of Mycobacteriology 7 (2018) 347–354

Badri M et al. (2001). Association between tuberculosis and HIV disease progression in a high tuberculosis Management of tuberculosis and HIV Co-infection prevalence are

Beyene Y., Geresu B., Mulu A., (2016) Mortality among tuberculosis patients under DOTS programme: a historical cohort study, BMC Publ. Health 16 883.

Belayneh M, Giday K, Lemma H. (2015). Treatment outcome of human immunodeficiency virus and tuberculosis co-infected patients in public hospitals of the eastern and southern zone of Tigray region, Ethiopia. Bras J Infect Dis Poverty;19(1):47–51.

Biadglegne F, Anagaw B, Debebe T, Anagaw B, Tesfaye W. (2013). Tuberculosis lymphadenitis and its treatment outcome in Felege Hiwot Referral Hospital, Northwest Ethiopia: a retrospective study. Int J Biol Med Res 4: 2942–2947

Castro KG, Dooley SW, Curran JW. (1992). Transmission of HIV-associated tuberculosis to health-care workers.

Central Statistical Agency (CSA), Ethiopia and ICF. (2018). Ethiopia Demographic and Health Survey, 2016. HIV Report. Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF.

Chakaya J , Kirenga B , Getahun H. (2016). Long term complications after completion of pulmonary tuberculosis treatment: A quest for a public health approach J Clin Tuberc Other Mycobact Dis, 3 (2016), pp. 10-12.

Cheru F, Mekonen D, Girma T, Belyhun Y, Unakal C, Endris M.(2013).

Comparison of treatment outcomes of tuberculosis patients with and without HIV in Gondar University Hospital: a retrospective study. J Pharm Biomed Sci.;3 :1606–13.

Corbett EL, Watt CJ, Walker N, et al. (2003).The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med; 163(9):1009–1021. Doi: 10.1001/ archinte.163.9.1009.

Corbett EL, Marston B, Churchyard GJ, De Cock KM. (2006). Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment .

Corbett E.L , Bandason T , Duong T , Dauya E , Makamure B , Churchyard G.J. (2010). Comparison of two active case-finding strategies for community-based diagnosis of symptomatic smear-positive tuberculosis and control of infectious tuberculosis in Harare, Zimbabwe (DETECTB): A cluster-randomised trial Lancet, 376 (9748) (2010), pp. 1244-1253.

Cruciani M . (2001). The impact of HIV1 on infectiousness of tuberculosis: a metaanalysis

Davies PD . (2003). The world-wide increase in tuberculosis: how demographic changes, HIV infection and increasing numbers in poverty are increasing tuberculosis. Ann Med 35: 235-243.

Dodd PJ, Yuen CM, Sismanidis C, Seddon JA, Jenkins HE. (2017). The global burden of tuberculosis mortality in children: a mathematical modelling study. The Lancet Global Health. ;5(9):e898-e906.

Dogru S, Doner P. (2016). Frequency and outcomes of new patients with pulmonary tuberculosis in Hatay province after Syrian civil war. Indian J Tuberc. 2017; 64.

Dooley K.E , Chaisson R.E. (2009). Tuberculosis and diabetes mellitus: convergence of two epidemics Lancet Infect Dis, 9 (12) (2009), pp. 737-746,

Drouin O, Bartlett G, Nguyen Q, Low A, Gavriilidis G, Easterbrook P, et al. (2016). Incidence and prevalence of opportunistic and other infections and the impact of antiretroviral therapy among HIV-infected children in low-and middle-income countries: a systematic review and meta-analysis. Clinical infectious diseases ;62(12):1586-94.

Ebonyi AO, Oguche S, Ejeliogu EU, Agbaji OO, Shehu NY, Abah IO. (2016). Prevalence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infected Nigerian children. Germs ;6(1):21-8.

Edmonds A, Lusiama J, Napravnik S, Kitetele F, Van Rie A, Behets F. (2009). Anti-retroviral therapy reduces incident tuberculosis in HIV-infected children. International journal of epidemiology; 38 (6):1612-21.

Ejeta E, Beyene G, Balay G, Bonsa Z, Abebe G. (2018). Factors associated with unsuccessful treatment outcome in tuberculosis patients among refugees andtheir surrounding communities in Gambela regional state ofEthiopia;13(10)

Ejeta E, Birhanu T, Wolde T. (2014). Tuberculosis treatment outcomes among tuberculosis/human immunodeficiency co-infected cases treated under directly observed treatment of short course in Western Ethiopia, J. AIDS HIV Res. 6, 164–171.

Ejeta E, Chala M, Arega G, Ayalsew K, Tesfaye L, Birhanu T, Disassa H. (2015). Outcome of tuberculosis patients under directly observed short course treatment in western Ethiopia, The Journal of Infection in Developing Countries 9 , 752–759.

Endris,M, Moges,F, Belyhun,Y. Woldehana,E., Esmael, A. and Unakal, C (2014).TreatmentOutcome of Tuberculosis Patients at Enfraz Health Center, Northwest Ethiopia: A Five-Year Retrospective Study. Tuberculosis Research and Treatment. 2014: 1-7.

Engelbrecht MC, Kigozi NG, Chikobvu P, Botha S. Rensburg HCJv. (2017). Unsuccessful TB treatment outcomes with a focus on HIV co-infected cases: a cross-sectional retrospective record review in a high-burdened province of South Africa. BMC Health Serv Res ; 17(470):1–10.

Federal democratic republic of Ethiopia (FDRE). (2012). Guidelines for clinical and programmatic management of TB, Leprosy and TB/HIV in Ethiopia, fifth edition Addis Ababa; April 2012.

Federal Ministry of Health (FMOH) . (2009). Federal Ministry of Health of Ethiopia Guideline for program and clinical manage.

Federal Ministry of Health (FMOH). (2011 - June 2012). Ethiopian Federal Ministry of Health. Preliminary report of Ethiopia national TB/HIV sentinel surveillance. One year Report (July 2013.

Federal Democratic Republic of Ethiopia, (2015). Annual Tuberculosis and Leprosy Bulletin

Federal Ministry of Health (FMOH). (2017). National guidelines for TB, DR-TB and Leprosy in Ethiopia, 6th, 2.

Federal Ministry of Health (FMOH). (2021). HIV Prevention and Control Office: Single Point HIV Prevalence Estimate Addis Ababa, Ethiopia; Available from: http://www .etharc.org/aidsineth/publications/singlepointprev.

Fentie, A. M.,,Jorgi, T. and Assefa, T. (2020).Tuberculosis treatment outcome amongpatients treated in public primary healthcare facility, Addis Ababa, Ethiopia: a retrospective study.78(12): 1-9.

Fiseha T, Gebru T, Gutema H, Debela Y. (2015). Tuberculosis treatment outcome among HIV co-infected patients at Mizan-Aman general hospital, Southwest Ethiopia: a retrospective study, J. Bioeng Biomed. Sci. (2015) 1–4.

Forni G , Mantovani A . (2021). COVID-19 vaccines: where we stand and challenges ahead Cell Death Differ (2021),

Garcıa-Basteiro B.A.L , Brew J , Williams B , Borgdorff M, Cobelens F . (2018).What is the true tuberculosis mortality burden? Differences in estimates by the World Health Organization and the Global Burden of Disease study Int J Epidemiol, 47 (5) (2018) pp. 1549-1560

Gebremariam G, Asmamaw G, Hussen M, Hailemariam M.Z, Asegu D, Astatkie A, Amsalu A.G. (2016). Impact of HIV status on treatment outcome of tuberculosis patients registered at Arsi Negele health center, southern Ethiopia: a six year retrospective study, PLoS One 11.

Gesesew H, Tsehayneh B, Massa D, Gebremedhin A, Kahsay H, Mwanri L. (2016). Predictors of mortality in a cohort of tuberculosis/HIV co-infected patients in Southwest Ethiopia. Infect Dis Poverty ;5(109):1–9.

Getahuna B, Amenia G, Medhin G, Biadgilignc S. (2013).Treatment outcome of tuberculosispatients under directly observed treatment in Addis Ababa, EthiopiaThe Brazilian Journal of Infectious Diseases7(5):521–528

Girardi E. (2000). Impact of the HIV epidemic on the spread of other diseases.

Grace A.G, Mittal A, Jain S, Tripathy J.P, Satyanarayana S, Tharyan P. (2019) .Shortened treatment regimens versus the standard regimen for drug-sensitive pulmonary tuberculosis Cochrane Database Syst Rev, 12 (2019).

Hamusse S.D, Demissie M, Teshome D, Lindtjørn B. (2014). Fifteen-year trend in treatment outcomes among patients with pulmonary smear-positive tuberculosis and its determinants in Arsi Zone, Central Ethiopia, Glob. Health Action 7 , 25382.

Harries AD, Nyangulu DS, Kang'ombe C et al. (1998). Treatment outcome of an unselected cohort of tuberculosis patients in relation to human immunodeficiency virus serostatus in Zomba hospital, Malawi.

Houben R.M.G.J, Dodd P.J. (2016). The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling PLoS Med, 13 (10) (2016), p. e1002152,

Huyen TTT, Nhung NV, Shewade HD, Hoa NB, arries AD. (2016). Collaborative activities and treatment outcomes in patients with HIV-associated tuberculosis in Viet Nam. Public Health Action.March ;6(1):8 - 15.

Ikushi Onozaki. (2008). Feasibility study and orientation.

Ikushi Onozaki, Philip, Anne. (2009). Preparatory WS and Basic design (group training in Geneva

Ikushi Onozaki. (2011). Coordination and advocacy, Protocol review and clearance.

Ikushi Onozaki, Marina Tadolini. (2011). Mid-term review, data management.

Ismail I, Bulgiba A. (2013). Determinants of unsuccessful tuberculosis treatment outcomes in Malaysian HIV-infected patients. Prev Med ;57:S27–30.

Johnston JC, Shahidi NC, Sadatsafavi M, Fitzgerald JM. (2009). Treatment outcomes of

Kassa J, Dedefo M, Korsa A, Dibessa T. (2018). Factors affecting treatment outcome of tuberculosis among tuberculosis patients in West Ethiopia, J. Bioanal. Biomed.10,24–29 multidrug- Resistant tuberculosis: a systematic review and meta-analysis

Kassu A, Mengistu,G, Ayele B, Mekonnen F D, Ketema F, Moges T.,Mesfin,A , Getachew B, Ergicho. (2007). Coinfection and clinical manifestations of tuberculosis in human immunodeficiency virus-infected and-uninfected adults at a teaching hospital, northwest Ethiopia, J. Microbiol. Immunol. Infect: 40 , 116.

Kefale,A.T, Anagaw Y.K . (2017). Outcome of tuberculosis treatment and its predictors among HIV infected patients in southwest Ethiopia, Int. J. Gen. Med. 10,161.

Kochi A. (1991). Government intervention programmes in HIV/tuberculosis infection. Outline of guidelines for national tuberculosis control programmes in view of the HIV epidemic. 66(1):33-6.

Krauss MR, Harris DR, Abreu T, Ferreira FG, Ruz NP, Worrell C. (2015). Tuberculosis in HIV-infected infants, children, and adolescents in Latin America. Brazilian Journal of Infectious Diseases ;19(1):23-9.

Kruijshaar ME, Abubakar I. (1999–2006). Increase in extra pulmonary tuberculosis in England and Wales. Thorax. 200; 64:1090–5.

Lee K.K , Bing R , Kiang J , Bashir S , Spath N , Stelzle D. (2020). Adverse health effects associated with household air pollution: a systematic review, meta-analysis, and burden estimation study Lancet Glob Heal, 8 (11) (2020), pp. E1427-E1434,

Li N, Manji KP, Spiegelman D, Muya A, Mwiru RS, Liu E. (2013). Incident tuberculosis and risk factors among HIV-infected children in Tanzania. AIDS (London, England).;27(8):1273-81.

Lienhardt C, Rodriques LC. (1997). Estimation of the impact of the human immunodeficiency virus infection on tuberculosis

MacPherson P, Lebina L, Motsomi K. (2020). Prevalence and risk factors for latent tuberculosis infection among household contacts of index cases in two South African provinces: analysis of baseline data from a cluster-randomised trial. PLoS One; 15 (3).

Madan C, Chopra K.K, Satyanarayana S, Surie D, Chadha V, Sachdeva K.S, Khanna A, Deshmukh R, Dutta L, Namdeo A. (2018). Developing a model to predict unfavourable treatment outcomes in patients with tuberculosis and human immunodeficiency virus co-infection in Delhi, India, PLoS One 13, e0204982.

Marina Tadolini, Ikushi Onozaki. (2009). Basic design and preparation (in Ethiopia).

Marks G.B , Nguyen N.V , Nguyen P.T.B , Nguyen T.-A , Nguyen H.B , Tran K.H. (2019). Community-wide screening for Tuberculosis in a high-prevalence setting N Engl J Med, 381 (2019), pp. 1347-1357,

Ngwatu Nsengiyumva, Ntwali Placide,Oxlade Olivia, Mappin-Kasirer Benjamin, Nguyen Nhat Linh, Jaramillo Ernesto. (2018) .The impact of digital health technologies on tuberculosis treatment: A systematic review Eur Respir J, 51 (2018).

Njuki, C, and Abera W. (2018). Forced displacement and mixed migration challenges in the IGAD region. GREAT insights Magazine- volume 7, Issue 1. Winter.

Oshi DC, Oshi SN, Alobu I, Ukwaja KN. (2014). Profile outcomes and determinants of unsuccessful tuberculosis treatment outcomes among HIV-infected tuberculosis patients in a Nigerian state. Hindawi Publishing Corporation Tuberculosis Res Treat 2014 :1–8.

Parwati C.G, Farid M.N , Nasution H.S , Basri C , Lolong D,(2020).Estimation of subnational tuberculosis burden: Generation and application of a new tool in Indonesia Int J Tuberc Lung Dis, 24 (2) (2020), pp. 250-257,

Peou Satha.(2010). Data management, TOT and Simulation (Field test) including Radiology Cambodian Field Survey.

Perriens JH, Mukadi Y, Nunn Ptubercu. (1991). loses and HIV infection: implications for Africa Refera H, Wencheko E, 2013. Survival of HIV-TB co-infected adult patients under ART in ambo referral hospital. Ethiop Ethiop J Health Dev ;27(2):88–93.

Proença R, Souza FM, Bastos ML, Caetano R, Braga JU, Faerstein E (2020). Active and latent tuberculosis in refugees and asylum seekers: a systematic review and meta-analysis. BMC Public Health.;20:838.

Reid M.J.A , Arinaminpathy N, Bloom A , Bloom B.R , Boehme C , Chaisson R. (2019). Building a tuberculosis-free world: The Lancet Commission on tuberculosis Lancet (2019)

Rocha M, Pereira S, Ferreira , Barros H. (2003).The role of adherence in tuberculosis IV-positive patients treated in ambulatory regimen, Eur. Respir. J. 21 785–788

Romanowski K , Baumann B , Basham C.A, Ahmad Khan F , Fox G.J , Johnston J.C. (2019).Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta- Lancet Infect Dis, 19 (10) (2019), pp. 1129-1137

Shastri S, Naik B, Shet A, Rewari B, Costa AD. (2013). TB treatment outcomes among TB-HIV co-infections in Karnataka, India: how do these compare with nonHIV tuberculosis outcomes in the province? BMC Public Health ; 13(838):1–6.

Sileshi B, Deyessa N, Girma B, Melese M, Suarez P, (2013). Predictors of mortality among TB-HIV Co-infected patients being treated for tuberculosis in Northwest Ethiopia: a retrospective cohort study, BMC Infect. Dis. 13 (2013) 297.

Sinshaw Y, Alemu S, Fekadu A, Gizachew M. (2017).Successful TB treatment outcome and its associated Factors among HIV/TB co-infected patients attending Gondar University Referral Hospital Sismandis Charalampos, Timimi Hazim,2011. Data cleaning.

Sismandis and Timimi Hazim. (2011). Data management review.

Subbaraman R, Nathavitharana R,Mayer K.H. , Satyanarayana S, Chadha V, Arinaminpathy N. (2019). Constructing care cascades for active tuberculosis: A strategy for program monitoring and identifying gaps in quality of care PLoS Med, 16 (2) (2019), p. e1002754,

Swindells S , Ramchandani R, Gupta A , Benson C.A , Leon-Cruz J , Mwelase N . (2019). One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis N Engl J Med, 380 , pp. 1001-1011.

Sumner T, Scriba T.J , Penn-Nicholson A, Hatherill M , White R.G. (2019). Potential population level impact on tuberculosis incidence of using an mRNA expression signature correlate-of-risk test to target tuberculosis preventive therapy Sci Rep, 9 (2019), p. 11126,

Tabarsi P, Chitsaz E, Moradi A, Baghaei P, Marjani M, Mansouri D. (2012). Treatment outcome and mortality: their predictors among HIV/TB co-infected patients from Iran. Int J MycobacterIology ;1:82–6.

Talha Burki. (2016) “Ethiopia shows it is single minded in tackling disease,” Lancet Infectious Disease 16, no. 2 (February 2016): 153–4

Tessema B, Muche A, Bekele A, Reissig D, Emmrich F.(2009). Sack, Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia. A five-year retrospective study, BMC Publ. Health 9, 371.

Tola A., Minshore K.M., Ayele Y., Mekuria A.N., (2019) Tuberculosis treatment outcomes and associated factors among TB patients attending public hospitals in Harar town, eastern Ethiopia: a five-year retrospective study, Tuberculosis research and treatment 11, 2019.

Trébucq A, . Schwoebel V. (2016). Numbers of tuberculosis cases: Dreams and reality Int J Tuberc Lung Dis, 20 (10) (2016), pp. 1288-1292.

United Nations High Commissioner for Refugees (UNHCR). (2013). Public Health Strategy for Tuberculosis among Syrian Refugees in Jordan,.http:// data. unhcr. org/Syrian refugees/ download. php? id=3791

United Nations High Commissioner For Refugees (UNHCR).(2019). Global Trends: Forced Displacement in 2018. Geneva: UNHCR.

United Nations High Commissioner for Refugees. (2017). Refugees and Asylum-seekers in Ethiopia.

UNAIDS Fact Sheet. (2017) .Latest Statistics on the Status of the AIDS Epidemic", available from http://www.unaids.org/en/resources/fact-sheet.

Uplekar M, Raviglione M., (2015) WHO's End TB Strategy: from stopping to ending the global TB epidemic, Indian J. Tubercul. 62 196–199.

Van Soolingen D. (2001). Molecular epidemiology of tuberculosis and other mycobacterium infections: main methodologies and achievements. J Intern Med. 249(1):1–26.

Vijay S, Kumar P, Chauhan LS, Rao SVN, Vaidyanathan P. (2011).Treatment outcome and mortality at one and half year follow-up of HIV infected TB patients under TB control Programme in a district of South India. PLoS One. July; 6(7):1–8.

Volmink J, Garner P. (2007). Directly observed therapy for treating tuberculosis Cochrane Database Syst Rev (2007),

World Health Organization. (1997). Tuberculosis control in refugee situations: An Inter-agency field manual. (WHO/TB/97.221).

World Health Organization. 2013. Definitions and reporting framework for tuberculosis- revision. Geneva: WHO; 2013. WHO/HTM/TB/2013.

World Health Organization. (2015).WHO Consultation Meeting to Enhance the Engagement of Communities, Nongovernmental and other Civil Society Organizations in the Implementation of the End TB Strategy," 2015

World Health Organization. (2016). Global tuberculosis report 2016. In. Geneva, Switzerland.

World Health Organization. (2017). International Organization for Migration, Ministry of Health of Lebanon. Joint review of the national tuberculosis programme of Lebanon. 2015.http://www. Data bank. com. lb/docs/ Tuberculosis %2 Report-MoPH- 2016. docx. Accessed 5

World Health Organization. (2018). Stop TB Initiative, Treatment of tuberculosis: guidelines.

World Health Organization. (2019). Global Task Force on TB Impact Measurement. World Heal Organ.

World Health Organization. (2020). Global Tuberculosis Report 2020.

Wondale, B., Medihn, G., Teklu, T., Mersha W., Tamirat, M. and Ameni, A. (2017).Aretrospective study on tuberculosis treatment outcomes at Jinka General Hospitalsouthern Ethiopia.BMC Research Notes. 1-7.

Yakob B, Alemseged F, Paulos W, Badacho A. (2018). Trends in treatment success rate and associated factors among tuberculosis patients in Ethiopia: a retrospective cohort study, Health Sci. J. 12 , 598.

Zenebe T, Tefera. (2016).Tuberculosis treatment outcome and associated factors among smear-positive pulmonary tuberculosis patients in Afar, Eastern Ethiopia: a retrospective study, Braz J. Infect. Dis. 20 , 635–636.

8 Appendixes

MADDA WALABU UNIVERSITY

SCHOOL OF GRADUATE STUDIES

ETHICAL APPROVAL APPLICATION FORM

Researcher: Mr. Tesfaye Dabi

School: MaddaWalabu University School of Graduate Studies

College: College of Natural and Computational Sciences

Department: Department of Biology

Title of the Research:Retrospctive analysis of TB and HIV among patients diagnosed in Zeway Hospital and Health Center from 2014-2019

Name of Supervisor _____

Type of Research: **Postgraduate**

2. **APPLICATION FORM CHECK LIST**

Please complete the ethics application form below and provide additional information as attachments.

My application includes the following documentation:	Included (mark as yes)	Not applicable(mark as N/A)
Participant information Leaflet	X	
Participant Informed Consent form	X	
Questionnaire/Survey		
Interview/Focus Group Questions		

3. RESEARCH DETAILS

a) Lay description

Tuberculosis (TB) remains one of the deadliest infectious diseases responsible for millions of deaths annually across the world. While TB is present in every country majority of TB

sufferers live in low income and middle income countries especially in regions such as Sub-Saharan Africa. In Ethiopia, tuberculosis is the leading cause of morbidity, the third cause of hospital admission, and the second cause of death in Ethiopia, after malaria. Routine monitoring of the extent of the treatment outcome and its determinants is important, but studies that have focused on evaluation of TB treatment outcome and associated factors that are lacking in Centeral Part of Ethiopia. This study aimed to Retrospective analysis of TB and HIV treatment outcomes and associated factors between January 1, 2014 to December 31, 2019 under the DOTS clinic of Batu Hospitaland Health Centeral Ethiopia. A retrospective data of TB and HIV patients registered at Batu Hospital between January 1, 2014 to December 31, 2019 will be obtained from hospital registry and used as source of data which will be collected from March 1 to April 8, 2020. Bivariate and multinomial logistic regression models will be used to analyze the association between treatment outcomes and potential predictor variables. At end of this study, the researcher will point out the treatment out comes and the factors that contribute to spread the disease.

Operational definitions of some terms:

Treatment outcome: study subjects who were cured, completed their treatment, new, relapsed defaulted, failure or transfer in during their treatment course in DOTs clinic in respective study area.

Treatment success: is defined as study subjects who were completely cured from the diseases and also completed their treatment. Unsuccessful treatment outcomes were study subjects who were new, relapse defaulted, failure or transfer in.

b) Research Objectives

The objective of this research is to assess Treatment outcome of Tuberculosis and HIV patients Associated risk factors in selected health centers and Batu Hospital.

c) Research location and duration

Location	Btu Sher Hospital and Health center
Research start date	2014
Research end date	2019
Approximate duration	6 years retrospective data analaysis

4. Participants

		Yes	No	N/A	Remark
Do participants fall into any of the following special groups?	Minors(under 18 years age)				
	People with learning or communication difficulties				
	Patients	✓			
	People in custody				If they attended their treatment at DOTs clinic
	People engaged in illegal activities(e.g. drug taking)				

5. Sample details

Inclusion Criteria

The inclusion criteria will be pulmonary TB (smear positive, PTB and smear negative, PTB), and extra pulmonary forms (EPTB) of TB cases which were registered in and HIV positive the TB clinic of the Zeway Hospital and selected Health centers will be included in the study.

Exclusion Criteria

Patients who transferred to other districts (transferred out), and patients with incomplete socio-demographic information (data) and with no clinical history will be excluded from the treatment outcome evaluation, as information on their treatment outcome was not available.

Justification for proposed sample size and for selecting a specific gender, age, or any other group if this is done in your research.

All registered TB patients with full socio-demographic information and clinical history that fulfilled the inclusion criteria during the study period will be sampled and included in the study.

6. Risk to participants

a) Please describe any risks to participants that may arise due to the research.

- ✓ The study will not cause any harm to the study participants as the research is a retrospective study that depend on the already registered socio-demographic and clinical history of the study participants.

7. Informed consent

	Yes	No	N/A
With questionnaires, will you give participants the option of omitting questions they do not want to answer?			
Will you tell participants that their data will be treated with full confidentiality and that, if published, it will not be identifiable as theirs?			
Will the data be anonymous?			
Will you debrief participants at the end of their participation?			
Will your research involve deliberately misleading participants in any way or will information be held?			

a) Please outline your approach to ensuring the confidentiality of data.

In order to maintain confidentiality and anonymity, data collector will be recruited from nurses. There is no use of individual identifiers and the data that will obtain the records will be only accessed by the investigator. During document review codes will be used and anonymity will be assured.

(b) There is an obligation on the lead researcher to bring to the attention of the College Ethics Committee any issues with ethical implications not clearly covered by this application form.

8. Declaration

I have read and understand the MWU guide lines for ethical practices in research and have read and understand the data protection guide lines.

Name Signature Date

(Researcher) :_____ _____ _____

(Supervisor)_____

Ethical Committee Name of the College

Head of College of Natural &

Computational Science:

Name (Chair person)	Signature	Date
_____	_____	_____
Department Head of Biology		
_____	_____	_____
Department Head of Chemistry		
_____	_____	_____
Department Head of Mathematics		
_____	_____	_____
Department Head of Environmental Science		
_____	_____	_____
Department Head of Physics		
_____	_____	_____

9. Statement of Ethical Approval

Chair of Ethics Committee (Chair person of the College)

This Research has been considered by the Ethics Committee and approval is granted.

Signed: _____ Name: _____

Date: _____