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Prevalence and Associated Factors of HIV Positive among Pulmonary Tuberculosis Patients in Woldia Comprehensive Specialized Hospital, Ethiopia

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Abstract*: Background: The bidirectional relationship between the twin epidemics of Tuberculosis (TB) and the Human Immunodeficiency Virus (HIV) causes major global health challenges in the twenty-first century. TB-HIV co-infected people face multifaceted problems like a high loss to follow-up rates, poor treatment adherence, high TB recurrence rate, and high mortality risk. Our objective was to assess the prevalence and associated factors of HIV patients among PTB patients in Woldia comprehensive specialized hospital, Ethiopia, 2021. Methods: A retrospective study was conducted among 584 TB/HIV co-infected patients registered from 2015 to 2019 in a hospital in Woldia town. The data were collected through document review by using a pre-tested structured data extraction checklist. The data were analyzed using SPSS Version 25. Bivariate and multivariate logistic regressions were determined at 95% confidence intervals. Results: Among the 584 PTB cases, the prevalence of HIV was 170, 29.1 %. PTB WHO stage 3 was 2.69 times more likely HIV positive than WHO stage 1 (AOR: 2.69, 95% CI (1.28-5.66). PTB patients who had an opportunistic infection were 5.27 times more likely to have HIV infection than patients who had not (AOR: 5.27, 95% CI (2.05-13.56)). The category of patient retreatment PTB cases was 5.02 times more likely HIV patient compared to new cases (AOR: 5.02, 95% CI (1.97-12.78). Conclusions: the prevalence of HIV infection among PTB cause is high. Late HIV stage, history of opportunistic infection and not taking opportunistic infection are associated with HIV infection. Therefore, diagnosing HIV among TB patients and treating TB cases to opportunistic parasitic infection could help prevent TB/HIV co-infections.*

Keywords: Prevalence, Pulmonary tuberculosis, HIV, Co-infection, Woldia

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硕 士 学 位 论 文

埃塞尔比亚迪亚地区肺结核病人艾滋病感染率及相关因素分析

Prevalence and Associated Factors of HIV Infection among Pulmonary Tuberculosis Patients in Woldia District, Ethiopia

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埃塞尔比亚迪亚地区肺结核病人艾滋病感染率及相关因素分析

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摘　要

背景：共同感染结核病和艾滋病病毒是全球公共卫生重大问题，共同感染面临者各种问题，比如追踪率低、治疗依从性差、结核病复发率和死亡率高。本文旨在评估分析 2021 年埃塞俄比亚沃尔迪亚综合专科医院 PTB 患者中艾滋病毒感染率和相关因素，为缓解共感染问题提供科学性指导。

方法：本研究对 2015 年至 2019 年在沃尔迪亚镇一家医院登记的 584 名结核病/艾滋病毒合并感染患者进行回顾性研究。采用预先测试的结构化数据，提取检查表通过文件审查收集，使用 SPSS 分析数据。

结果：在 584 名 PTB 患者中，感染 HIV 人数为 170，占 29.1% 。3 期的 PTB 患者 HIV 阳性率是 1 期患者的 2.69 倍(AOR: 2.69, 95% CI (1.28-5.66))。数据显示，机会性感染的 PTB 患者感染 HIV 的可能性是未感染患者的 5.27 倍(AOR: 5.27, 95% CI (2.05-13.56))。再治疗 PTB 病例的 HIV 感染率是新发病例的 5.02 倍(AOR: 5.02, 95% CI (1.97-12.78))。

结论：肺结核病人中 HIV 感染率较高。HIV 病毒的感染率与 HIV 晚期、有无机会性感染病史有关。因此，在结核病患者或机会性寄生虫感染的结核病病例进行检测 HIV 病毒，有助于预防结核病/艾滋病病毒合并感染。

关键词：患病率，肺结核，艾滋病，合并感染，沃迪亚。

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Abbreviations

PTB	Pulmonary Tuberculosis
EPTB	Extra-pulmonary Tuberculosis
ATT	Anti- Tuberculosis Treatment
AIDS	Acquired Immunodeficiency syndrome
ART	Anti-Retroviral Therapy
AFB	Acid-Fast Bacilli
BCG	Bacillus Calmette-Guerin
CD4 Cell	T-Cell Expressing CD4 Receptor
CDC	Centers for Disease Control
CPT	Cotrimoxazole Preventive Therapy
FMOH	Federal Ministry of Health
ANRS	Amhara National Regional State
HIV	Human Immunodeficiency Virus
OI	Opportunistic Infections
COR	Crude Odds Ratios
AOR	Adjacent odds ratios
PLWHA	People Living with HIV/AIDS
XDR TB	Extensively Drug-Resistant Tuberculosis
WHO	World Health Organization.

Chapter 1: Introduction

1.1 Background

TB is a chronic mycobacterial contagious disease caused primarily by M. tuberculosis and occasionally by M. Bovis and M. Africanism in humans. The disease is, spreading through the air by coughing, sneezing, or spitting, and it has remained a public health challenge in the world and is considered a major cause of morbidity and mortality [3]. Tuberculosis is a chronic infectious disease caused by Mycobacterium tuberculosis. It typically affects the lungs but can affect other parts of the body. The disease is spread via droplet infection when people with pulmonary TB expel the bacilli while coughing, sneezing, talking, etc. Without treatment, mortality rates are high [4]. The global TB report showed that there had been an estimated 10 million incident cases and 12 million prevalent cases of TB globally. Overall, 90% of the infection occurred in adults; of this 9% were people living with HIV (72% in Africa). About 26% of incident TB cases occurred in Africa, and 23% of the world's population are estimated to possess a latent TB infection and are thus in danger of developing active TB during their lifetime [2]. TB is a major public health issues in Ethiopia context. Currently, Ethiopia is ranked eighth among the 22 high TB burden countries worldwide and at rank three in Africa. The incidence rate of all styles of TB is estimated at 164 per 100,000 populations, resulting in an annual fatality rate of 27.5 per 100,000 Population [1,2]. Tuberculosis is exclusively transmitted supported environmental and private risk factors, especially during a social mixing setting (together with overcrowding) and conditions which prolong the length of exposure to an infectious patient like health system-related factor including delay in diagnosis can increase TB transmission [2,3].

Additionally, the chance of infection following TB exposure is primarily governed by exogenous factors and an intrinsic combination of the infectiousness of the source case, proximity to contact and social and behavioral risk factors, including smoking, alcohol, and indoor pollution [4]. Patients with asymptomatic phthisis transmit the bacilli to risky groups through inhalation. Identify and investigating infected individuals among contacts of patients with infectious tuberculosis is that the best method of preventing the later development of the disease in populations. Additionally, to the current situation, contact tracing is incredibly important to ascertain the first source of TB disease and detect those who are secondarily infected by proper diagnosis and prompt treatment [2]. Now a day, the world's population is estimated to be infected with tubercle bacilli phenomena's. Hence almost millions of people are at the risk of developing active disease per year. According to World Health Organization 2018 global TB report, an estimated 10 million people have developed TB disease in 2017, of which 5.8 million were men, 3.2 million among women, and 1 million were children. Overall, 90% were adults, and 9% were people living with HIV. There were also an estimated 1.3 million TB deaths in 2017 and an additional 0.3 million deaths resulting from TB disease among HIV-positive people [3].

The majority of the community lacks awareness that HIV-infected is increasing risk or suspected of Tuberculosis in Ethiopia. The analysis of any data is the backbone of interpreting any public health raw data. As a public health domain, the TB data also needs to be interpreted as other data since it is one of the public health concerns in Ethiopia context. There is lack of quality information concerning to the existing tuberculosis problem and trends of TB cases. Tuberculosis is exclusively transmitted based on environmental and personal risk factors, especially in a social mixing setting (together with overcrowding) and conditions which prolong the length of exposure to an infectious patient like health system-related factor including delay in diagnosis can increase TB transmission [4].

1.2 Statement of the problem

Tuberculosis is a major public health issue in Ethiopia context. Currently, **Ethiopia is ranked eighth among the 22 high TB burden countries within the world and at rank three in Africa [2].** TB is a chronic mycobacterial contagious disease caused primarily by M. tuberculosis and occasionally by M. Bovis and M. Africanism in humans. The disease is, spreading through the air by coughing, sneezing, or spitting, and it has remained a public health challenge in the world and is considered a major cause of morbidity and mortality [3]. Tuberculosis is a chronic infectious disease caused by Mycobacterium tuberculosis. It typically affects the lungs but can affect other parts of the body. TB is spread via droplet infection when people with pulmonary TB expel the bacilli while coughing, sneezing, talking. Without treatment, mortality rates are high [4]. The global TB report showed that there had been an estimated 10 million incident cases and 12 million prevalent cases of TB globally. Overall, 90% of the infection occurred in adults; of this 9% were people living with HIV (72% in Africa). About 26% of incident TB cases occurred in Africa, and 23% of the world's population are estimated to possess a latent TB infection and are thus in danger of developing active TB during their lifetime [2]. The incidence rate of all styles of TB is estimated at 164 per 100,000 populations, resulting in an annual fatality rate of 27.5 per 100,000 populations [1,2]. Tuberculosis is exclusively transmitted supported environmental and private risk factors, especially during a social mixing setting (together with overcrowding) and conditions which prolong the length of exposure to an infectious patient like health system-related factor including delay in diagnosis can increase TB transmission [2,3].

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disease in 2017, of which 5.8 million were men, 3.2 million among women, and 1 million were children. Overall, 90% were adults, and 9% were people living with HIV. There were also an estimated 1.3 million TB deaths in 2017 and an additional 0.3 million deaths resulting from TB disease among HIV-positive people [3,4]. Therefore, the aims of this study was to determine the trend in the magnitude of HIV infection among Pulmonary Tuberculosis patients in Woldia District, Ethiopia.

1.3 Significant Features and Innovation Points

- To evaluate the status of HIV infection among pulmonary TB and prevention and control measurements taken by the study area.
- To know the level of susceptibility to associated factors that may complicate the case of HIV infection among pulmonary TB in the study population.
- Other researchers and institutions will use the document as a reference.
- To share this study findings and recommendations of the research with relevant governments bodies

1.4 Objectives of the study

1.4.1 General objective

- ✓ To analyze the prevalence and Associated Factors of HIV infection among pulmonary Tuberculosis patients by using retrospective data from Woldia Comprehensive Specialized Hospital, Ethiopia.

1.4.2 Specific objectives

- ✓ To assess the prevalence of HIV infection among pulmonary Tuberculosis Patients in Woldia district, Ethiopia.
- ✓ To determine associated factors of HIV infection among pulmonary Tuberculosis patients
- ✓ To share the findings and recommendations of the research with relevant governments bodies

1.5 Research Questions

- ✓ What is the prevalence of HIV infection among pulmonary Tuberculosis patients in the study area?
- ✓ What are the associated factors of HIV infection among Pulmonary Tuberculosis Patients in the study area?

Chapter 2: Literature Review

2.1 Epidemiology of Tuberculosis

Tuberculosis is a chronic infectious disease which is caused by Mycobacterium tuberculosis problem. It typically affects the lungs but can affect other parts of the body as well [2]. The causative agent Mycobacterium tuberculosis (Mtb), has been estimated to be 3 million years old and probably originated in East Africa. Evidence of infection in humans includes identification of Mtb DNA in Egyptian mummies [43]. And, likely, a clinical condition called phthisis (or consumption) described in the Aphorisms of Hippocrates in ancient Greece was an early depiction of TB [44]. The pathogenesis of the disease was first outlined in 1819 by the French pathologist Laennec. Although controversies regarding the nature of TB as a genetic or a transmissible disease continued until 1882 when Robert Koch convincingly established that the etiology involved Mtb. This breakthrough was based on discovering a technique using a stain that could impregnate the waxy cell walls of the bacteria, thus rendering them visible under a light microscope [44]. In the 19th century, TB was common in Europe and the United States, causing up to 1,000 deaths per 100,000 persons annually [43]. A gradual decline was seen in the Western world from the 1920s, which is usually attributed to better living conditions and less crowding and a lesser extent to introducing BCG vaccination and anti-mycobacterial agents after discovering streptomycin in 1944 [45]. However, on a global scale, the rates did not decline and showed a dramatic increase in the latter part of the 20th century, primarily due to the emergence of HIV. Shortly after HIV was established as the cause of AIDS, increased numbers of TB cases were seen in the United States [46, 47]. A study indicated that TB had increased in 20 African nations from 1985 to1992 on average 7.7% annually [48].

According to the WHO global tuberculosis report, the total number of TB cases worldwide was 9.0 million in 2014 [4]. The same report also specified that incidence fell by approximately 1.5% yearly between 2000 and 2013, and mortality has decreased 45% between 1990 and 2013. However, TB still causes 1.5 million deaths annually (360,000 of those cases known to be HIV positive in 2013). Hence, TB is second only to HIV as the infectious disease with the highest mortality. Together, the following characteristics represent a successful approach from the perspective of the TB bacteria: the slow rate, at which a host is killed, the latent capabilities of the microbes within the host, and the primary focus in the host's lungs, which enables an effective route of transmission. Moreover, it is estimated that one-third of the global population is currently infected with a latent form of Mtb, and hence prospects of eradication of this pathogen seem implausible.

Tuberculosis is spread via droplet infection when people with pulmonary TB expel the bacilli while coughing, sneezing, and talking. Without treatment, mortality rates are high [4]. Tuberculosis remains a major public health problem in resource-limited countries, and it is the largest cause of death among people living with HIV/AIDS in the world. As WHO report, TB is an estimated about 9 million new cases occurred globally which is 13% were associated with HIV/AIDS infection. Whereas 78% of HIV/AIDS cases occurred in Africa context. The problem is further estimated that 1.49 million deaths from TB including 0.36 million among PLWHA. Besides to this, 96% of the death occurred in developing countries context. Moreover, Ethiopia has been classified 7th among the 22 high burden countries with TB and HIV/ AIDS infection in the world [1, 2]. HIV/AIDS predisposes to Mycobacterium tuberculosis infection and increases the probability of recently acquired TB infection to progress to active disease status and increases the rate of recurrent TB. The lifetime risk of developing active TB in immune-competent adults is estimated to be 10%. Still, in PLWHAs who have been infected with MTB, the annual risk of developing active TB disease exceeds 10% [3]. The current increasing HIV/AIDS-associated tuberculosis shifted the clinical pattern of TB towards smears negative pulmonary TB (PTB) and extra-pulmonary TB (EPTB), which in turn, causes difficulties in the diagnosis and treatment of TB due to unusual clinical picture with increased smear-negative acid-fast. Bacilli is a typical finding on chest radiography and increased prevalence of EPTB [4,9]. TB/HIV co-infection is associated with special diagnostic and therapeutic challenges and constitutes an immense burden on healthcare systems of heavily infected countries like Ethiopia. Studies indicated that certain HIV-infected people develop TB, while others do not. This phenomenon iterates that being HIV positive is not the only factor for being infected with TB, and various determinant factors contribute to the TB/ HIV co-infection [14, 15]. Understanding TB/HIV co-infection predictors in the local context are critical for Ethiopia to improve TB/HIV co-infected patients' management.

Therefore, this study main goal was to determine the prevalence and associated factors of TB co-infection among HIV patients in the HIV clinics in the Amhara Region, Ethiopia. It is anticipated that findings from this study will contribute to the body of knowledge that informs TB/HIV program planners, decision-makers, and project implementers by providing predictors of TB/HIV co-infection. (WHO clinical stage, baseline CD4 count, month on ART, functional status, and smoking status). Functional status was measured at baseline, and a person was categorized as working if "he/she was able to perform usual work in or out of the house" ambulatory if "he/she was able to perform activities of daily living" and bedridden if "he/she was not able to perform activities of daily living." Alcohol use was categorized as "yes" if a person was currently or previously an alcoholic beverages consumer and "no" if he/she had never been an alcoholic beverages consumer [11]. This account of end-stage phthisis, or tuberculosis (TB), could well be a description of a patient seeking care at a primary health center in Ethiopia and other low-income settings today. The tubercle bacillus is profoundly limited by the human immunodeficiency virus (HIV), which allows the unrestrained proliferation of TB and the development of disease within the host [1]. HIV can also mask early symptoms of TB due to the lack of adequate immune response, and patients with both TB and HIV in resource-limited settings often present with advanced disease that largely resembles the two-hundred-year-old description provided by Andrew Duncan. In this situation, with a severely debilitated immune response and widespread TB, combined with limited resources for diagnosing and monitoring patients, mortality is high despite improved access to effective treatment of both diseases. Since it was discovered, HIV has infected an estimated 75 million people [2], and the World Health Organization (WHO) estimates that there are around 35 million people are living with HIV (PLHIV) today [3]. In sub-Saharan African, HIV is one of the main reasons for the increase

in TB. TB is considered the most prevalent opportunistic infection and the most common cause of AIDS-related death in PLHIV [4]. A review of autopsy studies performed on HIV-positive patients 17 who died in sub-Saharan Africa up to 2010 showed that TB was detected in 21-54% of cases and was considered the main cause of death in 32-45% [5].

2.2 Clinical Manifestation of Tuberculosis

TB is commonly categorized as either latent or active, although this simplifies a spectrum between the two forms [54, 72]. Active TB can present as a primary progressive disease, which is relatively rare, develops within a few weeks after exposure, and mainly affects untreated HIV patients or children younger than 5 years of age. Reactivation of latent TB can also occur at a lifetime risk of 5–10% in those infected [54]. The most common presentation of active TB in an immune-competent host is pulmonary TB, which is characterized by cough and low-grade fever, and occasionally hemoptysis and weight loss [73]. Active TB can also involve extra pulmonary manifestations resulting from hematogenous dissemination. The symptoms and signs depend largely on the site of infection and the immune reaction triggered by the bacteria, and TB can arise in any location (e.g., pleura, lymph nodes, central nervous system, bones, and joints) and can also occur as a more diffuse spread to internal organs that is termed military TB. Atypical manifestations characterize HIV-associated TB, and patients more often present with extra pulmonary TB and have less common radiological findings consistent with TB [75].

2.3 Tuberculosis Diagnosis

Despite advances in research concerning the pathology of TB, diagnosis of the active form of the disease is a complicated matter even in high-resource countries. The gold standard for a definite diagnosis is the culture of the bacteria in a solid or liquid medium, which represents the most sensitive method to detect TB and the only technique to enable drug sensitivity testing. However, culture is hampered by the slow growth rate of Mtb, and diagnosis can require from 2 to 8 weeks. It represents a considerable length of time when dealing with a contagious disease. During this period, there are risks of both clinical deteriorations of the patient and further spread of TB [76]. The culture of the bacteria is prone to contamination [71]. It requires a PF3 laboratory (biosafety level 3) and a steady supply of electricity and reagents, which restricts the use of this method in resource-limited settings. The most commonly used point-of-care diagnostic tests include smear microscopy with Ziel-Neelsen (ZN) staining, a technique largely unchanged since it was first described by Robert Koch in 1882. In that it is rapid and cheap, ZN staining is widely used worldwide for the detection of TB, and it is still the only method for the definite diagnosis of this disease in many low-income countries, including Ethiopia. However, a limitation of this technique is that detection requires a substantial bacterial burden in sputum (10,000 bacteria/ml), which results in low sensitivity. It is especially problematic in immune-compromised individuals because they are known to have fewer bacteria in sputum. Moreover, ZN staining cannot distinguish between tuberculous and non-tuberculous mycobacteria, and it cannot identify mycobacterial resistance. Further development of ZN staining is fluorescence microscopy. thus, allowing a larger area to be investigated and also improving the visibility of and sensitivity for mycobacteria. [78, 79]. another method is to detect Mtb DNA using PCR for partial amplification of the genetic material present in a specimen. The newly developed Gene-Xpert MTB/RIF assay offers rapid automated and real-time detection of the rpoB gene, and this method requires minimal training to perform and is endorsed by the WHO for fast diagnosis of TB, especially in PLHIV and patients with suspected multidrug-resistant TB (MDRTB) [81]. The Gene-Xpert MTB/RIF test has the advantages of being easy to perform and providing results in less than 2 hours. This technique also furnishes information about resistance to rifampicin because it detects the most common resistance mutation [81], although a risk of false-positive reactions has been reported [82].

Furthermore, it should be noted that this assay is expensive, especially for the cartridges that are used, and it requires an uninterrupted power supply, an ambient temperature of 28 degrees, and an environment without extreme humidity or dust. These features make Gene-Xpert MTB/RIF less appealing for deployment in peripheral settings. It has even been suggested that building sustainable primary health care would be a better investment. Another widely used method is chest X-ray, which in some cases and if performed by experienced readers can add diagnostic information suggestive of TB. Unfortunately, chest X-rays of PLHIV are difficult to interpret. Thus, the diagnosis of TB remains elusive, especially in that patient group, particularly in peripheral low-income settings. Accordingly, TB is often diagnosed solely on clinical grounds when suspicion is high enough to initiate anti-TB treatment (ATT) [83].

2.4 Treatment of Tuberculosis

In 1995, when the increase in TB was recognized worldwide, the WHO endorsed an intervention program called Directly Observed Treatment, Short-Course (DOTS). It was done after a landmark study published by Styblo [87] had shown that short-course therapy regimens could achieve high cure rates in low-resource settings. In addition to stipulating that treatment should be given under supervision in a programmatic environment, the DOTS strategy also focused on political commitment. According to some investigators [88], the wide implementation of this global health program has led to increases in treatment success rates, but follow-up data are scarce [89]. Treatment of drug-sensitive TB is based on four drugs: rifampicin, isoniazid, pyrazinamide, and ethambutol [90], and it is divided into two phases: (i) an intensive phase including all four of these agents for 2 months; (ii) a continuation phase of 4 months with two of the compounds. In patients with extra pulmonary TB such treatment can be extended for up to one year, especially if there is CNS involvement. Data on the treatment of drug-resistant TB are limited, and the use of such treatment is often based on expert opinion. The second-line drug regimens administered to treat MDR-TB usually include a fluoroquinolone and an injectable agent, and these regimens have serious side effects, should be administered for 18–24 months [73], and have a poor cure rate of 54–64% depending on treatment strategy [91]. Also, less than 60% of notified MDR-TB cases were started on treatment in 10 countries with a high burden of such TB in 2014 [4]. Treatment for latent TB is given to patients considered an increased risk of reactivation of TB (e.g., immunosuppression).

The benefit of treatment was recognized as early as in the 1950s when it was noted that a 6–12-month course of treatment led to a risk reduction of up to 90% in immune-competent [92]. IPT for 6 up to 36 months is recommended [87], although treatment with a combination of rifampicin and isoniazid could be considered.

2.5 Epidemiology of HIV

In 1981, cases of pneumocystis pneumonia and Kaposi's sarcoma and unexplained lymphadenopathy occurred in previously healthy homosexual men on the west and east coasts of the United States [18]. It soon became clear that these cases represented a new concentrated epidemic characterized by pronounced cellular immunodeficiency and the development of rare opportunistic infections [19]. The condition was given the name acquired immunodeficiency syndrome, or AIDS, in 1982. Reports of AIDS cases emerged in 1982 from patients with hemophilia, women and children from separate states, and Haitian immigrants, suggesting that a transmittable agent caused this novel epidemic. The etiological agent was identified as a previously unknown retrovirus in 1984 [20]. It was given the name HIV in 1986. In 1985 ELISA-based blood tests were developed, and the genome of HIV was sequenced. After that, the search began to find molecules targeting different steps in the viral life cycle for therapeutic use. Cases of AIDS were identified in Zaire in 1984, and a study published in 1986 indicated that the condition was 15–30 times more common in that country than in the United States [21]. Late in the 1980s, it had become increasingly evident that AIDS was also widespread in other parts of Africa, where it was initially called" slim disease" [22]. The prevalence of the disease approached 30% in regions such as, rural Uganda by the end of the 1980s [23] and 34% in rural South Africa at the end of the 1990s [24]. It has been estimated that HIV has infected 78 million people globally and that 35 million are currently living with the disease [26]. There is an unequal distribution of PLHIV, with more than two-thirds (71%) of them (i.e., about 25 million people) living in sub-Saharan Africa [27]. There were 2.1 million cases of new HIV infections in 2013, which represents a 38% decline from 2001, and approximately half (48%) of the people infected were aware of their status. Approximately 1.5 million people die from this disease every year, making HIV the most common cause of death caused by an infectious agent worldwide [26].

In Ethiopia, the problem seems to be stable though it is not as to the national and WHO target. According to the Ethiopian Public Health Institute (EPHI) report, it was estimated that 722,248 population live with HIV, 22, 827 people develop new infections and 14,872 people die of AIDS in Ethiopia [101].

The government of Ethiopia had been working to enable all people tested for HIV disclose their test results to their sexual partners regardless of the status of their tests Nevertheless, literature shows the prevalence of disclosure of HIV positive status is not only at its lower level but also highly variable across different parts of Ethiopia, as low as 41.8% and as high as 93.1% [101,102]. there was no an attempt to compile those evidences together to show overall status of the country in the disclosure of HIV positive result to sexual partner and the common factors contributing to it. The finding should be helpful for the efforts that the country is making to develop efficient HIV prevention and control policies and strategies. Various data bases were explored to ensure if there were attempts to compile evidences of HIV status disclosure prevalence and associated factors in Ethiopia [103].

2.6 The Human Immunodeficiency Virus

HIV is a bilipid enveloped RNA virus that exists in two major types designated HIV-1 and HIV-2. HIV-1 is spread globally and is by far the most prevalent, whereas HIV-2 is geographically restricted to West Africa. Henceforth in this text, HIV will refer to HIV-1 because that is the predominant type of virus found in Ethiopia. HIV contains genomic RNA and viral proteins, the most important of which are a viral protease, a reverse transcriptase and an integrase [28]. HIV is a retrovirus, which means that it carries its genetic information in RNA that must be transcribed into DNA to enable replication. This is achieved through attachment of the virion to CD4 receptors and the chemokine receptors CXCR4 and CCR5 [29] on the host cell's surface, which results in the fusing of the membranes and injection of the RNA into the cell matrix. Inside the host cell, the RNA is transcribed into double-stranded DNA by the viral reverse transcriptase. This linear DNA then enters the nucleus and fuses with the host DNA with the help of integrase. New virus particles are transcribed through replication mediated by the host cell DNA polymerase. After assembly, these particles bud off the cell surface via the protease and are ready to attach to other cells. In an HIV-infected human host, in addition to the activated circulating CD4 cells, there are also latent reservoirs of infected cells in the body in "silent" or "quiescent." CD4 cells and other immune cells, which is why HIV cannot be cured by ART. Furthermore, HIV has a rapid mutation rate because the reverse transcriptase is prone to errors, and viral generation time is short [29]. It complicates the development of a vaccine [30] and explains the rapid emergence of drug resistance in HIV patients given monotherapy [31].

2.7 Pathogenesis of HIV

CD4+ T helper cells (CD4 cells) are the main target of HIV, although several other cell types can also be infected, such as dendritic cells and macrophages [33, 34]. CD4 cells orchestrate the adaptive immune response to pathogens through cytokine mediators that elicit responses in other immune cells to clear or contain microorganisms entering the host and orchestrate tumor immunology. Thus far, at least four distinct subtypes of CD4 cells derived from the naïve CD4 T cells have been elucidated. In the 1980s, it was found that Th1 CD4 cells predominantly direct the immune response to intracellular pathogens, and Th2 CD4 cells target extracellular helminthic infections and are important in the induction of allergic conditions and asthma. Since then, two additional major subtypes have been identified [34]: Th17 CD4 cells mediate immune response to extracellular bacteria and fungi; T-regulatory cells (Tregs), which play a critical role in regulating the immune response to avert tissue damage. HIV disease progression is characterized by increasing loss of

CD4 cells driven by immune activation and viral replication in peripheral blood; this usually occurs gradually for several years, although there is an early massive depletion in the gastrointestinal tract in acute HIV infection [38]. Viral replication proceeds continuously but is prominent during acute infection and late in the disease. Several mechanisms behind the successive depletion of CD4 cells in HIV infection are being investigated. It appears that such depletion entails apoptosis of infected cells [39], but in most cases, uninfected cells or "bystander" CD4 cells are destroyed [41]. In fact, only as little as 0.1%-1% of circulating CD4 cells are infected with HIV [43], and the remaining cells are thought to be destroyed by indirect means as the result of immune activation [40]. The term immune activation is a broad expression referring to a state including activation, proliferation, and death of immune cells and the release of soluble molecules from such cells [44]. Immune activation is physiological when it occurs in other viral infections, whereas when it arises in response to HIV, it ensures constant viral replication and depletion of immune cells. Immune activation in chronic HIV disease is thought to be multifactorial and to be induced by some events that occur during infection [45]. HIV-replication perse causes a chronic activation. However, a more important aspect is probably microbial translocation, which involves preferential depletion of Th17 CD4 cells of the gut mucosa primarily during the acute infection; this leads to increased permeability of bacterial components from the gut to the blood and, in turn, contributes to chronic immune activation [47]. Furthermore, there is evidence that concurrent viral infections such as cytomegalovirus (CMV) can contribute to chronic immune activation [46].

Acute opportunistic infections such as TB have increased viral load both in vitro and in vivo. A possible mechanism for this effect is related to the increased cellular immune response elicited by the concurrent infection [13]. Epidemiological data concerning the impact of TB on HIV disease progression are divergent. However, it should be noted that the studies providing such information used different outcome variables and, more importantly, they were carried out in the pre-ART era [48]. Today, it is difficult to investigate the effect of TB on the natural history of HIV due to the availability of effective treatments. The level of immune activation in PLHIV has been assessed using several different immune phenotypic and serum markers, such as expression of CD38, CD25, CD69, and CD70 expression on T-cells, and levels of neopterin, TNF and β2-microglobulin in serum [50]. Neopterin is of particular interest because it has been demonstrated to be strongly correlated with HIV-disease progression [51]. It is produced by macrophages upon stimulation with IFN-γ released from activated T-cells and has been shown to contribute to oxidative stress [52]. Neopterin enables cheap, stable and reliable measurement of immunosuppression [53]. Indeed, neopterin can be measured in both serum and urine, and there is even a dipstick essay makes it a suitable analyte in peripheral settings [54].

2.8 Clinical Manifestation of HIV

The clinical course of HIV disease is characterized by increased susceptibility to opportunistic infections and malignancies over several years. Early studies indicated that the median time from primary infection (seroconversion) to the development of AIDS was approximately 10 years in Western and African materials [55, 56]. However, there are large intra-individual differences, ranging from rapid progressors [57] to elite controllers [58], and considerable individual variation in the clinical spectrum due to differences in exposure to opportunistic infections. Initial infection can be asymptomatic or present with what is called an acute retroviral syndrome, which initially may present with skin rash, sore throat or oral ulcerations, fever and enlarged lymph nodes. It is followed by a longer period of up to several years when the patient is largely asymptomatic or can exhibit persistent generalized lymphadenopathy. During this period, there is continuous viral replication of the virus at a viral "set point," albeit at a lower level than during the acute retroviral syndrome, and there is a slow decline in peripheral CD4 cells [59]. At the end stages of infection, the patient develops AIDS, the clinical syndrome characterized by a debilitated immune response and an array of opportunistic infections and malignancies.

2.9 Diagnosis of HIV-infection

Diagnosis of HIV infection is made by detecting antibodies, the detection of the p24 antigen, or viral RNA or DNA. The most common method entails antibody detection with enzyme-linked immune sorbent assay (ELISA). This technique is sensitive in chronic HIV, but antibodies against the virus do not develop until about 3-4 weeks after initial infection. Therefore, an assay detecting the p24 antigen of the virion is used to reduce the time elapsed before diagnosis by about a week. The earliest possible detection that can be achieved is by polymerase chain reaction (PCR) analysis of HIV RNA. Still, even this method cannot identify infection until there is active replication of the virus, which occurs 10-14 days after infection [60]. Rapid diagnostic tests have been developed to detect antibodies and are widely used. Ideally, if the result of these assays is positive, they should be confirmed by Western Blot assay. However, in resource-limited settings, diagnosis is based on two to three rapid tests as recommended by the WHO. An independent evaluation has shown that the rapid tests used in Ethiopia have a reasonable sensitivity of 97.3% and a specificity of 98.8% [62]. However, there have also been recent reports of false-positive rates of up to 7.7% with the Ethiopian HIV-diagnostic procedures [62].

2.10 Global Response to HIV

In the 1990s, it became clear that HIV was treatable, but high costs still kept most of PLHIV in resource-limited settings from access to treatment [90]. Besides, there was concern that treating HIV in low-resource areas was not possible due to the lack of health care infrastructure. A large-scale intervention could even lead aggravate the epidemic by leading to the development of drug-resistant strains ART anarchy" [7,8]. However, it became increasingly apparent that the prevalence of HIV in sub-Saharan Africa was reaching disastrous proportions, with a prevalence approaching one in three adults in some areas up to the end of the 1990s [24]. Moreover, the AIDS pandemic was beginning to have a detrimental social and societal impact, thus calling for prompt action to address a decreased life expectancy, massive numbers of children without parents and the threat of impending economic collapse and rising political instability. Through efforts of the joint United Nations Program on HIV/AIDS (UNAIDS), the Drug Access Initiative was launched in 1997, which

led to the piloting access to ART in Uganda and Côte d'Ivoire in 1998 and at about the same time also in rural Haiti through the HIV Equity Program launched by the non-governmental organization Partners in Health [91]. Brazil had already initiated nationwide treatment for PLHIV in 1996 and started production of generic antiviral drugs from 2001 [92]. Encouraged by the success of these early treatment efforts, UNAIDS collaborated with the World Bank and major drug companies to reduce costs and provide affordable treatment to more patients in resource-limited settings, mainly in sub-Saharan Africa [93]. In 2003 the WHO launched 2003 the initiative designated "3 by 5" [94] to provide free ART to three million PLHIV living in low- and middle-income countries by 2005.

It was intended to be a stepping stone towards the overall target of ensuring universal access to ART for all PLHIV, as had already been stated by Kofi Annan in his inaugural speech at the first African summit on HIV/AIDS, tuberculosis, and other infectious diseases held in 2001 in Abuja, Nigeria. The funding for 3 by 5 initiative was established mainly through the Global Fund, which was also proposed at the summit in Abuja and through the Presidential Emergency Plan for AIDS Relief (PEPFAR) initiated by the United States in 2003 [90]. The 3 by 5 initiative resulted in approximately 1.3 million people being on ART by the end of 2005, thus less than half of the projected goal. Nevertheless, this program successfully proved the feasibility of universal access to ART, and it showed that this intervention averted between 250,000 and 350,000 deaths [95]. The number infected of people on treatment has subsequently increased. In 2013 alone, 2 million people were enrolled in ART care, and in 2014, 13.6 million people, or about 37% of infected in the Africa region, were on ART [6].

2.11 Interaction between HIV and TB

HIV and TB have reciprocal interactions that benefit the proliferation of both pathogens [2]. HIV raises the risk of TB approximately tenfold. However, this cannot be entirely explained by a low CD4 cell count because the increase is seen even during the early stages of infection [64], and the risk is not eliminated (albeit is lowered considerably) by ART [65]. The growth and proliferation of Mtb can be augmented during several stages of HIV infection. Increased survival of Mtb has been observed in infected macrophages [65], and it is also clear that the lack of a cell-mediated immune system plays an essential role in the increased risk of TB seen in HIV patients. The importance of CD4 cells is illustrated by an investigation showing that both progressions to active TB after exposure to Mtb and reactivation of latent TB occurred to a higher degree in macaques depleted of CD4 cells than in control animals with normal CD4 cell levels [67]. In human HIV patients with severely depressed CD4 cell counts, granulomas are ill-formed, necrotic, and multibacillary [2].

Furthermore, preferential depletion of Mtb-specific CD4 cells during HIV infection has been observed [12, 69]. Conversely, TB has been found to increase the risk of both HIV-related death and other opportunistic infections [69]. It has been explained by increased viral loads [71] in co-infected patients. Still, it is also possible that other mechanisms of immune activation related to TB can contribute to this exacerbation of HIV.

2.12 Treatment of HIV/TB Co-Infected Patients

Treatment of TB in HIV-positive patients follows the same guidelines as in HIV-negative patients, although the underlying evidence is not as strong. The most effective approach to prevent TB infection in HIV patients is to give ART, which has been shown to provide a risk reduction of 54–92% [93]. As in HIV-negative patients, it is also recommended that IPT be given for at least 6 months to patients with positive or unknown TST results and in whom the active disease has been ruled out [73], although only 30% of patients eligible for IPT were given such treatment in 2012 [5]. A meta-analysis recently showed that this approach is beneficial in that it reduces morbidity of TB even if it does not affect mortality in HIV/TB-co-infected patients [92]. However, as IPT is part of a scheme including screening for TB, this interventional package may still have an important impact on survival [94]. The timing of ART in TB patients has been heavily debated, starting with early concerns about drug interactions, and it was recommended, if possible, to defer ART until after ATT [95]. After a series of randomized trials [97], it was evident that mortality was decreased if ART was introduced during treatment of TB; in a sub-analysis from one of the studies, there was also a trend towards improved survival if treatment was initiated early (within 2 weeks) and in patients with severe immunosuppression (<50cells/mm3) [99]. These observations resulted in a change in the WHO recommendations in 2013 to recommend that ART be started within 2 weeks in patients with a CD4 cell count of < 50/mm3 and within the intensive phase (8 weeks) in patients with less severe immunosuppression [85]. However, in 2014 a large multicenter study carried out in Africa [99], showed no increase in survival in patients with CD4 cell counts of > 220/mm3, and the authors suggest that ART could be deferred in patients above this threshold. Furthermore, Török et al. [100] found that early ART led to increased mortality in patients with TB meningitis.

2.13 Treatment of HIV infection-related TB

In principle, TB treatment in individuals with HIV infection should be the same as that for patients with TB who do not have HIV disease. Standard first-line therapy for TB with a 4-drug intensive treatment phase of 2 months, followed by 4 months of treatment with a 2-drug regimen, is highly effective in patients with HIV-infection-related TB. Unlike the treatment of HIV-uninfected patients, however, treatment of HIV-infected patients with TB presents a myriad of clinical challenges regarding the duration of treatment, frequency of administration, management of drug interactions, and complications of therapy, such as drug toxicity and immune reconstitution disease. Because such patients are being treated for 2 diseases, the goals of therapy must be balanced so that optimal outcomes in terms of treatment response and prevention of drug resistance are achieved for both conditions. Early reports of treatment outcomes in patients with HIV-infection-related TB revealed that initial outcomes were generally very good. Still, long-term outcomes were poor because of HIV infection-related mortality [9]. In recent years, because of the more effective treatment of HIV infection, long-term outcomes of TB therapy have improved, and additional problems, such as recurrent TB, drug-drug interactions, and

overlapping drug toxicities, have emerged. Duration of treatment. Because initial responses to therapy are most excellent in both HIV-infected and HIV-uninfected patients, the optimal duration of TB treatment is determined by the risk of relapse. Currently, treatment guidelines recommend that the duration of TB therapy should be the same for both HIV-infected and HIV-uninfected persons [11–13]. For pulmonary infection with drug-susceptible Mycobacterium tuberculosis, a 6-month course of rifamycin-based therapy is the standard of care [11], because of comparable rates of TB relapse among persons receiving 6-month regimens of rifamycin-based therapy (e.g., rifampin or rifabutin) [14–17]. However, most of the studies that have shown equal efficacy were relatively small and not randomized. Only 2 randomized trials have been reported on relapse rate among HIV-infected persons with TB, compared with that among HIV-uninfected patients with TB, who receive 6 months of rifamycin-based therapy [18, 19]. These studies, both performed in settings with very high community rates of TB, showed that a longer duration of therapy was associated with a lower short-term recurrence rate. Perriens et al. [18], working in former Zaire, found that 12 months of standard rifampin-based therapy resulted in a significantly lower recurrence rate at 18 months than a 6-month regimen. Fitzgerald et al. [19] studied HIV-infected and HIV uninfected patients with TB in Haiti and found that recurrences were significantly reduced only among HIV-infected patients when isoniazid was continued for 1 year after a 6-month standard regimen for TB. In neither study were the investigators able to distinguish relapse from reinfection, and patients did not have access to antiretroviral therapy.

Nonetheless, these trials suggest that, in high-burden areas, the likelihood of recurrent TB is reduced by either longer treatment of the initial episode or secondary prophylactic (suppressive) therapy with isoniazid. In addition to this, various surved studies have suggested that the relapse rate after such therapy may be higher among HIV-infected persons than among HIV-uninfected persons, with rates of ~2% among HIV-uninfected persons and as high as 9% among HIV-infected persons [21–23]. In an observational cohort study involving South African gold miners, Churchyard et al. [24] found that secondary isoniazid preventive therapy reduced the risk of recurrent TB substantially. The primary risk factor for TB recurrence among HIV-infected patients with TB appears to be low CD4+T lymphocyte count, with the risk highest among persons with a CD4+ T lymphocyte count 100 cells/mm3 [22, 23]. Low CD4+ T lymphocyte count appears to be a stronger risk factor than the factors associated with relapse in HIV-seronegative persons: cavitary pulmonary disease, positive sputum culture result after 2 months of treatment, bilateral pulmonary disease, low body weight, and white race [22, 25]. However, large-scale comparative studies of risk factors for relapse in HIV-infected persons with TB are needed in HIV-uninfected patients with TB. A recent study from Botswana found that low pyrazinamide concentrations were associated with poor treatment outcome (defined as treatment failure or death) after adjusting for HIV infection and CD4+ T lymphocyte count [25].

2.14Prevention and Control Method of Tuberculosis TB

There are several TB prevention activities. It includes preventing people with latent TB from developing active and infectious TB disease. TB infection control consists of masks and respirators. It means preventing the transmission of TB in such setting is accessible in hospitals and prison houses.

The pasteurization of milk helps to prevent humans from getting bovine TB cases. There is a vaccine for TB. Even though, it takes only a small contribution to TB prevention. It makes little interrupt on the transmission of TB among adults [23].

2.15 Tuberculosis Protections Cough Protocol

Tuberculosis is caused when a person breathes in TB bacteria. Therefore, people with TB who are not on effective treatment, they cannot release TB bacteria. If you have TB cases or you might have TB cases event, you will be cough etiquette, you should cover your mouth and nose with a tissue. You should put your used tissue in a bin. If you don't have a tissue, you should cough or sneeze into your upper sleeve or elbow. You should not cough into your hands. After you have coughed, you should wash your hands [22, 23].

2.16 TB Prevention the BCG Vaccine

The vaccine is named as Bacillus Calmette-Guerin was developed in 1920s; it is one of the most widely used of all current vaccines, and it reaches more than 80% of all newborn children and infants in countries where it is part of the national childhood immunization program. The BCG vaccine has shown to provide children with excellent protection against the disseminated forms of tubtuculosis. Protection against pulmonary TB in adults is viable. Transmission originates from adult cases of pulmonary tubtuculosis. The BCG vaccine is used to protect children insteady of the interrupt transmission among adults. The BCG vaccine will often result in the person vaccinated positively resulting in a TB skin test [22].

Bacillus Calmette-Guerin vaccination is highly effective in preventing childhood TB. BCG immunization has also been protective of other mycobacterial infections, such as leprosy, Buruli ulcer and glandular disease. It has been used since 1921 for TB prevention. In Ethiopia, the Expanded Program on Immunization (EPI) was initiated in 1980 by the Ministry of Health (MOH) in close cooperation with WHO, UNICEF and other partners and implemented in each region by the Regional Health Bureaus to reach 90% coverage among children under one year of age by the year 1990 which targeted against six diseases recommended by world health organization [21]. For the past time, Health Sector Development Programs and the current Health Sector Transformation Plan is Expanded Program on Immunization. In this Programme, the BCG vaccine has given to the newborn if asymptomatic for TB screening to protect against TB infection. BCG is the most widely administered vaccines in infancy and most cost-effective mthods in the case of low-income countries. WHO recommends BCG vaccination is more valuable to young children, particularly infants. It was expected that adolescent and adult vaccine with 60% efficacy delivered to 20% of the population at risk could prevent about 30–50 million new cases of TB by 2050.1 Similar to the global pattern over the same period, BCG coverage in Africa currently stands at 89% compared with 16% in 1980. Each year more than 100 million children are immunized worldwide [21, 22].

In Ethiopia, four to ten children age 12–23 months (39%) received all basic vaccinations at some time. furthermore 22% received these vaccinations before their first birthday. In Senegal, BCG immunization coverage at birth was 94.7%, as indicated by Senegal Demographic and Health Survey (DHS), 2010–2011. Full immunization coverage can affected by the mother's education, marital status, mother's ability to show a vaccination card, access to information from television and place of delivery. In industrialized countries, higher childhood vaccination rates have been associated with family characteristics, such as higher household income and older maternal age, child characteristics, such as younger age, early birth order and good health, and healthcare organization factors including easy access to immunization facilities [22].

2.17Tuberculosis Education

Tuberculosis education is necessary for people with a TB cases. People with TB need to know how to take their TB drugs properly. They also need to know how to make sure that they do not pass TB on to other people. But TB education is also necessary for the general public. The public needs to know basic information about Tsomereasons, including reducing the stigma associated with TB [23].

2.18Tuberculosis Treatment as Prevention

Tuberculosis drug treatment for prevention, also known as chemoprophylaxis, can reduce the risk of the first episode of active TB occurring in people with latent Tuberculosis. Isoniazid is one of the drugs used to prevent latent TB from progressing to active TB or TB disease. Isoniazid is a cheap drug, but in a similar way to using the BCG vaccine, it is mainly used to protect individuals rather than interrupt transmission between adults. Because children have infectious of TB. It is hard to administer isoniazid adults on a large scale those who do not have any symptoms. Taking isoniazid daily for six months is difficult in respect of adherence. As a result, many individuals who could benefit from the treatment stop taking the drug before the end of six months. There have concerns about the possible impact of TB treatment for prevention programs concerning to drug resistance. A review of the scientific evidence has show that has no concern. The benefit of isoniazid preventative people living with HIV and who have or may have had latent TB which has also recently been emphasized [23].

2.19Preventing TB Transmission in households, masks

The houses should adequately ventilated, anyone who cough should be educated on cough etiquette and respiratory hygiene and should follow such practice at all times and While smear-positive, Tuberculosis patients should spend much time as possible outdoors. If possible sleep alone, adequately ventilated room spend as little time as possible on public transport and Spend as little time as possible in places where large numbers of people gather together.

2.19 Physical Measures for TB Prevention

Before drug treatment for TB cases became available, removing TB patients from their homes and putting them in isolation in sanatoria was the main way to reduce TB transmission. The policy has changed in the vast majority of countries after studies demonstrated that if patients stayed at home and were treated on an "outpatient" basis, it did not increase the risk of TB among the household contacts of the people with TB. It is because drug treatment quickly makes a TB patient uninfectious. Most household contacts who become infected will have already become infected before diagnosing TB has been made [22].

To conclude, there is no need of people to leave their homes because they have tuberculosis. When someone has infectious extensively drug-resistant Tuberculosis which is not feasible to isolate them in home. Besides, people may still need to go into a health care facility because complications arise from condition. There may be a need people to reduce the chances of transmission within a health care facility. The measures described mainly apply to resource-poor settings, and the recommendations can be different where more resources are available [23].

2.20 Tuberculosis Prevention in Health Care Facility

From the prevention side, doctors and other health care workers, who provide care for TB, must follow infection control procedures to ensure that TB infection is not passed from one person to another. Every country should have infection control guidance that needs to consider local facilities and resources and the number of people served with care particularly, infection control guidance must not only be written but also implemented.
The World Health Organization has established the WHO Global TB Programme. This program aims to advance universal access to TB prevention, care and control, guide the global response to threats, and promote innovation. Their core functions include Provision of global leadership on TB, Development of evidence-based policies, strategies and standards for TB prevention, care and control, Provision of technical support and capacity building for the Member States, Monitoring the global TB situation measuring progress in TB care, control, and financing, Shaping the TB research agenda with the dissemination of valuable knowledge and Facilitation of partnerships for TB action.

2.21 Administrative control measures

The administrative controls for TB infection control are placed at the top of the hierarchy. They are the most effective way to reduce the production of TB aerosols in the local environment. Early diagnosis of TB remains the most important intervention to reduce TB transmission. Several steps and role players are needed to ensure early diagnosis. These include A patient-centered service**,** Heightened clinical suspicion of TB**,** Rapid specimen collection and processing**,** Directed patient flows to avoid mixing of coughing adults with

vulnerable patients (e.g., immune compromised, young or older people)**,** Implementation of strict cough triage and respiratory hygiene (separate coughing patients and provide them with surgical masks)**,** Effective patient tracking and recall to commence treatment**,** Treatment adherence by patients and Active case-finding among household TB contacts (people who have been exposed to a TB case) [24].

Chapter 3: Material and Methods

3.1 Description of Study area

North Wollo is the one among ten zones of the Amhara Region in Ethiopia. It is bordered on the south by Debub Wollo (South Wollo), on the west by Debub Gondar (South Gondar), on the north by Wag Herma, on the northeast by Tigray Region, and on the east by Afar Region; the Mille River defines part of its southern border. It is located 521 kilometers away from Addis Ababa. The global positioning system coordinates of Woldia in terms of latitude and longitude indicate that 11° 49' 59.99" N and 39° 40' 59.99" E, respectively. The elevation is 2,112 meters above sea level. Woldia has an estimated total population of 46,139 people. Out of this 23, 000 are males, and 23,139 are females [20].

Figure 1: Map of the study area.

3.2 Source and Study Population

3.2.1 Source of population

- The Pulmonary TB diagnosed people in the study area

3.2.2 Study population

- The HIV infection among Pulmonary Tuberculosis Patients **in 2015-2019** In Woldia Comprehensive Specialized Hospital, Ethiopia.

Those who have been diagnosed with Pulmonary TB in Woldia Comprehensive Specialized Hospital and have accurate information and peoples who have HIV and have been diagnosed with Pulmonary TB during the study period.

3.3 Study design and period

- ✓ The Prevalence and Associated Factors of HIV infection among Pulmonary Tuberculosis Patients Retrospective Study was conducted based on data collected from Woldia Comprehensive Specialized Hospital, Ethiopia (2015-2019).

3.4 Source of data

- **The five years (2015-2019) retrospective data were collected from the** Woldia Comprehensive Specialized Hospital **health records to review and analyze HIV infection among pulmonary TB and associated factors in the study area.**
- Additionally, data was collected from Amhara Regional State Health bureau, North Wollo Zone Health Department and the Woldia District Health Office.

3.5 Inclusion and exclusion criteria

3.5.1 Inclusion criteria

The Pulmonary TB diagnosed (WHO, Golden Standard TB test) people in 2015-2019 In Woldia Comprehensive Specialized Hospital, Ethiopia, at the time of the study

3.5.2 Exclusion criteria

People who did not have Pulmonary TB when they were diagnosed and did not have accurate information in Woldia Comprehensive Specialized Hospital, Ethiopia, at the time of the study

3.6 Study Variables

3.6.1 Dependent variable

HIV positive among pulmonary tuberculosis patients

3.6.2 Independent variables

Socio-demographic characteristics: Age, sex, residence, educational status of patients, occupational status, marital status and monthly income

Behavioral factors; smoking and alcohol dirking

3.7 Clinical characteristics of patients

Previous History of PTB, Year of TB Diagnosis conducted, Category of Patient, Types of PTB, WHO stage, CD4 count cells, Duration on ART, CPT initiated, History of Opportunistic, Asthma, Nutritional status, Pretreatment weight, Pretreatment BMI Kg/m2, DM, Cough, Cough length, Fever and Night sweet

3.8 Data analysis

All Data was entered into an MS Excel spreadsheet and analyzed using SPSS statistical software package (version 25). Frequency, percentage and range were used to present the data. The logistic regression was used to assess the association between dependent and independent variables. Associations between variables were determined using the odds ratio and 95 % confidence interval (CI). A *p*-value of <0.05 was considered statistically significant.

3.9 Quality control

Standardized protocols and checklist were used in study site by the health officer to collect data during the study period. The data collector was supported the additional information by the TB clinic doctors and were given information about TB and HIV patients medical

record from the Woldia comprehensive specialized hospital during the data collection time.one supervisor from the Woldia hospital periodically monitored data collection.

3.10 Ethical consideration

This study's ethical approval was obtained from the institutional ethical review committee of Southern Medical University, School of public health. The supportive letter was obtained from SMU School of public health, EPHI/PHEM, Federal Ministry of Health, Amhara Public Health Institute and Woldia Comprehensive Specialized Hospital, where the research was carried out. The study's purpose will clearly explain to all study participants before obtaining verbal/written informed consent.

3.11Dissemination of the research findings

The findings of this study could be submitted and presented to Southern Medical University (SMU) School of Public Health, Amhara Regional State of Health bureau, in north Wollo Zone Health Department, Woldia Comprehensive Specialized Hospital, as well as Woldia town Health office distributed for different purposes. The findings were also presented in various seminars and workshops and published in a scientific journal.

Chapter 4: Result

4.1 Socio-demographic Characteristics of the Study Participant

A total of 584 TB infected patients under PTB treatment were included. Out of those respondents, 170 (29.1%) were HIV patients, whereas 414 (70.89%) were done not have HIV. Of the 584 patients, 221 (37.8%) were female, and 363 (62.2%) were males. Regarding the marital status patients, 120 (20.5%) were single, 367(62.2%) were married 48 (8.2%) were widowed, and 49(8.4%) were divorced. Among resident patients, 319 (54.6%) were urban and 265(45.4%) rural.

Table 1. Socio-demographic characteristics of HIV patients among PTB patients at Woldia comprehensive specialized hospital, Woldia town, northeastern Ethiopia, 2021

Variable	Total number	percentage
Sex		
Male	363	62.2
Female	221	37.8
Age		
≤24	360	61.6
25-45	148	25.3
≥46	76	13.0
Occupation status		
Housewife	80	13.7
Daily labor	62	10.6
Government employed	104	17.8
Merchant	167	28.6
Farmer	171	29.3
Marital status		
Single	120	20.5
Married	367	62.8
Widowed	48	8.2
Divorced	49	8.4
Income		
<1000	156	26.7
1000-2000	332	56.8
>2000	96	16.4
Educational status		
No education	228	39
Primary	142	24.3
Secondary	91	15.6
Certificate and Above	123	21.1
Residence		
Urban	319	54.6
Rural	265	45.4

4.2 The prevalence of IHV among PTB patients

Among the total PTB cases, the proportion of HIV infection among males was 31.4 % (114/170) which is higher than the HIV infection among females 25.4 % (56/170). In the age group of ≤24 years, the proportion of HIV 54.7% (93/170) was higher than the prevalence 31.1% (53/170) among the 25-45 age groups.

The overall prevalence shows that the number of tuberculosis patients is high in 2016, 2017 and 2019 respectively and in 2017, 2018, and 2019 indicates that the number of people living with HIV is high.

Of the 601 patients screened, 584 were positively diagnosed with pulmonary TB Figs. (1 and 3) giving the overall prevalence rate of 70.9 % Fig. (2). in the present study, more than a half (*n*=148; 25.3%) of participants had CD4 count ranged between 200-500/µl, 54.6% (*n*=319) of respondents had CD4 count <200/µl and 20 % (*n*=117) of respondents had CD4 count >500/µl.

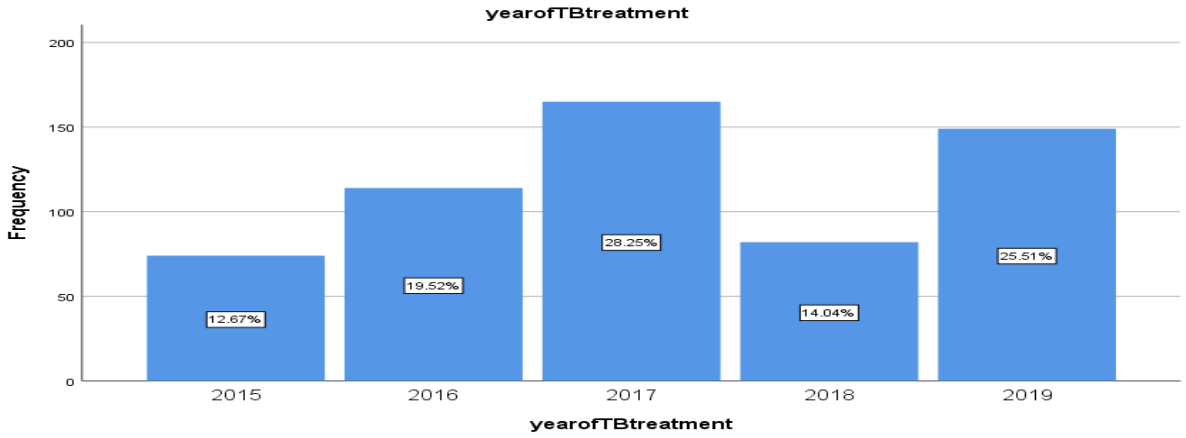

Figure 2. Year of TB treatment in Woldia Comprehensive Specialized Hospital

Table 2. The prevalence of HIV patients among PTB patients at Woldia comprehensive specialized hospital, Woldia town, northeastern Ethiopia, 2021

Variables		HIV status		COR (95%CI)	P-value
	Total (No, %)	Negative (No, %)	Positive (No, %)		
Sex					
Male	363(62.2%)	249 (68.6)	114 (31.4)	0.74 (0.509-1.07)	0.118 *
Female	221(37.8%)	165 (74.6)	56 (25.4)	1	
Age					
≤24	360(61.6%)	267(74.1)	93(54.7)	1.33 (0.74-2.27)	0.305
25-45	148(25.3%	95(64.2)	53(31.1)	0.83 (0.46-1.49)	0.53
≥46	76(13.0%)	52(68.4)	24(14.1)	1	
Occupation status					
Housewife	80(13.7%)	63(78.7)	17(21.3)	1.8 (0.99-3.45)	0.052
Daily labor	62(10.6%)	41(66.2)	21(33.8)	0.98 (0.53-1.805)	0.94
Government employed	104(17.8%)	73(70.2)	31(29.8)	1.18 (0.69-1.99)	0.54
Merchant	167(28.6%)	123(73.6)	44(26.4)	1.4 (0.87-2.23)	0.161
Farmer	171(29.3%)	114(66.6)	57(33.4)	1	
Marital status					
Single	120(20.5%)	82(68.3)	38(31.7)	0.30 (0.12-0.77)	0.12
Married	367(62.8%)	251(68.4)	116(31.6)	0.30 (0.125-0.73)	0.008
Widowed	48(8.2%)	38(79.2)	10(20.8)	0.53 (0.18-1.59)	0.26
Divorced	49(8.4%)	43(87.7)	6(12.3)	1	
Income					
<1000	156(26.7%)	118(75.6)	38(24.4)	1.28 (0.722-2.27)	0.40
1000-2000	332(56.8%)	228(68.7)	104(31.3)	0.93 (0.55-1.49)	0.69
>2000	96(16.4%)	68(70.8)	28(29.2)	1	
Educational status					

No education	228(39.0%)	157(68.8)	71(31.2)	1.15 (0.78-1.82)	0.565
Primary	142(24.3%)	108(76)	34(24)	1.65 (0.96- 2.81)	0.068
Secondary	91(15.6%)	68(74.7)	23(25.3)	1.53 (0.840-2.78)	0.164
Certificate and above	123(21.1%)	81(65.9)	42(34.1)	1	
Residence					
Urban	319(54.6%)	228(71.5)	91(28.5)	1.064 (0.744-1.52)	0.734
Rural	265(45.4%)	186(70.2)	79(29.8)	1	
Total	584	414(70.9)	170(29.1)		

1 Reference category

* Variables from Bivariable analysis of *p<0.05*

4.3 Clinical characteristics of the study participant

The majority (96.2%) (95% CI: 2.25-14.6) of the study participants category were retreatment TB cases. Four hundred fifteen (71.1%) of the study participants had smear-positive Pulmonary TB,93, (15.9%) had smear-negative Pulmonary TB, and the remaining 76, (13.0%) had Extra pulmonary TB, and 68 (11.6%) were categorized to WHO stage 3 HIV disease during the initiation of their TB treatment. 66 (11.5%) of the patients had experienced opportunism. The majority (88.8%) with 95% CI: 0.14–0.650) of study participants did not take CPT. from 584 PTB patients 66 (11.3%) were Smokers and 518 (88.7%) were nonsmoker.

From Bivariable analysis clinically characteristics factors, participants smoker 1.21 were higher odds of who were nonsmoker patients (COR: 1.21, 95% CI (0.674-2.16) Participants WHO stage 3 were 3.11 higher times odds of HIV positive compared with stage 1 (COR: 3.11, 95% CI (1.5-6.48). among participants who have a history of opportunistic infection were 5.7 higher odds of HIV positive compared with who do not have an opportunistic infection (COR: 5.7, 95% CI (2.25-14.6). Among PTB patients, the retreatment case was 5.63 were higher odds of HIV than new cases (COR:5.6, 95% (CI 2.25-14.06). (Table 2)

Table 3. Clinical characteristics of HIV patients among PTB patients at Woldia comprehensive specialized hospital, Woldia town, Ethiopia, 2021

Variables	**HIV status**			**COR (95%CI)**	**P-value**
	Total (No %)	**Positive (No %)**	**Negative (No %)**		
Previous History of PTB					
Yes	140 (24.0%)	107	33	1.165 (0.79-1.71)	0.434
No	444 (76.0%)	307	137	1	
Year of TB Diagnosis conducted					
2015	74(12.7%)	45	29	0.88 (0.497 -1.57)	0.668
2016	113(19.3%)	90	23	2.24 (1.26-3.92)	0.006*
2017	166(28.4%)	132	34	2.020 (1.33- 3.65)	0.002*
2018	82(14.0%)	52	30	0.956 (0.56-1.7)	0.96
2019	149(25.5%)	95	54	1	
Category of Patient					
New	22(3.8%)	7	15	1	
Retreatment	562(96.2%)	407	155	5.63 (2.25-14.06)	0.000*
Types of PTB					
Smear positive (SPP TB)	415(71.1%)	283	132	252 (0.08-0.54)	0.000*
Smear negative (SNP TB)	93(15.9%)	63	30	247 (0.105-0.58)	0.001*
Extra PTB	76(13.0%)	68	8	1	
WHO stage					
Stage I	385(65.9%)	261	124	1	
Stage II	60(10.3%)	45	15	1.42 (0.76-2.65)	0.264
Stage III	68(11.6%)	59	9	3.11 (1.5-6.48)	0.002*
Stage IV	71(12.2%)	49	22	1.06 (0.61-1.82)	0.84
CD4 count cells					

<200	319(54.6%)	212	107	0.384 (223-0.66)	0.001*
200-500	148(25.3%)	104	44	0.46 (0.250- 0.84)	0.011*
>500	117(20.0%)	98	19	1	
Duration on ART					
<5Yrs	87(14.9%)	61	26	0.95 (0.58-1.57)	0.86
≥5yrs	497(85.1%)	353	144	1	
CPT initiated					
Yes	66(11.3%)	58	8	1	
No	518(88.7%)	356	162	0.303 (0.14-0.650)	0.002*
History of Opportunistic					
Yes	66(11.5%)	61	5	5.7(2.25-14.46)	0.000*
No	518(88.8%)	353	165	1	
Smoking					
Yes	66(11.3%)	49	17	1.21 (0.674-2.16)	0.525
No	518(88.7%)	365	153	**1**	
Alcohol drinking					
Yes	90(15.4%)	69	21	1.42 (0.84-2.34)	0.19*
No	494(84.6%)	345	149	1	
Asthma					
Yes	58(9.9%)	44	14	1.325 (0.76-2.49)	0.38
No	526(90.1)	370	156	1	
Nutritional status					
Normal	334(57.2%)	237	97	0.87 (0.55-1.38)	0.545
Moderate(MAM)	124(21.2%)	84	40	0.75 (0.43-1.29)	0.292
SAM	126(21.6%)	93	33	1	
Pretreatment weight					
20-29Kg	385(65.9%)	261	124	0.95 (0.55-1.62)	0.84
30-39Kg	60(10.3%)	45	15	1.35 (0.62- 2.9)	0.45
40-54Kg	68(11.6%)	59	9	2.94 (1.24- 6.98)	0.014
>54Kg	71(12.2%)	49	22	1	
Pretreatment BMI Kg/m2					
Under weight	81(13.9%)	64	17	1.15 (0.42- 3.12)	0.79
Normal weight	135(23.1%)	97	38	0.78 (0.30- 1.96)	0.59
Over weight	338(57.9%)	230	108	0.65 (0.270-1.56)	0.33
Obese	30(5.1%)	23	7	1	
DM					
Yes	46(7.9%)	37	9	1.76 (0.83-3.72)	0.142*
No	538(92.1%)	377	161	1	
Cough					
Yes	46(7.9%)	37	9	0.93 (0.52- 1.64)	0.79
No	538(92.1%)	377	161	1	
Cough length					
1 weak	22(3.8%)	7	15	1	
≥2 week	562(96.2%)	407	165	5.63(2.25-14.06)	0.000*
Fever					
Yes	527(90.2%)	369	158	0.62(0.32-1.21)	0.162*
No	57(9.8%)	45	12	1	
Night sweet					
Yes	501(85.8%)	350	151	0.69 (0.4-188)	0.180*
No	83(14.2%)	64	19	1	

1 Reference category

* Variables from Bivariable and multivariable analysis of *p<0.05*

4.4 Factors associated with HIV infection among PTB from multivariable and Bi-variable analysis

All P-value < 0.25 were taken from Bivariable, and multivariable analysis entered into multiple logistic regression models by using backward logistic regression to control confounders and get P- value < 0.05 significant association to HIV among PTB patients.

In the multivariable analysis from clinically characteristics factors WHO stage 3, category of patient and history of opportunistic infection was a significant association with HIV patients among PTB. WHO 3 was 2.69 times more likely HIV positive than WHO stage 1 (AOR: 2.69, 95% CI (1.28-5.66). Patients who had opportunistic infection were 5.27 times more likely HIV patients than patients who had not (AOR: 5.27, 95% CI (2.05-13.56)). And the category of patient retreatment cases was 5.02 times more likely HIV patients compared to new cases (AOR: 5.02, 95% CI (1.97-12.78)).

Table 4. The univariate and multivariate analysis of factors associated with HIV infection at Woldia comprehensive specialized Hospital, Woldia town, Ethiopia, 2021

Variables		HIV statues		COR (95%CI)	P-value	AOR (95%CI)	P-value
		Negative (No %)	Positive (No %)				
Sex	Male	249	114	1.35(0.92-1.96)	0.118	0.74(0.51-1.08)	0.118
	Female	165	56	1			
Age	≤24	267	93	1.081 (0.71-1.64)	0.713	0.45(0.23-0.85)	0.014
	25-45	95	53	2.22 (1.17-4.19)	0.014	0.48(0.24-0.97)	0.042
	≥46	52	24	1			
Smoking	Yes	49	17	0.83 (0.46-1.48)	0.525	1.208(0.67-2.16)	0.525
	No	365	153	**1**			
Alcohol drinking	Yes	69	21	0.705 (0.42-1.2)	0.191	1.42 (0.84-2.4)	0.191
	No	345	149	1			
Asthma	Yes	44	14	0.755 (0.402-1.42)	0.38	1.33(0.71-2.49)	0.38
	No	370	156	1			
Nutritional status	Normal	237	97	0.87 (0.55-1.38)	0.545	1.15(0.73-1.83	0.545
	Moderate	84	40	0.75 (0.43-1.29)	0.292	0.86(0.55-1.34)	0.504
	SAM	93	33	1			
WHO staging	Stage I	261	124	1			
	Stage II	45	15	1.42 (0.77-2.6)	0.264	1.26 (0.65-2.43)	0.496
	Stage III	59	9	3.11 (1.5-6.48)	0.002	2.69 (1.28-5.66)	**0.009**
	Stage IV	49	22	1.06 (0.61-1.82)	0.84	0.95 (0.54-1.68)	0.87
History of Opportunistic	Yes	61	5	5.7(2.25-14.46)	0.000	5.27(2.05-13.56)	0,001
	No	353	165	1			
Category of Patient	New	7	15	1			
	Retreatment	407	155	5.63(2.25-14.63)	0.000	5.02(1.97-12.78)	0.001
	<200	212	107	0.38 (0.22-0.66)	0.001	2.63(1.51-4.48)	0.001

CD4 count cells	200-500	104	44	0.46(0.250-0.84)	0.011	1.19(0.78-1.82)	0.413
	>500	98	19	1			

1 Reference category

** Variables from Univariate and multivariable analysis of $p<0.05$

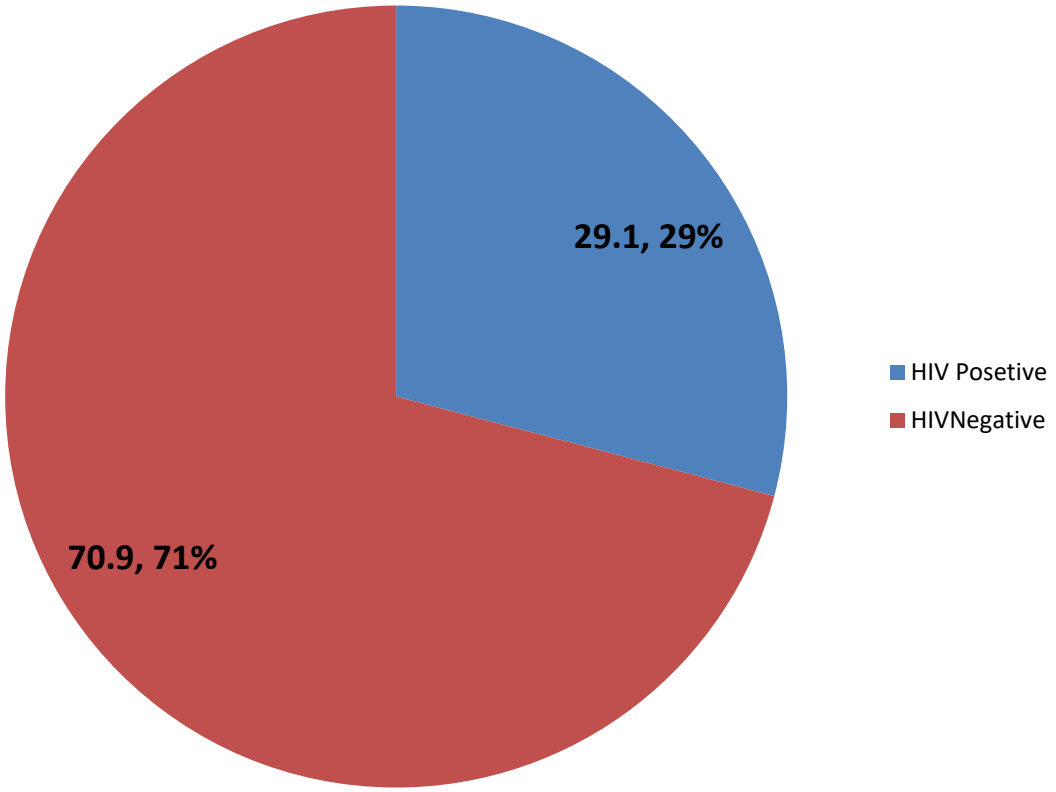

Figure 3: the prevalence rate of HIV infection among PTB patients in Woldia Comprehensive specialized Hospital, Ethiopia

Chapter 5: Discussion

5.1 Discussion of Results

This study used a retrospective design to assess the prevalence and associated factors of HIV patients among PTB patients in Woldia comprehensive specialized Hospital, Woldia, North-Eastern Ethiopia. The study found that the prevalence of HIV patients among PTB was 29.1%. The North Wollo Zone has a high prevalence of HIV infection among the Amhara region in Ethiopia. It is concerned with the Community living standard, lack of awareness of the transmission of HIV, and there is a balance between unemployment and job creation. It has increased the prevalence of HIV in the context of the study area.

In this study, WHO stage 3, opportunistic infection and category of patient retreatment were significantly associated with HIV patients among PTB. Tuberculosis and HIV are incorporated with the main burden of infectious disease in those whose resources are limited countries [26, 27]. The TB treatment TB-HIV outcome co-infected patients in various settings could provide evidence for evaluating the country's TB control program and determining future directions.

According to WHO 2017 report, the global treatment success rate for HIV-associated TB cases among the 2015 cohort was 78%, and in the WHO Africa region, it was 80% [38]. In this study, among those HIV screened TB patients, the proportion of TB/HIV co-infection was 29.1% that was much higher than reports from Ethiopia, 6.3–20 % [40]. Similar to Bahirdar University (2016) similarly to North-

Eastern Ethiopia (2015), this was 24.3% it has better finding results when compared to other similar studies such as Nigeria on 20.5% [35].

Overlapping comorbid diseases are growing in resource-limited countries like Ethiopia (30); it might be due to multi-TB and HIV-related risk factors. These are: the communities are well-known in this area with the practice of dating sisters-in-law or brothers-in-law. The practices have a significant impact on HIV transmission. Second, the community, especially the farmers, is a well-known drinker of local beer or Teji (local Amharic Language) in the study area. Their actions might push the community to have unprotected sexual practices. Finally, because the area is prone to draughts and lacks access to food, many divorced women migrate to the Middle East to work as housemaids. Furthermore, due to financial constraints, many beautiful women are forced to perform sex work. The link between poverty and tuberculosis has also been established [37, 39]. Hence, it might increase TB/ HIV co-infection cases in the area. Fourth, the presence of many illegal private TB-drug sellers in the area might contribute a high TB and drug-resistant-TB. It will be HIV-associated tuberculosis when a high number of HIV cases happened.

It has an observed variation due to the difference of quality of service in the TB/HIV clinic, proper counseling, health education, and appropriate follow concerning the clinician. The inclusion of transferred outpatients on the final analysis of previous studies could be another other potential issue. TB/HIV co-infected patients were transferred out in proportions ranging from 3.8% in Nigeria's Ebonyi State to 64.2% in Ethiopia's Mizan Aman [33].

The TB treatment outcomes in TB/HIV co-infected patients are heavily influenced by various factors. In this regard, our research found that the patient's age, type of TB, WHO staging, and history of opportunistic infection were all associated with the success of TB treatment. The retreatment group of TB/HIV co-infected patients had a higher rate of unsuccessful treatment outcomes rather than new patients. Other socio-demographic characteristics were factors that influenced TB/HIV infection, with older people having a higher risk.

The current study's ART coverage was higher (76.3%) than a WHO report from Ethiopia (68%) but fell short of the WHO target of 100% [40, 41]. According to other reports, ART coverage in Ethiopia and the Amhara region was 50.5 percent and 40.2 percent, respectively [41]. This could be due to the health centers' proximity to the community. Furthermore, local stakeholders may use communication and social mobilization to diagnose and link more patients to ART. Furthermore, unpublished community reports show that while safe sex and condom use are low, people's awareness of the value of ART is high.

5.2 Limitation

- The limitation of this study was delimited on 5 years' retrospective records of secondary data.
- COVID-19 pandemic was negative impact in overall research procedure, data collection it was difficult because this data collect form my home town and the data were collected from patients' medical records.
- The medical record of the system does not incorporated adherence level, drug resistance, and behavioral factors (knowledge, attitude, and illicit drug use problem) were not well-recorded.

Chapter 6: Conclusions and Recommendation

6.1 Conclusion

The findings conclude that the overall TBHIV co-infected patients in this study were higher than many previous studies. TB/HIV patient's retreatment TB advanced HIV late WHO clinical stage, history of opportunistic infection and no CPT initiated were at a high risk of HIV disease. Therefore, HIV treatment facilities should give special attention to those TB-HIV co-infected patients with a higher risk of TB treatment.

6.2 Recommendation

To all Woreda/ district and Zone health institutions:

- Information regarding HIV/TB con infection should be provided to the public through available channels and practical models. Promoting messages focusing on Patients' proper use of treatment should be scaled up into the community throughout. Providing enough information about HIV treatment
- Based on the study findings, the spread of tuberculosis shows that the problem is serious and that the institutions need to raise public awareness and address the problem.
- I recommended other researches should conduct a research work to explain the Clinical features of treatment outcomes in the retrospective data obtained from the Woldia comprehensive specialized hospital.

To the community:

- According to the results of the findings, the study recommends that the North Wollo zonal health department use participatory approaches to promote community behavioral change for long-term HIV/TB treatment.
- The community-level should be strengthened and enhance the agenda of TB/HIV co-infection closer to the community.
- A committee established and responsible to promote TB/HIV activities
- Social mobilization activity

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ANNEX

Checklist to collect secondary data from Medical Records Prevalence of HIV infection among Pulmonary TB Patients In Woldia Comprehensive Specialized Hospital (from 2015-2019)						
Patient codes						
Age category	1= ≤24 years	2=25-45years	3=≥46 years			
Sex	1=male	2=female				
Occupation status	1=Housewife	2=Daily laborer	3= Government employee	4= Merchant	5= Farmer	6=Other
Martials status	1=Single	2=Married	3=Widowed	4=Divorced		
Monthly Income	1= <1000	2=1000-2000	3=>2000			
Educational status	1=No education	2=Primary	3=Secondary	4=Certificate and Above		
Residence	1=Urban	2=Rural				
Previous history of PTB	1=yes	2=No				
Category of PTB patient	1=new	2=retreatment				
Type of PTB	1=smear positive (SPP TB)	2=smear negative (SPP TB)	3=extra PT			
Year of TB Diagnosis conducted	1=2015	2=2016	3=2017	4=2018	5=2019	
WHO stage	1=Stage I	2=Stage 2	3=Stage 3	4=Stage 4		

CD4 count cells	1=<200	2=200-500	3=>500			
Duration on ART	1=<5Yrs	2=≥5yrs				
CPT initiated	1=yes	2=No				
History of Opportunistic	1=yes	2=No				
Smoking	1=yes	2=No				
Alcohol drinking	1=yes	2=No				
Asthma	1=yes	2=No				
Nutritional status	1=Normal	2=Moderate(MAM)	3=SAM			
Pretreatment weight	1=20-29Kg	2=30-39Kg	3=40-54Kg	4=>54Kg		
Pretreatment BMI Kg/m2	1=Under weight	2=Normal weight	3=Over weight	4=Obese		
DM	1=yes	2=No				
Cough	1=yes	2=No				
Cough length	1=1 weak	2=≥2 week				
Fever	1=yes	2=No				
Night sweet	1=yes	2=No				
HIV status	1=yes	2=No				

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