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ORIGINAL RESEARCH

Magnitude and Associated Factors of Pulmonary Tuberculosis Among HIV/AIDS Patients Attending Antiretroviral Therapy Clinic at Debre Tabor Specialized Hospital, Northwest Ethiopia, 2019

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Teklehaimanot Kiros[1]
Eninur Dejen[1]
Mulu Tiruneh[2]
Tegenaw Tiruneh[1]
Tahir Eyayu[1]
Shewaneh Damtie[1]
Kefyalew Amogne[3]

[1]Department of Medical Laboratory Sciences, College of Health Sciences and School of Medicine, Debre Tabor University, Debre Tabor, Ethiopia; [2]Department of Social and Public Health, College of Health Sciences and School of Medicine, Debre Tabor University, Debre Tabor, Ethiopia; [3]Debre Tabor College of Health Sciences, Debre Tabor, Ethiopia

Background: Tuberculosis (TB) has remained as a top global public health concern of the 21st century. It is the leading cause of morbidity and mortality among people living with human immunodeficiency virus (HIV) worldwide.

Objective: The study aimed to investigate the magnitude of pulmonary tuberculosis and its associated factors among HIV-positive patients attending antiretroviral treatment (ART) clinic in Debre Tabor specialized hospital, Northwest, Ethiopia.

Methods: A hospital-based cross-sectional study was conducted among 362 HIV-positive adult participants attending the ART clinic from October 1st to December 30th 2019. Socio-demographic data were collected using a pre-tested questionnaire. Sputum was collected aseptically into a sterile and leak-proof container. Following aseptic techniques, each sample was processed using the GeneXpert assay based on the manufacturer's instructions. Similarly, about 3–5 mL of whole blood was drawn for CD4+ T-cell count and plasma viral load tests following standard blood collection procedures. CD4+ T-cell count was performed using the BD FACS caliber flow cytometry while the plasma viral load was performed by using a quantitative real-time polymerase chain reaction. Then, collected data were double-checked, cleaned and entered into Epi-Info version 7.2.0.1 and exported to SPSS version 20.0 for further statistical analysis. The bivariate and multivariate logistic regression were conducted to address risk factor analysis. The 95%confidence interval with its corresponding cure and adjusted odds ratio was computed. Finally, p-value ≤0.05 was considered as a statistically significant association.

Results: In this study, the overall prevalence of tuberculosis among HIV-positive patients was 18 [(5%), 95% CI: 2.8–7.5]. A high viral load (≥1000 copies/mL) was positively associated [AOR (95% CI: 6.4 (1.6–25.7)), $p < 0.001$] with developing tuberculosis among HIV-positive patients.

Conclusion: The prevalence of TB is low among ART-receiving patients in our study site.

Keywords: ART, GeneXpert, pulmonary tuberculosis, predictors, sputum, viral load

Background

Tuberculosis (TB) is an airborne disease caused by a bacterium *Mycobacterium Tuberculosis* (MTB), which is a non-motile rod-shaped and an obligate aerobe.[1]

MTB affects any parts of the body but generally affects the lung. *Mycobacterium* enters the alveoli by airborne transmission. Subsequently, it resists destruction by alveolar macrophages, forms the tubercle and then spread to other

Correspondence: Teklehaimanot Kiros
College of Health Sciences and School of Medicine, Debre Tabor University, Debre Tabor, Ethiopia
Tel +251911009588
Email tkt0932@gmail.com

systems.[2] Furthermore, based on the site of infection, TB infection can be either pulmonary tuberculosis or extra tuberculosis. Infections involving the lung parenchyma are classified as pulmonary tuberculosis (PTB) whereas extrapulmonary tuberculosis (EPTB) is confined to organs other than the lungs, such as the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones.[3] TB is the leading cause of morbidity and mortality among people living with the human immune virus (HIV) and is the manifestation of acquired immune deficiency syndrome (AIDS) worldwide. It is the most common opportunistic disease and cause of death for those infected with HIV. It is responsible for more than a quarter of deaths in people living with HIV/AIDS (PLWHA).[4,5]

Globally, nearly 10% of TB cases are HIV-positive and the figure reaches up to 30% in African countries. In sub-Saharan Africa, up to 80% of individuals with active TB are HIV-positive.[6–8] Globally, there were an estimated 10 million incident cases and 1.5 million TB deaths (251000 among HIV-positive) according to the 2018 report of the world health organization (WHO).[3,6] In Ethiopia, TB remains one of the leading causes of mortality, especially multi-drug resistant TB (MDR-TB). It has been estimated that about 13% of all new TB cases are HIV co-infected in Ethiopia.[9,10] Despite various efforts made to prevent and control the disease, TB and HIV infection has remained the major threat to community health worldwide leading to mortality and morbidity.[11] TB has remained as the most serious opportunistic infection in HIV-positive patients in more than 50% of cases in developing countries.[12] MTB can occur at any time during HIV infection. As a result, it substantially altered the epidemiology of the infection by increasing the risk of reactivating latent TB, increasing the chance of TB infection (re-infection), and increasing the risk of rapid progression soon after infection.[13]

HIV infection is the most important deriving risk factor for triggering active TB infection through increasing susceptibility to other infections.[14] In persons infected with PTB, the risk of developing TB varies in between 10% and 20%[4] compared to a person co-infected with TB and HIV.[15] Consequently, HIV does not only increase the prevalence but also complicates the follow-up period and compromises the immune response against TB. Also, the co-existence of several opportunistic microbial infections may lead to diminished treatment outcomes. This may be due to TB/HIV co-infection together with the concomitant use of antiretroviral treatment (ART) and the intensive phase of TB treatment.[16] The coexistence of TB/HIV among ART-receiving HIV-positive patients may increase the chance of drug-related problems such as organ toxicity and metabolic distress due to superimposed pharmacokinetics and pharmacodynamic interruptions. The drug-related adverse outcome such as increased mortality, morbidity and tremendous colonization with several opportunistic microbial infections due to immune suppression is greatly manifest. As the combined effect, the decreased ART adherence will lead to the evolution of drug-resistant organisms.[17,18] HIV also complicates appropriate diagnosis and treatment of PTB mainly due to unusual clinical pictures, increased smear-negative PTB, atypical findings on chest radiography together with increased prevalence of EPTB.[19,20] That is why HIV and TB can individually be the major causes for public health threats and the combination of the two has proven to have a far greater impact on the epidemiology progression and consequences on global health.[21]

TB-HIV co-infection have remained challenging for diagnosis and treatment.[4] Also, the emergence of MDR-TB is complicating the disease control effort.[19,22] Therefore, diagnosis of TB can be by chest X-ray, smear microscopy, culture, serological tests, and molecular techniques.[10,19,23–25] TB is a curable and preventable disease. Since co-infections complicate both diagnosis and treatment, understanding the predictors of TB/HIV co-infection in the local context is critical to improving the management.[22] Although there is an increasing burden of the twin pandemics,[5,10,16,24–26] no study is available regarding the magnitude and associated factors of PTB among HIV-positive patients who are attending the antiretroviral therapy clinic in our setting. Therefore, the present study aims to determine the magnitude of PTB and its associated risk factors among PLWHA who are attending the ART clinic at Debre Tabor specialized hospital.

Materials and Methods

Study Setting

The study was conducted at Debre Tabor specialized hospital (DTSH), Northwest, Ethiopia. Debre Tabor is a town located in the Southwest of Gondar Zone in the Amhara Region which is about 666 kilometers far from Addis Ababa (the capital city of Ethiopia). The town has a latitude and longitude of 11°51′N 38°1′E with an elevation of 2706 meters above sea level. It has only one public specialized hospital, seven primary hospitals, and three

other private health facilities. Currently, DTSH is providing a comprehensive service to both outpatients and inpatients admitted to an emergency, medical, surgical, obstetric/gynecologic, neonatal, and pediatric wards. It is providing a comprehensive service including for about 2249 enrolled HIV-positive patients attending ART.

Study Design and Period

A hospital-based cross-sectional study was conducted among HIV-positive patients who were attending the ART clinic of DTSH from October 1st to December 30th 2019.

Source Population and Study Participants

The source populations for this study were all HIV-positive individuals attending DTSH during the study period. All adult ages 18 years and above HIV-positive patients attending at ART centre in the study period were included for study participation.

Eligibility Criteria

All adult HIV patients who were willing to participate in the study, who were in the chronic ART care, and those did not take anti-TB drugs either due to treatment missed, loss to follow-up or naïve to anti-TB drugs for the last couple of weeks were included in the survey. However, HIV-positive patients who were severely ill, who had a serious mental problem or psychosocial disorder, HIV-positive patient who is already PTB diagnosed and already initiated to co-treatment for TB-HIV co-infection are excluded from our survey, unable to give consent and those who were absent during the time of data collection were excluded from the study. Moreover, participants with incomplete secondary medical data records, particularly for laboratory (baseline CD4+ T-cell count) and other related missed clinical data were excluded from the study.

Sample Size Determination and Sampling Technique

The sample size for this study was determined using a formula for the estimation of a single population proportion ($n = (Z\ \alpha/2)^2\ P\ (1\text{-}P)/d2$) by using the prevalence, p= 27.7% (0.277) which was taken from previously done studies,[27] using a 95% confidence interval, Zα/2=1.96, and the margin of error, d= 0.05. Then, the required sample size for the study by substituting the above values was approximately 310. By adding 20% non-response rate, the total sample size required for this study was 372 HIV-positive patients attending the ART clinic at DTSH. There was an average of 35 HIV-positive individuals per day for their follow-up in the ART clinic in our setting. A systematic random sampling technique was used to select HIV-positive study participants. The total number of PLWHA at DTSH-ART centre was 2249. The Kth value for the study was computed using the formula, K= 2249/372=6.00. Then, the first study participant was selected using the lottery method. That means among ART attendants at the period of sampling, the first study participant was selected blindly or using simple random way. However, next, every study participant was selected in the order of every K^{th} interval of ART attending until the final sample size was reached.

Study Variables

The dependent variable was the magnitude of PTB among HIV-positive patient attending the ART clinic of DTSH. Whereas the independent variables include sociodemographic characteristics (age, gender, marital status, level of education, residence, and current occupation), past and current clinical characteristics (ART duration, CD4+ status both baseline and current count, plasma viral load, level of ART adherence, previous history of PTB, hemoglobin level and the like), anthropometric measurements (body mass index or BMI), and related personal behaviours like alcoholic drinking and smoking of study subjects.

Data Collection Tools

Sociodemographic and Clinical-Related Data Collection

Ahead of data collection, verbal and written participant's student information was given to all study participants including the caregivers. At the same time, before data collection, a pre-designed semi-structured questionnaire to address the primary outcome measure was adopted from various relevant kinds of literature to assess the sociodemographic variables, including age, gender, level of education, and other related characteristics of each study subject. However, 10% of the questionnaires were pretested outside of the study area (Addis Zemen primary hospital) before the actual study was made to ensure its completeness, simplicity, and clarity based on the objective of the study.

HIV-positive participants were also asked for the associated risk factors for PTB upon attending the ART clinic of DTSH. Importantly, essential clinical data such as ART duration, baseline CD4+ count, treatment switching were

extracted from their medical records through careful chart review. Furthermore, laboratory data were obtained using standard microbiological methods such as CD4+ count, GeneXpert and viral load determinations.

Laboratory Investigation Procedures

Sample Collection, Processing, Transport, and Handling

Ten patients were excluded from enrolment as they refused to give consent. Adequate instruction for participant on how to collect appropriately sputum sample for the investigation was given. Later on, properly labelled, leakproof and dry sputum cup or equivalent container was given to all volunteer participants. For each volunteer study participant, a single spot sputum sample was collected aseptically giving a total of 362 specimens from HIV-positive participants and submitted to the laboratory immediately for further examination.

Similarly, transportation of the sputum specimen was made according to the standard operating procedure (SOP) designed for this study, in addition to the manufacture's safety instructions and general leaflet. Sputum specimens were transported to the laboratory for analytical processing within two hours of collection. In case of delay, sputum specimens were kept at 2–8°C until ready for transport to mycobacteriology laboratory for testing.[28,29]

Upon arrival at the laboratory, the macroscopic examination was made, along with the verification for completeness of the test request to minimize the potential pre-analytical errors.

Sputum processing was made using the semi-automated GeneXpert assay as described previously.[16,26] The assay machine uses a plastic cartridge with lyophilized reagents and buffers for sample processing, amplification, detection particularly for rifampin resistance (RIF).[4,26,30]

The results of GeneXpert assay can be interpreted as (1) RIF resistance detected means positive for MTB/RIF resistance, (2) RIF resistance not detected means positive for MTB only, and finally (3) RIF resistance indeterminate indicates that positive for MTB/indeterminate for RIF.[28–31]

Regarding CD4+ T-cell count and viral load tests, about 3–5 mL of whole blood was drawn from each study participant following standard blood collection procedures. Following to SOPs, collected specimens were transported to the DTSH-ART laboratory for CD4+ T-cell count. The CD4+ count was conducted by adding 50 µL whole blood to a reagent tube containing 20 µL of monoclonal antibodies.[32] Then, appropriate vortexing followed by incubation for 30 minutes was made. Finally, the determination of absolute CD4+ T-cell count was performed using the BD FACS caliber flow cytometry system (BD, CA, USA) through the strict following to the manufacturer's instruction.[33] On the other hand, for viral load testing, the plasma was prepared for transportation on dry ice to the Amhara Public Health Institute (APHI) and processed following the standard protocol and Biosafety precautions as described elsewhere.[34–36] At APHI, viral load was performed by using a quantitative real-time polymerase chain reaction (QRT-PCR) HIV-1 assay with the COBAS® instrument (Roche, Homburg, Germany).

Data Quality Assurance

The reliability of the study findings was guaranteed by implementing quality control (QC) measures for questionnaires, specimen collection and the final laboratory work-up through an SOPs. All materials, equipment, reagents, and procedures were adequately controlled. Pre-analytical, analytical and post-analytical stages of quality assurance were strictly followed by SOP to ensure the sample was correctly processed and interpreted. The GeneXpert assay has both sample processing control and probe check control system to measure the fluorescence signal if the acceptance criteria are met.[28,30] At the same time, CD4+ T-cell count and viral load tests were performed by strictly following the manufacture's instruction manuals. A semi-structured questionnaire for face to face interview was pre-tested before data collection regarding socio-demographic characteristics, clinical data, and associated risk factors. That means 10% of the questionnaire was pre-tested before the actual data collection process. In addition to this, the semi-structured questionnaire was prepared in the English version and translated in the local language (Amharic version) and then transcribed back to English to maintain its consistency. Moreover, adequate training was given for data collectors and supervisors. Generally, the process of the study was supervised daily so that any incompletely filled questionnaires and test requests were discarded based on the available specimen rejection criteria for any good clinical practice.

Data Processing and Statistical Analysis

All data were entered into epi info manager version 7.2.0.1 and analyzed taking care for completeness,

consistency, and coding using SPSS version 20. Before any statistical analysis, normal distribution of data was checked by using the Kolmogorov–Smirnov and Shapiro–Wilk test. Statistical analysis for descriptive statistics of the variables was computed to summarize the data. For categorical variables, frequencies and percentages were computed while for the continuous variables mean and the standard deviation was calculated. For the associated risk factor analysis of independent variables with the outcomes, the bivariable and multivariable logistic regression model was fitted. Odds ratios (OR) with 95% confidence intervals (95% CI) was calculated. All variables with p-value <0.25 (to control the effect of confounding) in the bivariate analysis was included in the multivariate logistic regression model for risk factor analysis so that adjusted odds ratio (AOR) with 95% confidence intervals was calculated. However, the model fitness of the final binary logistic regression was tested by using Hosmer and Lemeshow test at a p-value >0.05. In all cases, p-value ≤0.05 was taken as a statistically significant association. Finally, the findings were represented with texts and tables.

Ethical Clearance

The study was approved by the Debre Tabor University, College of Health Sciences and School of Medicine, Research and Ethical Review Committee (Permission letter's reference number: chs/224/2012 in Ethiopian calendar). Permission letter was obtained and sent to all concerned bodies and the study was secured at all levels. The purpose, the potential benefits, and possible risks associated with participation in this research work have been cleared so that participants were decided either to proceed or withdraw from the entire study. Also, study participants were informed both verbally and written so that a written consent form was given after a brief explanation of the study. All results were kept confidential and the process was solely made through coding to maintain individuals' privacy concerns. However, the participants were given the full right to withdraw at any time from participating in the research process. We all authors confirm that this study was conducted following the declaration of Helsinki. The study is conducted based on medical research and ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

Results

Socio-Demographic Characteristics of the Study Participants

Among a total of 362 HIV-positive patients, 207 (57.2%) were female participants. The mean age of the study participants was 39.6 years ± 12.2 standard deviations (std) and majority, 191 (52.8%) were in the age group of 25–44 years. Similarly, out of the total, 297 (82%) lived in urban areas while 172 (47.5%) of the study participants were married followed by 155 (42.8%) singles as shown in (Supplementary file 1: Table S1).

Clinical Characteristics of the Study Participants Attending the ART Clinic

The medical and clinical-related history of PLWHA is presented in (Supplementary file 2: Table S2). The mean baseline CD4+ count was 258.89 cells/mm^3±181.89 std. In the meantime, 136 (37.6%) of the study subjects had a current CD4+ count of more than 350 cells/mm^3. However, the majority of the study participants were with 132 (38.3%) CD4+ count of <200 cells/mm^3. Besides, out of the total, 119 (32.9%) of the PLWHA had a hemoglobin level less than 11gm/dl. Similarly, around 72 (19.9%), 50 (13.8%), 28 (7.7%), and 54 (14.9%) of the study participants had the previous history of TB infection, history in the family, history of cigarette smoking, and alcohol drinking, respectively. Furthermore, HIV duration since confirmation for greater than five years has shown a statistical association with the risk of developing TB in the bivariate logistic regression [COR (95% CI): 4.45 (1–19.7, p-value: 0.004)] with PTB among PLWHA in DTSH.

The Magnitude of Tuberculosis Among Peoples Living with HIV/AIDS

Among 362 study subjects, only 18 (5%) were positively diagnosed with PTB using the semi-automated GeneXpert method. As a result, the overall prevalence rate of PTB among HIV-positive patients attending to ART clinic of DTSH was 5.0% (95% CI: 2.8–7.5). For HIV-positive patients with the previous history of TB, we have conducted smear microscopy (Acid-fast stain) to adequately control the study results (ie the likelihood of falsely positive GeneXpert results). A smear microscopy (Acid-fast stain) examination for the participants with a previous history of TB was a control protocol. This enhances to

confirm previous TB case rates. Unless and otherwise, GeneXpert has to be confirmed by sputum smear microscopy, it will have a great chance to yield a falsely positive result which may result in affecting the prevalence among the study participants. Therefore, the Acid-fast stain shall be done to confirm previous TB case rates.

Associated Risk Factors Analysis

In the bi-variable analyses, duration of HIV, being low BMI, having the previous history of TB, high viral load, WHO clinical stage three, baseline CD4+ count <200cells/mm^3, no cotrimoxazole therapy usage was statistically associated with the risk to develop PTB among PLWHA attending ART clinic of DTSH. Fitting to the final multivariate logistic regression model revealed that duration of HIV more than 5 years, being WHO stage three, having a high viral load (more than 1000copies of RNA), and low BMI was identified as independent predictors of tuberculosis among HIV/AIDS patients as shown in (Supplementary file 3: Table S3). In this study, HIV patients who have a lower BMI (<18.5 kg/m^2) was four times (AOR (95% CI) =4.2 (95% CI: 1.2, 15.08)) more likely to developed tuberculosis as compared to HIV patients who have normal BMI. Whereas, patients who have greater than or equal to 1000 HIV RNA copies/mL in their blood were 6 times (AOR (95% CI) =6.4 (95% CI: 1.6, 25.7)) more likely to infect with tuberculosis than those with fewer RNA copies in their blood.

Discussion

TB remains one of the tops of the leading causes of mortality among many other infectious diseases provided that the consequences are devastating especially among PLWHA globally.[16] Although ART initiation has shown has improved outcome of PLWHA, the intimate link of TB-HIV co-infection has remained the world's top important public health problem. Co-existence complicates appropriate diagnosis and treatment.[37,38]

The present study revealed that the overall prevalence of PTB among PLWHA was 5.0% (95% CI: 2.8–7.5). This finding was comparatively lower than a study conducted in different areas of Ethiopia like Amhara region Northwest Ethiopia 27.7%,[27] to a study conducted among 12,980 Ethiopian study participants 25.59%,[38] to a study that was done in Bahir Dar Flege Hiwot specialized hospital 10.1%,[39] a facility-based retrospective study conducted at Hawassa University referral hospital of Ethiopia reported that 18.2%,[40] another cross-sectional study (n=1153) that was done at private health institutions in Ethiopia 20%,[41] and a retrospective study at Butajira Zonal hospital, Ethiopia that founds 20.3%.[9]

Not only from local studies but also abroad studies have shown that the higher magnitude of PTB among HIV-positive individuals including from South India 60.58%,[42] Nigeria 42.3%,[43] Tanzania (11.0%) participants developed TB while receiving ART,[37] and the prevalence rate of TB while receiving ART from South Africa reported 10%.[44] The discrepancy in the magnitude of TB among HIV-positive participants may be explained by the difference in the health-care system among ART centres, variation in study design,[45] the diagnostic methods[46] employed (smear microscopy, culture, GeneXpert), ART regimens and its adherence[47] and adverse drug-related problems that trigger MTB-MDR. Besides, the variation may be attributed due to the course of infection[8] and the presence of concomitant opportunistic infections[48] that alters the host immunity, the socio-economic condition[49] of study subjects, and awareness of the community to seek health care for both TB and HIV.[4,5,16,24,25,31,50] For example, the GeneXpert assay is essential due to its rapid diagnosis for MTB disease and its drug resistance (MTB/RIF) simultaneously in less than 2 hours. This takes advantage over conventional TB culture detection methods that take at least two to six weeks for detection.[47,51]

On the contrary, the present finding is nearly in line with the previous research studies including to hospital-based retrospective follow-up study (n=496) conducted at Arba-Minch general hospital, Ethiopia that shows a -5.36%,[24] a cross-sectional study conducted at the University of Gondar ART clinic, Ethiopia that founds 7.5%,[11] 9.7%,[5] and 6%,[31] respectively. However, the present finding is higher than a cross-sectional study conducted at St. Paul's Hospital Millennium Medical College, Ethiopia conducted in 2014 that founds 1.1%,[16] a study involving 1824 ART participants from Mexico where only 45 (2.47%) developed active TB.[52] The discrepancies may be due to the variation in the study detection methods, course of infection and target groups enrolled for the study.

In the present study, lower BMI was significantly associated with TB among study participants living with HIV/AIDS. PLWHA of a lower BMI (ie <18.5 kg/m^2) was four times more likely to acquire TB [AOR (95% CI: 4.2 (1.2–15.1, p-value: 0.03)] as compared to those with a normal BMI. This finding was consistent with a study conducted in Felege-Hiwot hospital Northwest, Ethiopia

that shows five times more likely to develop tuberculosis[39] and another similar study.[53] This could be hypothesized by PLWHA are more likely to become malnourished due to reduced food intake, poor absorption of nutrients, and changes in the way the body uses nutrients it receives or has stored in addition to the psychosocial-related factors.[54]

Regarding the WHO clinical stage, HIV patients in stage three were more than five times more likely to develop PTB infection [AOR (95% CI: 5.4 (1.3–22.8, p-value: 0.02))] as compared to those who were in the WHO stage one. This finding is supported by a study conducted in Pakistan,[55] Tanzania,[37] and South Africa.[56] According to the WHO staging of HIV/AIDS, those HIV patients in stage 3 are more likely to develop TB. Furthermore, atypical pulmonary presentation is common in more advanced HIV disease.[24,52] Another study has shown that WHO clinical stages III and IV have significant effects on the likelihood of malnutrition development and immune impairment among HIV/AIDS patients that subsequently produce a poorer clinical outcome. Malnutrition combined with other aggravating factors to TB-HIV co-infection is usually encountered at the advanced phase of the HIV infection.[57] A retrospective cohort study in Tanzania also indicated that WHO clinical stage 3 and 4 (p-value: 0.029) was associated independently with the development of TB among ART-receiving participants.[37]

In this study, duration since confirming HIV test was significantly associates with tuberculosis among PLWHA [AOR (95% CI: 5.7 (1.08–30, p-value: 0.04))]. Patients ≥5 years in the ART since confirming the HIV test was six times more likely to developed tuberculosis. This may due to careless nesses that triggers personal behaviours like alcoholic drinking, desire to smoke, and inclinations to poor ART adherence. As the duration of ART increases, there is a likely hood of diminishing the protective immunity.[9,47,58] Similarly, chronic ART patients are probably exposed to other infectious diseases including sexually transmitted diseases that finally result in increasing regimens and pain.[40,58,59]

In the multivariate logistic regression, the viral load test result of study participants has shown that patients who have ≥1000 HIV RNA copies/mL in their blood were 6 times more likely to infect with TB. This is because a patient having detectable viral load (≥ 10000copies/mL) is exposed to ongoing virus replication in its body leading to clinical and/or immunological failure but virological success. Such conditions substantially increase the risk for disease progression, disease transmission, immune suppression, poor ART adherence, weight loss, severe malnutrition (diarrheal diseases), susceptibility to over dozens of opportunistic infections (OIs), and eventually accelerate morbidity and mortality.[4,5,10,16,31,38,50]

Conclusion

In conclusion, the overall prevalence of pulmonary tuberculosis among PLWHA was 5%. Despite lower in the present finding, tuberculosis has remained the world's most common public health threat posing significant mortality and morbidity among patients receiving ART. Meanwhile, the risk factor analysis has shown that longer duration on ART (≥5 years), being WHO stage three, having a high viral load, and underweight were identified as a strong independent predictor of developing tuberculosis among HIV-positive patients. Therefore, early screening of PTB among PLWHA and its potential predictors are imperative to contain TB spreading generally in Ethiopia and particularly in the study setting. The results of the present study will provide a local clinical and epidemiological interest for further studies since TB is considered a threat to ART-receiving patients worldwide. Furthermore, the outcome of the study is expected to facilitate periodic surveillance and monitoring practices to TB-HIV co-infections. Besides, it provides secondary information for health professionals, policymakers, and other governmental and non-governmental organizations in our country.

Abbreviations

AIDS, acquired immune deficiency syndrome; ART, antiretroviral treatment; DTSH, Debre Tabor specialized hospital; HIV, human immune virus; MDR-TB, multi-drug resistant TB; MTB, *Mycobacterium tuberculosis*; PLWHA, people living with HIV/AIDS; PTB, pulmonary tuberculosis; TB, tuberculosis; WHO, World Health Organization.

Data Sharing Statement

All the data used in this research article are presented within the manuscript and additional file.

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Author Contributions

TK was the primary researcher who conceived the study, designed the study methodology, participated in supervision, conducted laboratory investigation, involved in execution, acquisition of data, data statistical analysis, results interpretation, drafting the manuscript and introducing changes into the manuscript during proofing stage, engaged in critically revising of the manuscript. Have agreed on the journal to which the article will be submitted and finalized the manuscript for publication. ED participated in clinical data collection, sputum specimen collection for laboratory investigation, execution, acquisition of data, participated in statistical analysis, result interpretations, have participated in drafting and substantially revising the manuscript and have agreed on the journal to which the article will be submitted. MT, TT, TE, SD and KA participated in study design, involved in execution, acquisition of data, data statistical analysis, results interpretation, drafting the manuscript, engaged in critically revising of the manuscript including and any significant changes that were introduced at the proofing stage, have agreed on the journal to which the article will be submitted. All the authors agree to take responsibility and be accountable for the contents of the manuscript. Besides, all authors read the last version of the manuscript and approved for publication.

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Disclosure

The authors declare that they have no conflicts of interest.

References

1. Murray PR, Rosenthal KS, Pfaller MA. *Medical Microbiology E-Book*. Elsevier Health Sciences; 2020.
2. Sastry AS, Bhat S. *Essentials of Medical Microbiology*. Jaypee Brothers, Medical Publishers Pvt. Limited; 2018.
3. Organization WH. *Global Tuberculosis Report 2017*. Vol. 2018. World Health Organization; 2017.
4. Wondimeneh Y, Muluye D, Belyhun Y. Prevalence of pulmonary tuberculosis and immunological profile of HIV co-infected patients in Northwest Ethiopia. *BMC Res Notes*. 2012;5(1):331. doi:10.1186/1756-0500-5-331
5. Damtie D, Yismaw G, Woldeyohannes D, Anagaw B. Common opportunistic infections and their CD4 cell correlates among HIV-infected patients attending at antiretroviral therapy clinic of Gondar University Hospital, Northwest Ethiopia. *BMC Res Notes*. 2013;6(1):534.
6. Organization WH. *Global Tuberculosis Report 2019*. World Health Organization; 2019.
7. van Halsema CL, Okhai H, Hill T, Sabin CA. Incidence of and risk factors for tuberculosis among people with HIV on antiretroviral therapy in the United Kingdom. *Aids*. 2020;34(12):1813–1821.
8. Siika AM, Yiannoutsos CT, Wools-Kaloustian KK, et al. Active tuberculosis is associated with worse clinical outcomes in HIV-infected African patients on antiretroviral therapy. *PLoS One*. 2013;8(1):e53022.
9. Mohammed S, Gebremariam TT. Tuberculosis among HIV-positive patients at Butajira Hospital, South-Central Ethiopia. *Int J Pharma Sci Res*. 2015;6(12):1406–1411.
10. Negussie A, Debalke D, Belachew T, Tadesse F. Tuberculosis co-infection and its associated factors among People living with HIV/AIDS attending antiretroviral therapy clinic in southern Ethiopia: a facility based retrospective study. *BMC Res Notes*. 2018;11(1):417. doi:10.1186/s13104-018-3530-3
11. Sileshi B, Deyessa N, Girma B, Melese M, Suarez P. Predictors of mortality among TB-HIV Co-infected patients being treated for tuberculosis in Northwest Ethiopia: a retrospective cohort study. *BMC Infect Dis*. 2013;13(1):297. doi:10.1186/1471-2334-13-297
12. Giri PA, Deshpande JD, Phalke DB. Prevalence of pulmonary tuberculosis among HIV positive patients attending antiretroviral therapy clinic. *N Am J Med Sci*. 2013;5(6):367. doi:10.4103/1947-2714.114169
13. Gebremichael DY, Hadush KT, Kebede EM, Zegeye RT. Food Insecurity, Nutritional Status, and Factors Associated with Malnutrition among People Living with HIV/AIDS Attending Antiretroviral Therapy at Public Health Facilities in West Shewa Zone, Central Ethiopia. *Biomed Res Int*. 2018;2018.
14. Sinshaw Y, Alemu S, Fekadu A, Gizachew M. Successful TB treatment outcome and its associated factors among TB/HIV co-infected patients attending Gondar University Referral Hospital, Northwest Ethiopia: an institution based cross-sectional study. *BMC Infect Dis*. 2017;17(1):132. doi:10.1186/s12879-017-2238-7
15. Bucher HC, Griffith LE, Guyatt GH, et al. Isoniazid prophylaxis for tuberculosis in HIV infection: a meta-analysis of randomized controlled trials. *Aids*. 1999;13(4):501–507. doi:10.1097/00002030-199903110-00009
16. Solomon S. Prevalence of Tuberculosis among HIV Positive Individuals with Asymptomatic Disease States at St. Paul?s Hospital Millennium Medical College, Addis Ababa, Ethiopia. *J Med Microbiol Diagnosis*. 2015;4(02):2. doi:10.4172/2161-0703.1000192
17. Gassama O, Kao C. Factors Associated with Adherence to Antiretroviral Therapy among HIV Infected Adults in the Gambia. *J AIDS Clin Res*. 2018;9(07):2. doi:10.4172/2155-6113.1000771
18. Alexander PE, De P. The emergence of extensively drug-resistant tuberculosis (TB): TB/HIV coinfection, multidrug-resistant TB and the resulting public health threat from extensively drug-resistant TB, globally and in Canada. *Canadian J Infect Dis Med Microbiol*. 2007;18.
19. Jacobs DS, Kasten BL, Demott WR, Wolfson W. *Laboratory Test Handbook*. Lexi-Comp Incorporated; 1996.
20. Organization WH. *The Global Plan to Stop TB 2011–2015: Transforming the Fight Towards Elimination of Tuberculosis*; 2010.
21. Chandrasekaran V, Kamath R, Sharma V, Pattanshetty S. HIV-TB coinfection: clinico-epidemiological determinants at an antiretroviral therapy center in Southern India. *Lung India*. 2013;30(4):302. doi:10.4103/0970-2113.120605
22. Organization WH. *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis-2011 Update*. Geneva: World Health Organization; 2011.
23. Parsons LM, Á S, Gutierrez C, et al. Laboratory diagnosis of tuberculosis in resource-poor countries: challenges and opportunities. *Clin Microbiol Rev*. 2011;24(2):314–350.
24. Dalbo M, Tamiso A. Incidence and predictors of tuberculosis among HIV/AIDS infected patients: a five-year retrospective follow-up study. *Adv Infect Dis*. 2016;6(02):70. doi:10.4236/aid.2016.62010

25. Mama M, Manilal A, Tesfa H, Mohammed H, Erbo E. Prevalence of pulmonary tuberculosis and associated factors among HIV positive patients attending antiretroviral therapy clinic at Arba Minch General hospital, southern Ethiopia. *Open Microbiol J*. 2018;12(1):163. doi:10.2174/1874285801812010163
26. Gebretsadik D, Ahmed N, Kebede E, Mohammed M, Belete MA. <p>Prevalence of Tuberculosis by Automated GeneXpert Rifampicin Assay and Associated Risk Factors Among Presumptive Pulmonary Tuberculosis Patients at Ataye District Hospital, North East Ethiopia. *<![CDATA[Infection and Drug Resistance]]>*. 2020;13:1507–1516. doi:10.2147/IDR.S248059
27. Mitku AA, Dessie ZG, Muluneh EK, Workie DL. Prevalence and associated factors of TB/HIV co-infection among HIV Infected patients in Amhara region, Ethiopia. *Afr Health Sci*. 2016;16 (2):588–595. doi:10.4314/ahs.v16i2.29
28. Moussa HS, Bayoumi FS, Ali AM. Evaluation of GeneXpert MTB/RIF assay for direct diagnosis of pulmonary tuberculosis. *Saudi Med J*. 2016;37(10):1076. doi:10.15537/smj.2016.10.14998
29. Rachow A, Zumla A, Heinrich N, et al. Rapid and accurate detection of Mycobacterium tuberculosis in sputum samples by Cepheid Xpert MTB/RIF assay—a clinical validation study. *PLoS One*. 2011;6(6): e20458. doi:10.1371/journal.pone.0020458
30. Iram S, Zeenat A, Hussain S, Yusuf NW, Aslam M. Rapid diagnosis of tuberculosis using Xpert MTB/RIF assay-Report from a developing country. *Pakistan j Med Sci*. 2015;31(1):105.
31. Alemayehu M, Gelaw B, Abate E, et al. Active tuberculosis case finding and detection of drug resistance among HIV-infected patients: A cross-sectional study in a TB endemic area, Gondar, Northwest Ethiopia. *Int j Mycobacteriology*. 2014;3(2):132–138. doi:10.1016/j.ijmyco.2014.02.004
32. Hailu GG, Hagos DG, Hagos AK, Wasihun AG, Dejene TA. Virological and immunological failure of HAART and associated risk factors among adults and adolescents in the Tigray region of Northern Ethiopia. *PLoS One*. 2018;13(5):e0196259.
33. Sisay C, Bekele A, Sisay A, Mekonen H, Terfa K. Incidence and Predictors of Anti-Retroviral Treatment (ART) Failure among Adults Receiving HIV Care at Zewditu Memorial Hospital, Addis Ababa, Ethiopia. *J AIDS Clin Res*. 2017;8(12):2. doi:10.4172/2155-6113.1000749
34. Manaye GA, Abateneh DD, Kebede KM, Belay AS. Immunological Response During HAART and Determinants of Current CD4+ T-Cell Count Among HIV/AIDS Patients Attending University of Gondar Referral Hospital, Northwest Ethiopia. *HIV/AIDS*. 2020;12:295.
35. Ma Y, Zhao D, Yu L, et al. Predictors of Virologic Failure in HIV-1–Infected Adults Receiving First-Line Antiretroviral Therapy in 8 Provinces in China. *Clin Infect Dis*. 2010;50(2):264–271. doi:10.1086/649215
36. Hassan AS, Nabwera HM, Mwaringa SM, et al. HIV-1 virologic failure and acquired drug resistance among first-line antiretroviral experienced adults at a rural HIV clinic in coastal Kenya: a cross-sectional study. *AIDS Res Ther*. 2014;11(1):9. doi:10.1186/1742-6405-11-9
37. Gunda DW, Maganga SC, Nkandala I, et al. Prevalence and risk factors of active TB among adult HIV patients receiving ART in northwestern Tanzania: a retrospective cohort study. *Canadian J Infect Dis Med Microbiol*. 2018;2018.
38. Tesfaye B, Alebel A, Gebrie A, Zegeye A, Tesema C, Kassie B. The twin epidemics: prevalence of TB/HIV co-infection and its associated factors in Ethiopia; A systematic review and meta-analysis. *PLoS One*. 2018;13(10):e0203986. doi:10.1371/journal.pone.0203986
39. Belay A. Magnitude and correlates of tuberculosis among HIV patients at Felege Hiwot Referral Hospital, Bahir Dar city, northwest Ethiopia. *Clin Med Res*. 2013;2(4):77–83. doi:10.11648/j.cmr.20130204.18
40. Fekadu S, Teshome W, Alemu G. Prevalence and determinants of Tuberculosis among HIV infected patients in south Ethiopia. *J Infect Dev Countries*. 2015;9(08):898–904. doi:10.3855/jidc.5667
41. Alemie GA, Gebreselassie F. Common types of tuberculosis and co-infection with HIV at private health institutions in Ethiopia: a cross sectional study. *BMC Public Health*. 2014;14(1):319. doi:10.1186/1471-2458-14-319
42. M. N, Prasad RB. Epidemiological surveillance of tuberculosis among HIV/AIDS seropositive individuals attending ART center at a tertiary care teaching hospital. *Int J Community Med Public Health*. 2017;4(8):2816–2824. doi:10.18203/2394-6040.ijcmph20173329
43. Oku AO, Owoaje ET, Ige OK, Oyo-ita A. Prevalence and determinants of adherence to HAART amongst PLHIV in a tertiary health facility in south-south Nigeria. *BMC Infect Dis*. 2013;13(1):401. doi:10.1186/1471-2334-13-401
44. Van Rie A, Westreich D, Sanne I. Tuberculosis in Patients Receiving Antiretroviral Treatment: incidence, Risk Factors, and Prevention Strategies. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2011;56(4):349. doi:10.1097/QAI.0b013e3181f9fb39
45. Ngowi BJ, Mfinanga SG, Bruun JN, Morkve O. Pulmonary tuberculosis among people living with HIV/AIDS attending care and treatment in rural northern Tanzania. *BMC Public Health*. 2008;8(1):341. doi:10.1186/1471-2458-8-341
46. Mu W, Zhao Y, Sun X, et al. Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study. *AIDS Care*. 2014;26(9):1127–1135. doi:10.1080/09540121.2014.882492
47. Liu E, Makubi A, Drain P, et al. Tuberculosis incidence rate and risk factors among HIV-infected adults with access to antiretroviral therapy. *Aids*. 2015;29(11):1391–1399. doi:10.1097/QAD.0000000000000705
48. Chepkondol GK, Jolly PE, Yatich N, Mbowe O, Jaoko WG. Types and prevalence of HIV-related opportunistic infections/conditions among HIV-positive patients attending Kenyatta National Hospital in Nairobi, Kenya. *Afr Health Sci*. 2020;20(2):615–624. doi:10.4314/ahs.v20i2.9
49. Guehi C, Badjé A, Gabillard D, et al. High prevalence of being Overweight and Obese HIV-infected persons, before and after 24 months on early ART in the ANRS 12136 Temprano Trial. *AIDS Res Ther*. 2016;13(1):12. doi:10.1186/s12981-016-0094-y
50. Alemu YM, Awoke W, Wilder-Smith A. Determinants for tuberculosis in HIV-infected adults in Northwest Ethiopia: a multicentre case–control study. *BMJ Open*. 2016;6(4):4. doi:10.1136/bmjopen-2015-009058
51. Umanah T, Ncayiyana J, Padanilam X, Nyasulu PS. Treatment outcomes in multidrug resistant tuberculosis-human immunodeficiency virus Co-infected patients on anti-retroviral therapy at Sizwe Tropical Disease Hospital Johannesburg, South Africa. *BMC Infect Dis*. 2015;15(1):478. doi:10.1186/s12879-015-1214-3
52. Martin-Echevarria E, Serrano-Villar S, Sainz T, et al. Development of tuberculosis in human immunodeficiency virus infected patients receiving antiretroviral therapy. *Int J Tuberculosis Lung Dis*. 2014;18(9):1080–1084. doi:10.5588/ijtld.13.0757
53. Worodria W, Massinga-Loembe M, Mayanja-Kizza H, et al. Antiretroviral treatment-associated tuberculosis in a prospective cohort of HIV-infected patients starting ART. *Clin Dev Immunol*. 2010;2011.
54. Ababa A. *Federal Democratic Republic of Ethiopia Ministry of Health*. Ethiopia: Postnatal Care; 2003.
55. Ali A, Ahmad F, Imran M, Atif M, Noor Y, Imran S. Prevalence of pulmonary tuberculosis in HIV/AIDS subjects. *Austin Virol Retrovirology*. 2016;3(2):1023.
56. Gupta A, Wood R, Kaplan R, Bekker L-G, Lawn SD. Prevalent and incident tuberculosis are independent risk factors for mortality among patients accessing antiretroviral therapy in South Africa. *PLoS One*. 2013;8(2):e55824.
57. Piwoz EG, Preble EA. *HIV/AIDS and Nutrition*. A review of the literature and recommendations for nutritional care and support in Sub-Saharan Africa: Support for Analysis and Research in Africa (SARA) Project; 2000.

58. Farley JE, Ram M, Pan W, et al. Outcomes of multi-drug resistant tuberculosis (MDR-TB) among a cohort of South African patients with high HIV prevalence. *PLoS One*. 2011;6 (7):e20436.

59. Cui Z, Lin M, Nie S, Lan R. Risk factors associated with Tuberculosis (TB) among people living with HIV/AIDS: A pair-matched case-control study in Guangxi, China. *PLoS One*. 2017;12(3):e0173976.