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SCHOOL OF PUBLIC HEALTH

DETERMINANT FACTORS FOR THE OCCURRENCE OF TUBERCULOSIS AMONG PEOPLE LIVING WITH HIV AFTER ART INITIATION IN ADDIS ABABA, ETHIOPIA: A CASE CONTROL STUDY

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Abbreviations/ Acronyms

AFB; Acid Fast Bacilli

AHR ; Adjusted Hazard Ratio

AOR; Adjusted Odd Ratio

AIDS; Acquired Immune Deficiency Syndrome

ART; Antiretroviral Therapy

AZT; Zidovudine

CI; Confidence Interval

COR; Crude Odd Ratio

d4t; Stavudine

EFV; Efaviren

EPTB; Extra Pulmonary Tuberculosis

IPT; Isoniazid Preventive Therapy

IRIS; Immune Reconstitution Inflammatory Syndrome

HAART; Highly Active Antiretroviral Therapy

HIV; Human Immunodeficiency Virus

Hgb; Hemoglobin

NNRTI; Non-Nucleoside Reverse Transcriptase Inhibitor

NRTI; Nucleoside Reverse Transcriptase Inhibitor

NVP; Nevirapine

OR; Odd Ratio

PI; Protease Inhibitor

PLWHIV; People Living With Human Immune deficiency Virus

PTB; Pulmonary Tuberculosis

3TC; Lamivudine

TLC; Total Lymphocyte Count

WHO; World Health Organization

Abstract

Introduction: Tuberculosis is the leading killer of people with HIV/AIDS and the first presenting sign in the majority of AIDS patients. The risk of developing tuberculosis is estimated to be between 20- 37 times greater in people living with HIV than among those without HIV infection in their life time. In the developing world, many patients either have a history of tuberculosis when they initiate antiretroviral therapy, or they develop TB while receiving ART. ART diminishes the risk for TB as the CD4 count rises, yet the excess risk for TB is never eliminated even if CD4 levels return to normal levels.

Objective: To assess determinant factors for the occurrence of TB among PLWHIV after ART initiation in public hospitals and health centers in Addis Ababa.

Methodology: A case control study was conducted from December 2011 to February 2012 in selected 2 public hospitals and 13 health centers in Addis Ababa. The sample size of the study was 613 (204 cases and 409 controls). Cases were adult people living with HIV who developed TB after ART initiation and on anti TB treatment in the last 6 months prior to data collection and Controls were adult people living with HIV who did not develop TB after ART initiation. An interviewer administered structured questionnaire was used to collect information. Bivariate and multivariate analysis was performed by using logistic regression to determine independent factors of TB among PLWHIV after ART initiation.

Result: After adjustment for potential confounders, having separate kitchen (AOR=0.50; 95% CI: 0.26, 0.96), the presence of INH prophylaxis (AOR=0.35; 95% CI: 0.125, 0.69) and cotrimoxazole prophylaxis (AOR=0.19; 95%CI: 0.06, 0.62) had an independent protective benefit against risk of tuberculosis. In contrary being bedridden (AOR= 9.36; 95%CI: 3.39, 25.85), having WHO clinical stage III or IV (AOR= 3.40; 95% CI: 1.69, 6.87), having opportunistic infection at ART initiation (AOR=5.22; 95%CI: 2.67, 10.27), the ART regimen initiated at base line and hemoglobin level less than 10mg/dl (AOR=0.35 ;95% CI: 0.125, 0.69) were an independent predictors for increased risk of tuberculosis in people living with HIV after ART initiation.

Conclusion: Increasing coverage of INH preventive therapy and cotrimoxazole preventive therapy reduced the overall risk of TB among HIV patients who initatiated treatment. Targeting special attention is need to be provided for patients who have advanced condition(WHO clinical stage III or IV disease, being bedridden and having hemoglobin level less than 10mg/dl) would also reduce the risk of development of new TB infection. Improving housing condition and living standard is also recommended.

1. Introduction

1.1. Background Information

The human immunodeficiency virus (HIV) pandemic presents a massive challenge to the control of tuberculosis (TB). In high HIV prevalence population, TB is a leading cause of morbidity and mortality, and HIV is driving the tuberculosis epidemic in many countries, especially in sub-Saharan Africa (1). There were an estimated 1.1 million HIV positive TB patients globally in 2009, around 80 % of patients live in sub-Saharan Africa. At least one-third of the 33.3 million people living with HIV worldwide are infected with TB (2).

HIV and TB are so closely connected that the term 'co-epidemic' or 'dual epidemic' is often used to describe their relationship, which is also referred to as TB/HIV (or HIV/TB) co-infection. Throughout the 1990s and up to 2004, the HIV epidemic led to a dramatic increase in the number of TB cases in the African Region, from less than 200 to more than 350 cases per 100 000 population. Within the African Region, the highest rates of HIV infection among TB patients are in countries in southern and eastern Africa, where more than 50% of TB patients are estimated to be infected with HIV (3).

To tackle TB/HIV burden different responsive measures have been tried (2). World Health Organization (WHO) recommends the three "I's" for TB/HIV (Isoniazid preventive therapy, Intensified case finding for TB, and infection control) to reduce the burden of TB among people living with HIV. In addition to this WHO also recommends the following; provide HIV testing and counseling, introduce HIV infection prevention methods, introduce cotrimoxazole preventive therapy, ensure HIV/AIDS care and support introduce antiretroviral therapy. People living with HIV need early diagnosis and treatment of active TB. If TB is not present, they should receive isoniazid preventive treatment (IPT). However by the end of 2009, globally only 85 000 (less than 1%) people living with HIV enrolled on IPT and only 5% of people living with HIV reported screened for TB (2, 4, 5).

1.2. Statement of the Problem

Tuberculosis is the leading killer disease of people with HIV and the first presenting sign in the majority of AIDS patients (6). Almost one in four deaths among people with HIV is due to TB. It is also the most common presenting illness among people living with HIV, including those who are taking antiretroviral treatment. People living with HIV are facing emerging threats of drug-resistant TB. Worldwide, there were an estimated 440,000 MDR-TB cases in 2009 (2) and 650 000 MDR-TB cases in 2010 (7). The risk of developing tuberculosis (TB) is estimated to be between 20- 37 times greater in people living with HIV than among those without HIV infection in their life time. Globally there were 8.8 million new cases of TB, of which 1.1 (13%) million were among people living with HIV in 2010, 0.35 million deaths (range, 0.32 million–0.39 million) among people who were HIV-positive (3, 7, 8). Most of the estimated number of TB cases in 2010 occurred in Asia (59%) and Africa (26%). The proportion of TB cases co infected with HIV is highest in countries in the African Region , accounted for 82% of TB cases among people living with HIV(7)

The 22 high burden countries (HBCs) that have received particular attention at the global level since 2000 account for 81% of all estimated TB cases worldwide in 2010 (7). A high rate of previously undiagnosed TB is common among people living with HIV. Despite major reductions with ART, however, the risk of TB remains high in Africa(9).

According to the 2010 WHO global TB control report, Ethiopia ranks 8th among the 22 high-burden countries in the worlds and 3rd in Africa. As Ethiopia ranks 8th among the world's 22 high-burden tuberculosis countries, there were 12 % HIV positive incident TB cases of all TB cases in 2009 (5). According to the World Health Organization's Global TB report of 2011, the country had an estimated prevalence rate of 394 cases per 100,000 populations in 2010, with an estimated incidence rate of 261 cases per 100,000 populations and mortality rate of 35 per 100,000 population (7). In HIV positive people, new all forms of TB cases were 74 per 100 000 pop/year). The number of TB cases is likely to increase in the country as HIV/AIDS epidemic expands; while 16 percent of notified TB patients tested for HIV, 40 percent are HIV positive (10).

However the introduction of provider initiated counseling and testing in most public health facilities in the country has improved HIV screening among TB patients from 16% in 2007 to 38% in 2009. A total of 56,040 TB patients were tested for HIV, of which 11,118 (20%) were found to be HIV positive. In addition, a total of 24,112 HIV-positive people were referred from chronic HIV and ART clinics for TB screening out of which 4,154 (17.2%) were found to have active TB and 2,403 (10%) with latent TB, and hence put on IPT (11).

Rationale of the Study

In the developing world, many patients either have a history of tuberculosis (TB) when they initiate antiretroviral therapy (ART), or they develop TB while receiving ART. When patients start ART, it has not been well delineated what influence development of TB, especially in patients who consistent HIV suppression on ART (12). In sub-Saharan Africa including Ethiopia, the incidence of tuberculosis in adults receiving highly active antiretroviral therapy (HAART) is higher than in HIV-negative adults (8). Studies on risk factors of TB were done in the general population but determinants of active TB among HIV patients are not well elucidated in countries with limited resources. There are no enough studies in Ethiopia on factors associated with development of TB among HIV infected patients on ART. This study is intended to examine determinant factors for occurrence of TB in PLWHIV during ART. It would provide basic information to program designers and implementers at national, regional and district level on predisposing factors of TB in PLWHIV and started ART treatment. It may also helps for policy makers to make right decision in TB/HIV prevention.

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2. Literature Review

2.1. Over View of TB - HIV Co-infection

Tuberculosis is an airborne infectious disease that kills 2 million people per year, making it the greatest curable infectious killer on the planet. TB is a growing global epidemic to which we are all vulnerable (6). Among the 22 high burden countries (HBCs), the five countries with the largest number of incident cases in 2010 were India (2.0 million-2.5 million), China (0.9 million-1.2 million), South Africa (0.40 million-0.59 million), Indonesia (0.37 million-0.54 million) and Pakistan (0.33 million-0.48 million). India alone accounted for an estimated one quarter (26%) of all TB cases worldwide, and China and India combined accounted for 38% (7).

The lifetime risk of developing active TB in HIV-negative individuals is approximately 10%; but the annual risk among HIV-infected patients is ~10%, while the lifetime risk approaches 50% among them (13). It is estimated that about one-third of people with HIV are also infected with TB (6). The ecological study in Oromia National Regional State revealed that a positive and strong ecological association (r=0.69 p=0.01) between the prevalence of HIV infection and the incidence of all forms of TB (14). Even though ART known to minimizes incidence of TB, still studies have reported TB incidence from HIV patients on ART. A retrospective cohort study done in Addis Ababa, Ethiopia showed that 11.8 % of patients develop TB within 6 months after HAART initiation, of which 5.4% and 4.3 % were pulmonary and extra pulmonary TB (15). A retrospective review study done in five Medicines Sans Frontiere's HIV programmes (Cambodia, Thailand, Kenya, Malawi and Cameroon) shows 62.3% of pulmonary TB and 54.9% of extra-pulmonary TB were diagnosed within 3 months after HAART initiation (16). A prospective cohort study conducted in Abidjan also reported that during follow-up under HAART, TB incidence of 4.8/100 P-Y (95% CI, 2.5–8.3) (17). Another retrospective cohort study from Uganda shown that of the 271 HAART naïve patients without TB at baseline, 5.9% developed active TB within 6 months and 2.7% after 6 months after initiating HAART(18). Likewise a cohort study from Europe and America revealed the incidence rate of TB among HIV patients receiving HAART was 3.1 after 6 months of follow up and 4.69 cases /1000 PY during the first 3 years of follow up (19).

Time to initiate antiretroviral therapy in co-infected patients

All HIV-positive TB patients are considered eligible for ART according to the latest WHO guidelines on provision of ART (5)**.** The actual ART commencement time during TB treatment remains poorly defined although expert groups and the World Health Organization (WHO) recommend that public health programs make treatment of TB the first priority and ideally begin ART after anti-TB treatment (ATT) is tolerated and CD4 cell count is measured (20). Some observational studies have now documented that ART reduces the likelihood of death during anti TB therapy of HIV-infected TB patients. In Thailand, mortality occurred in 5/71 (7%) of patients among those who received ART compared to 94/219 (43%) among those who did not; 80% reduction in the odds of death was found with ART commencement even after adjusting for CD4 cell counts, smear status, cotrimoxazole use and treatment facility (21).

What ART regimen to start? The recommended first-line ART regimen comprises 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus 1 non-nucleoside reverse transcriptase inhibitor (NNRTI). There are few drug interactions between TB drugs and the 2 NRTIs. The situation is more complex with the NNRTI class because NNRTI levels are reduced in the presence of rifampicin. However, accumulating data support the use of first-line NNRTIs-containing ARV regimens in patients receiving rifampicin containing treatment for TB. Here EFV is the preferred option, because the interactions with rifampicin are easier to manage; the second alternative is to use a triple NRTI regimen in patients undergoing TB treatment. Two triple NRTI regimens (zidovudine + lamivudine + abacavir and zidovudine + lamivudine + tenofovir) can be used safely with rifampicin. A third less favored option is the use of two NRTIs with nevirapine (NVP), though its level is decreased in the presence of rifampicin. Hepatotoxicity is a significant complication of both ART and anti- TB treatment and liver function should be monitored (20).

There are two issues to consider in patients who are diagnosed with TB while on ART. The first concerns the modifications of ART, if any, which should be recommended for patients developing active TB within 6 months of initiating first-line or second-line ART (20).

The second issue is whether the presentation of active TB on ART constitutes ART failure. In cohort studies, ART has been found to decrease the incidence of TB in treated patients. Rates of TB among treated patients nevertheless remain persistently higher than among HIV-negative individuals(18). Subclinical or undiagnosed TB often presents within the first 6 months after initiation of ART, frequently as part of immune reconstitution inflammatory syndrome (IRIS). If an episode of TB occurs during the first 6 months following initiation of ART, this should not be considered a treatment failure event and the ART regimen should be adjusted for co-administration with rifampicin-containing regimens. If there is good

response to anti-TB therapy, the decision to switch to a second-line regimen can be delayed until short-course TB therapy has been completed (20).

2.2. Determinant Factors for the occurrence of Tuberculosis in People Living with HIV receiving ART

2.2.1. Socio economic related determinants of TB

Socio economic determinants have been shown to be an important determinant of TB occurrence, especially in developing countries. For instance, a case control study from West Africa reveal that marital status (single OR= 1.67; 95 % CI 1.21–2.30; Widowed OR = 1.48; 95 % CI: 0.89–2.47)), found to be risk factors for tuberculosis. This study also showed that ownership of the house by the TB-HIV patients' family (OR = 1.42; 95 % CI 1.07–1.90 P = 0.016) associated with Tuberculosis (22). A case control study done in south west Ethiopia to assess risk factors of active TB in PLWHIV showed that a low level of education (OR=2.8; 95% CI**:** 1.1, 7.1), was found to be risk factors for the occurrence of active TB in PLWHIV (23).

2.2.2. Host related factors for the occurrence of Tuberculosis

As studies have shown that different host related factors are associated with the development of TB. Different Studies have demonstrated male gender was found to be at higher risk of developing TB. In case control study in West Africa, male gender (OR=1.43) is independently associated with risk of TB (22). From another observational cohort study done in South Africa also found that male patients had 1.42 times greater hazard ratio for the occurrence of active TB compared with female patients(24). Similarly, a case control study in south west Ethiopia (23) and retrospective cohort study in Uganda also documented that being male was at higher risk of acquiring TB (25). In retrospective cohort analysis of all incident TB cases recorded in San Diego County from 1993 through 2007, a TB–HIV co-infected patient was more likely to be male (adjusted odds ratio (AOR)=2.86; 95% confidence interval CI=1.97, 4.14) and aged 30 to 39 years (AOR=3.23; 95% CI=2.11, 4.95) compared with patients infected only with TB (26).

Baseline CD4+ T-lymphocyte count is another important predictor for development of TB. A retrospective review study done in five Medicines Sans Frontiere's HIV programmes (Cambodia, Thailand, Kenya, Malawi and Cameroon) to measure the incidence rate of notified TB in people receiving HAART showed that 90% had a CD4 cell count of < 200 cells/ml (16). A longitudinal cohort study of 804 adult factory workers (95 HIV-positive, 709 HIV-negative) in Ethiopia demonstrated that the incidence of TB increased as CD4 counts decreases (CD4 counts (/µl) ≥500 IR = 0.0 , 200–499 IR= 41.2 and <200 IR =

107.6 (27). Similarly, in prospective cohort study over 3 years follow up among 944 patients accessing a community-based ART programme in South Africa found that during ART, an increase of CD4 by 100 cells/ ml was associated with a 25% lower risk of developing TB (P = 0.007) (28) . A retrospective cohort study in Uganda also showed that a baseline CD4 count of 50 cells/mm3 (hazard ratio [HR] 1.84 (1.25–2.70), P=0.002) was significantly associated with an increased risk of TB (25). Furthermore, a case control study done in south west Ethiopia, CD4 lymphocyte count less than 200 cells/μL (OR=9.8; 95% CI: 5.5, 17.5) was found to be risk factors for the occurrence of TB in PLWHA (23). However, in observational cohort study in South Africa , for late occurring TB risk (>6months) , CD4 count was marginally significant (p=0.06) (12) and over one year of follow up study in Uganda reported that CD4 cell count < 50 (cells/μL) AHR = 2.22 (0.49–10.16), p = 0.304 (29) was not statistically significant risk factors for TB. And also in prospective cohort study conducted in Abidjan an increase of CD4 by 50cels /mm^3 (AHR 1.01, p = 0.85) was not significantly associated(18).

In the HIV positive patients, as the WHO clinical stage advances different opportunistic infections have been developed, one of these is TB. In an observational cohort study done in South Africa , patients with baseline advanced WHO stage (stage III/IV) had 1.35 times greater hazard ratios for early occurring TB compared with those mild WHO stage . This study also show that for late occurring of TB (>6 months), advanced baseline WHO stage was marginally significant risk factor (p=0.06 (12). A case control study done in south west Ethiopia also reveal that a WHO clinical stage IV (OR=4.3) found to be risk factors for the occurrence of active TB in PLWHA (23). But over one year of follow up of 219 HIV-infected patients starting ART at the infectious diseases clinic in Kampala, Uganda reported that WHO clinical stage 3 and 4 with AHR = 1.82 (0.33–10.18) P =0.495 was not significantly associated with TB occurrence (29). Similarly a prospective cohort study over 3 years follow up among 944 patients accessing a community-based ART programme in South Africa reported that WHO Stage 3 (IRR = 1.53 (0.72–3.24), P = 0.27) and WHO stage 4 (IRR = 1.59 (0.69–3.66) P = 0.271) was not significantly associated with TB occurrence (28).

Those patients with a unit increase in BMI and hemoglobin were at risk of active TB with the hazard ratio of 1.06 (1.02, 1.09) and 1.10 (1.02, 1.18) respectively. For the early occurring TB events (<6 months), baseline BMI and hemoglobin were significant factors (12). Over one year of follow up of 219 HIV-Infected Patients Starting ART at the Infectious Diseases Clinic in Kampala, Uganda found that low BMI (<18.5 kg/m2) were predictors of ART-

associated TB (29). Correspondingly, a case control study done in south west Ethiopia documented that a BMI less than 18.5 kg/m2 (OR=4.1; 95% CI: 2.3, 7.4) and hemoglobin level less than 10.0 g/dl (OR=2.8; 95%CI: 1.5, 5.2), found to be risk factors for the occurrence of active TB in PLWHA (23). But hemoglobin < 12.5 (mg/dL) (AHR= 2.31 (0.23–23.43) P = 0.477) was not significantly associated with TB in the over one year follow up study of 219 HIV-Infected Patients Starting ART (29).

According to a clinic-based case-control study in West Africa, TB was found to be associated with smoking (current OR=2.03; 95 % CI 1.22–3.39, past OR = 1.53) (with a dose–effect relationship), with a persistent dose–response effect according to duration of smoking (22). However in a case control study in Gambia revealed that in the combined multivariate host - environmental analysis, smoking was not an independent risk factor for TB (smoker in the past 6 months OR = 1.88 (0.83–4.26), p= 0.13)(24).

A systematic review of existing scientific data on the association between alcohol consumption and TB shows a strong association between heavy alcohol use/alcohol use disorders and TB. A meta-analysis on the risk of TB for these factors yielded a pooled relative risk of 2.94 (95% CI: 1.89-4.59). Heavy alcohol use strongly influences both the incidence and the outcome of the disease and was found to be linked to altered pharmacokinetics of medicines used in treatment of TB, higher rate of re-infection, higher rate of treatment defaults and development of drug-resistant forms of TB. Based on the available data, about 10% of the TB cases globally were estimated to be attributable to alcohol (30). *Another* systematic review study also reveal that the risk of active tuberculosis is substantially elevated in people who drink more than 40 g alcohol per day, and/or have an alcohol use disorder with the pooled relative risk across all studies 3.50 (31).

A case control analysis of the hospital discharge dataset from the Texas Health Care Information Council from 1999–2001 showed that Diabetes patients were almost twice as likely to have tuberculosis after adjusting by sex, age, and race/ethnicity (32). Case control study in West Africa, History of asthma appeared strongly protective against TB in that population (OR = 0.28) (22). However Case control study in Gambia, history of asthma (OR =1.0 (0.09–11.03)) was not an independent risk factor for TB (24).

2.2.3. Environmental related determinants

Overcrowding and history of household exposure to a known TB case are the standout risk factors for TB occurrence. Since TB is contagious air born disease, contact with TB patients in the family increase the risk. In case control study in West Africa, those patients who had family history of TB have around 3 times greater risk of TB (OR = 3.24; P<0.001)

(19)(22). Another case control study in Gambia also documented that history of TB in another household member (AOR = 10.17 (4.08–25.63) ($p < 0.0001$) was significant risk factor (24). Similarly a study in south west Ethiopia showed that history of contact with a TB patient in the family (OR=2.0; 95% CI: 1.2, 3.3) was increase risk for the occurrence of active TB in PLWHA (23). Tuberculosis also found to be associated with number of adults in the household (6-10 adult/house hold OR = 1.37; 95 % CI 1.03–1.82, $P< 0.001$; > 10 adult/ house hold (OR = 2.80; 95 % CI 1.71–4.57) (31). In case control study in West Africa, those patients who lived in the number of adults in the household between 6-10 have had 1.37 times more likely at risk of TB (CI: 1.03,1.82, P.0.0001) (25). A Case control study in Gambia revealed that Being in the highest crowding category index 3 ($p = 0.003$) was significant risk factors. Increasing crowding across the three categories was significantly associated with TB by the likelihood ratio test for linear trend ($p = 0.0038$) (24). In contrary, in case-control study in Greenland there is no significant difference being in the crowding category index >1 person/room or ≤ 1person/room (OR=1.41 ; 95% CI=0.922.16) (33).

Prophylaxis with the isoniazid (INH) has been shown to reduce the incidence of TB in HIV infected persons either by eradicating latent infection and or preventing progression of new infection to active TB (34). A Meta analysis of (seven randomized trials) six months preventive therapy with INH was shown that reduces in incidence of TB in HIV infected people with relative risk (RR) of 0.58 (95% CI, 0.43-0.80), P=0.03 on INH treated Vs placebo for TB. Another retrospective study carried out in Rio D Janeiro, Brazil, reported that the combination of ART and IPT has the greatest impact on TB incidence when compared to IPT or ART alone (35). Another meta analysis of 11 trials involving over 73 000 non-HIV-infected participants, use of IPT was associated with a tuberculosis risk reduction of 60% (95% CI 48–69%) over a follow-up period of at least 2 years (36). Another cohort study showed that there was a significantly lower incidence of TB among the IPT cohort compared with the control cohort (IRR,0.45;95%CI,0.26,0.78) (37).

3. Objective

3.1. General Objective

To assess determinant factors for the occurrence of TB in PLWHIV on ART in public hospitals and health centers, Addis Ababa.

3.2. Specific Objectives

To identify potential determinant factors for the development of TB in HIV positive patients after ART initiation.

4. Methodology

4.1. Study Area and Period

This case control study was conducted in Addis Ababa in selected health facilities from December 15, 2011 to February 30, 2012 and a total of two hospitals and thirteen health centres were included in the study.

Addis Ababa is the capital city of Ethiopia and seat of African Union & Economic Commission for Africa, having three layers of Administration: City Government at the top, 10 Sub City Administrations in the Middle, and 116 woreda Administrations at the bottom. Addis Ababa has a population size of over 3 million (3038096) with annual growth rate of 2.1. It is established in 1887 by Emperor Menelik II and Empress Taitu. Its average altitude is 2,500 meters above sea level, covers an area of 540 square kilometers with an overall average maximum and minimum temperature of 22.9 and 10.8 degree centigrade respectively .

The city has 48 hospitals. Thirteen are public hospitals of which, five are under Addis Ababa Regional Health Bureau (AARHB) and 5 are specialized referral (central) Hospitals. Two are defence forces (military) referral hospitals and one hospital under police force. Furthermore the city has 27 health centres under the Addis Ababa health bureau and five newly opened health centres. There are two hospitals, three health centres and 31 different level clinics established by non-government organizations (NGOs). The city also has 33 private hospitals and more than 700 different level private clinics. TB/HIV cares have been given in almost all public health facilities.

4.2. Study Design

A Case control study was conducted in selected public hospitals and health centers in Addis Ababa to assess determinant factors for the occurrence of TB in PLWHIV who initiated ART.

Cases: - were adult people living with HIV who developed TB after ART initiation and on anti TB treatment in the last 6 months prior to data collection

Controls: - were adult people living with HIV who did not develop TB after ART initiation and have no any of the following problems for two to four weeks or longer:

- Chronic Cough (greater than 2 weeks)
- Fever , Fatigue/Tiredness , Night Sweats
- Weight loss , loss of appetite

4.3. Population

4.3.1. Source population

All People living with HIV, ≥18 years of age and started ART treatment in Addis Ababa public hospitals and health centers were source population.

4.3.2. Study population

All People living with HIV, ≥18 years of age and started ART treatment in 2 Hospitals & 13 health centers in Addis Ababa and fulfilling the following criteria

Inclusion criteria

People living with HIV, who were ≥18 years of age and started ART treatment and have, follow up at the study site.

Exclusion criteria

HIV patients presenting with TB before commencing ART

Patients who were taking TB therapy at the time of HAART initiation

PLWHIV who were not on ART or discontinued

TB -HIV co-infected patients who were severely ill will be excluded

4.4. Sample Size Determination and Sampling Technique

4.4.1. Sample size determination

The sample size was calculated using Epi Info version 3.5.1 software (Center for Disease Control and Prevention, Atlanta, 2004) using the following parameters: the exposure variable was CD4 < 50cells/µl with proportion of 31.8 % among the controls and 43.9 % among cases (38), 5% significance level, power of 80%, a case to control ratio of 1:2 and by using the following formula

$$n1 = \frac{\left[Z\alpha/2\sqrt{\left(1+\frac{1}{r}\right)p(1-p)} + Z\beta\sqrt{P1(1-P1) + \frac{p2(1-p2)}{r}}\right]2}{(p1-p2)^2}$$

$$p = \frac{p1 + rp2}{1+r} \qquad r = \frac{n2}{n1}$$

Where; n1 = the required sample size for the cases

n2 = the required sample size for the controls

n_1: n_2 = 1:2

p_1 = Proportion of exposure in case

p_2 = Proportion of exposure in controls

α = type -I error (0.05)

$Z_{\alpha/2}$= Critical value at 95% level of confidence (1.96)

Z_β = standard normal distribution value corresponding to power (0.84)

Sample size was calculated for exposure status in different variables. The most significant predictors of TB were used. Due to financial and time constraints, I took the second maximum sample size, which was CD4 cell count less than 50 cell/µl as exposure variable (38, 39).

Table 1: **Sample Size Determination**

Variables (exposure)	Proportion of exposure in cases (%)	Proportionof exposure inControls(%)	Sample size for case(No)	Sample size for Controls (No.)	Total sample Size (No.)
Sex (male)	40	26	130	259	389
BMI< 18 kg/m^2	50	23	41	82	123
CD4< 50cell/µl	**43.9**	**31.8**	**186**	**372**	**558**
WHO stage IV	43.3	33.9	312	624	936
LowHgbmg/dl)	63.5	45.3	96	192	288

The Calculated sample size was 186 for n_1 (cases) and 372 for n_2 (controls) adding 10% for none response, the resulting minimum sample size was 613 (204 cases and 409 controls).

4.4.2. Sampling Technique / Procedure

First the governmental hospitals and health centers were assessed whether they have adequate cases or not. Two hospitals and thirteen health centers was found to be eligible and considered as study site

Different sampling scheme was used for cases and controls to have reasonably comparable groups. All TB–HIV patients after ART who were on anti TB treatment and fulfill inclusion criteria included in the study for their relative small number. Since controls were adequate enough to be sampled, they were selected by simple random sampling method. For those

controls that fulfill inclusion criteria, unique ID number was given in increasing order. Then simple random sampling technique was employed to select samples from each facility using computer generated random number table. If that selected subject is not eligible, the next number was taken as a study participant and exit interview was conducted. Controls were selected from each facility based on the number of cases available in each facility.

4.5. Data Collection Procedure and Quality Control

The data was collected by structured questionnaire. The questionnaire was initially prepared in English and then translated in to Amharic. The Amharic version was again translated back to English to check for any inconsistencies. The data was collected from two sources: the primary data was collected by face to face interview of patients and to supplement clinical and laboratory information, record review was conducted from ART log books. Nurses who were working in ART and TB clinics in the selected hospitals and health centers were recruited as data collectors and supervisors for their respective hospitals. Identification of cases and controls was done by the principal investigator through the help of the ART and TB registers.

Training was given for supervisors and data collectors. Then Pre-testing of the questionnaire for its clarity, understandability, completeness and reliability was conducted prior to actual data collection. The overall activity was controlled by the principal investigator of the study. Data quality was controlled by designing the proper data collection materials and through continuous supervision. All completed questionnaire was examined for completeness and consistency during data management, storage and analysis. The data was entered by trained data clerk and cleaned by principal investigator before analysis.

4.6. Data Entry, Processing and Analysis

Data were entered and cleaned using Epi-info version 3.5.1 and exported to SPSS software version 16 for analysis. Frequencies and proportions were used to describe the study population in relation to relevant variables.

Bivariate analysis was performed to examine the effect of each variable of interest on the risk of TB. Odds ratios (OR) and their 95% confidence intervals (CIs) were estimated using binary logistic regression, with TB as an outcome.

To identify independent predictors of developing tuberculosis, a multivariate logistic regression model was fitted with the variables having a P-value < 0.05 in the bivariate logistic regression analysis.

4.7. Study Variables

4.7.1. Independent variables

The independent variables include Socio demographic characteristics (age, sex, religion, ethnicity, marital status, employment and educational status), Clinical and immunological variables at ART initiation (CD4 cell count (cells/μL), hemoglobin level mg/dl, WHO Stage, functional status, opportunistic infection, Chemoprophylaxis), use of substances such as smoking, alcohol and Chat, presence of asthma and history of diabetes mellitus, Contact history with a TB patient in the family, crowding , availability of separate kitchen in the house hold, presence of latrine in the compound.

4.7.2. Dependent variables

TB development after ART initiation

4.8. Ethical Considerations

The proposal was reviewed and ethical clearance was obtained from the Institutional Review Board (IRB) of the AAU, college of Health science and also from Addis Ababa City Health Bureau Ethics Review committee. Following the approval by IRB, official letter of co-operation was written to selected hospitals and health centers by Addis Ababa City Government Health Bureau and written permission was obtained from the respective hospital and health centers administration before starting data collection.

The data collectors explained about the study and informed verbal consent was obtained from each study participants and confidentiality assured for all the information provided. To preserve the confidentiality, the data collectors were nurses or counselors working in ART and TB clinic of the respective selected hospitals and health centers. Moreover, personal identifiers were not included on data collection questionnaire. The recorded data were not accessed by a third person except the principal investigator, and was kept confidentially.

4.9. Operational Definition

Tuberculosis defined and categorized according to the National Tuberculosis and Leprosy Control manual of Ethiopia (42).

- **Definite case of tuberculosis**. A patient with *Mycobacterium tuberculosis* identified from a clinical specimen, either by culture or sputum smear examinations positive for acid-fast bacilli (AFB).
- **Pulmonary tuberculosis** (PTB) refers to a case of TB (defined above) involving the lung parenchyma. Miliary tuberculosis is classified as pulmonary TB because there are lesions in the lungs.

- **Smear-positive pulmonary TB (PTB+)** refers to patient with at least two initial sputum smear examinations positive for AFB by direct microscopy, Or patient with one initial smear examination positive for AFB by direct microscopy and culture positive, Or A patient with one initial smear examination positive for AFB by direct microscope and radiographic abnormalities consistent with active TB as determined by a clinician.

- **Smear-negative pulmonary TB (PTB-)** A patient having symptoms suggestive of TB with at least 3 initial smear examinations negative for AFB by direct microscopy, and (1) No response to a course of broad-spectrum antibiotics, and (2) Radiological abnormalities consistent with pulmonary tuberculosis, and (3) Decision by a clinician to treat with a full course of anti- tuberculosis Or A patient whose diagnosis is based on culture positive for M. tuberculosis but three initial smear examinations negative by direct microscopy

- ***Extra* pulmonary** TB refers TB in organs other than the lungs, without radiographic abnormalities in the lungs, proven by one culture-positive specimen from an extra-pulmonary site or histo-pathological evidence from a biopsy. Or TB based on strong clinical evidence consistent with active EPTB and the decision by a physician to treat with a full course of anti-TB therapy.

- **"Presumptive" pulmonary TB:** (*1*) consistent clinical picture > 30 days, (*2*) positive smear for acid-fast bacilli in sputum or broncho alveolar lavage sample or absence of microbiological evidence of pneumonia from any other known pathogen, (*3*) unsuccessful response to standard antibiotic therapy, and (*4*) successful response to standard anti tuberculosis therapy.

- **"Presumptive" extrapulmonary TB:** (*1*) Consistent clinical picture > 30 days, (*2*) positive smear for acid-fast bacilli in normally sterile body fluid or tissue from a site other than lungs or no other microbiologic explanation, and (*3*) successful response to standard anti tuberculosis therapy.
- **A history of active TB at HAART initiation** a history of TB on admission to the ART clinics or if they had an episode of active TB that was considered to be cured between their admission to the ART clinics and HAART initiation;
- **Prevalent episode of active TB** if they had an episode of active TB that was under treatment on HAART initiation, or if an episode of active TB was documented after HAART initiation and the date of the first symptoms recorded in the ART center medical record preceded the date of HAART initiation

- **An incident episode of active TB** if TB was documented after HAART initiation and the date of the first symptoms was posterior to HAART initiation
- WHO clinical staging system was considered to staging HIV/AIDS
- Functional status
  - Working = able to perform usual work in or out of the house
  - Ambulatory= able to perform activities of daily living
  - Bedridden= not able to perform activities of daily living

4.10. Dissemination of Study findings

Findings of this study will be disseminated to corresponding Hospitals and health centers where the study was conducted and to school of public health through hard copy and presentation. The findings will also finally be published to access others outside as well.

5. Result

5.1. Socio demographic characteristics of HIV and TB/HIV infected patients

Of 613 participants selected, 593 study subjects were responded (196 (33%) cases and 397(67%) controls) with over all response rate of 96.7 % (96.1 % for cases and 97.1% for controls).

The mean and inter quartile range (IQR) for the age of cases were 36.7 and 29-42.75 years, respectively. The corresponding values for controls were 35.7 and 30-40 years. More proportion of case and control patients was in the age group of 30-39; 37.2 % and 45.6% respectively. High proportion of women was in both groups; 56.6% (111) in cases and 69.3% (275) in controls respectively. But the proportion of women in controls was more than in cases. More than three fourth of the patients were completed primary school and above; 83.2% in cases and 80.9 % in controls. The majority of subjects were married; 39.8 % in cases and 40.1% in controls. When we see the occupation of the participant, 26.5% (52) of cases and 29.5% (117) of controls have no job and 17.3% (34) of cases and 24.9% (99) of controls were none governmental organization employee (Table-2).

Table 2: Socio-demographic characteristics of HIV and TB/HIV infected patients in Addis Ababa, 2012

Sociodemographic variables	Cases n (%)	Controls n (%)	Total n (%)
Sex			
Male	85(43.4)	122(30.7)	207(34.9)
Female	111(56.6)	275(69.3)	386(65.1)
Age			
18-29	53(27)	96(24.2)	149(25.1)
30-39	73(37.2)	181(45.6)	254(42.8)
≥40	70(35.)	120(30.2)	190(32.0)
Religion			
Muslim	30 (15.3)	43 (10.8)	73 (12.3)
Orthodox Tewahdo	14 1(71.9)	320 (80.6)	461(77.7)
Protestant	24(12.2)	32(8.1)	56(9.4)
Other*	1(0.5)	2(0.5)	3(0.5)
Ethnicity			
Amhara	90(45.9)	198(49.9)	288(48.6)
Oromo	51(26.0)	111(28.0)	162(27.3)
Tirgie	25(7.6)	30 (7.6)	55 (7.6)
Gurage	23 (11.7)	43 (10.8)	66 (11.1)
Other❖	7(3.6)	15(3.8)	22(3.7)
Educational status			
No education	33 (16.8)	76 (19.1)	109 (18.4)
primary	85 (43.4)	159 (40.1)	244 (41.1)
secondary	61 (31.1)	122 (30.7)	183 (30.9)
Tertiary	17 (8.7)	40 (10.1)	57(9.6)
Marital status			
Single	63(32.1)	93(23.4)	156(26.3)
Married	78(39.8)	159(40.1)	237(40.0)
Divorced & Widowed	55(28.1)	145(36.5)	200(33.7)
Occupation			
Merchant	24 (12.2)	21 (7.8)	55(9.3)
Governmental employee	23 (11.7)	26 (6.5)	49(8.3)
NGO employee	34 (17.3)	99 (24.9)	133(22.4)
Day laborer	18 (9.2)	58 (14.6)	76(12.8)
Jobless	52(26.5)	117 (29.5)	169(28.5)
driver	10 (5.1)	5 (1.3)	15(2.5)
Private	21 (10.7)	41(10.3)	62(10.5)
Other♣	14(7.)	20(5)	34(5.7)

* Catholic, Adventist

❖ Argoba, Eritrea, Gamo, Kefa, Kembata , Sidama, Silte , Somali ,wolayta

5.2. Host and Environmental variable characteristics of study subjects

More than one third of cases (32%) and one forth of controls (27%) had previous history of TB. Likewise 16.8% of cases and 18.9% controls had a contact history with TB patients in their family. But low proportion of cases and controls had history of Diabetes Mellitus, asthma and imprisoned. Regarding substance use, 35.7% of cases and 19.4 % of controls had history of chat chewing. Similarly 36.6 % and 19.1% of cases and controls had history of alcohol use respectively. Moreover, one fourth of cases; 25% but 9.1% controls had history of smoking.

More proportions of cases; 44.4% than controls; 35.3% had no separate kitchen. Seventy six percent (149) of cases and eighty five percent (337) of controls had the family size of between 1-5. Less than one tenth of cases (7.7%) and controls (9.8%) were imprisoned. Similarly 20% of cases and 12.8% of controls lived in other place for more than 6 months in the last 5 years (Table 3).

♣ House wife, student, guard, waiter, retirement, house worker, beggar, cleaner

Table 3: Host and Environmental related variables of HIV and TB/HIV infected patients in Addis Ababa, 2012.

variables	Cases n (%)	Controls n (%)	Total n (%)
Chat chewing			
Yes	70 (35.7)	77 (19.4)	147 (24.8)
No	126 (64.3)	320 (80.6)	446 (75.2)
History of Smoking			
Yes	49(25.0)	36(9.1)	85(14.3)
No	147 (75.0)	361(90.9)	508 (85.7)
Alcohol drinking			
Yes	71 (36.2)	76 (19.1)	147 (24.8)
No	125 (63.8)	321 (80.9)	446 (75.2)
Past history of TB			
Yes	63 (32.1)	108 (27.2)	162(27.3)
No	120 (61.2)	223(56.2)	352(59.4)
I don't know	13(6.6)	66(16.6)	79(13.3)
History of Asthma			
Yes	11(5.6)	16(4.0)	27(4.6)
No	181(92.3)	343(86.4)	524(88.4)
I don't know	4(2.0)	38(9.6)	42(7.1)
History of Diabetes Mellitus			
Yes	5 (2.6)	5(1.3)	10(1.7)
No	187(95.4)	354(89.2)	541(91.2)
I don't know	4(2.0)	38 (9.6)	42 (7.1)
Family history of TB			
Yes	33(16.8)	75(18.9)	108 (18.2)
No	159(81.1)	306(77.1)	465(78.4)
I don't know	4(2.0)	16(4.0)	20(3.4)
History of Imprisoned			
Yes	15(7.7)	39(9.8)	54(9.1)
No	181(92.3)	358 (90.2)	539 (90.9)
Lived other place			
Yes	40(20.4)	51 (12.8)	91 (15.3)
No	156(79.6)	346(87.2)	502(84.7)

Availability of separate kitchen			
Yes	109(55.6)	257(64.7)	366(61.7)
No	87(44.4)	140(35.3)	227(38.3)
Owen house			
Yes	52 (26.5)	137 (34.5)	189(31.9)
No	144(73.5)	260(65.5)	404(68.1)
Availability of Latrine			
Yes	160(81.6)	352(88.7)	512 (86.3)
No	36 (18.4)	45 (11.3)	81 (13.7)
Kerosene (Gas) as source of energy in the house			
Yes	139(70.9)	196(49.4)	335(56.5)
No	57(29.1)	201(50.6)	258(43.5)
Number of people in the house hold			
1-5	149(76.0)	337(84.9)	486 (82.0)
6-9	44(22.4)	52(13.1)	96 (16.2)
>=10	3(1.5)	8(2.0)	11(1.9)
Number of adult people in the house hold			
1-5	172(87.8)	370 (93.2)	542 (91.4)
6-9	21(10.7)	24(6.0)	45(7.6)
>=10	3(1.5)	3(0.8)	6(1.0)

5.3. Clinical and immunological Characteristics of the Study Subjects at the ART initiation

Clinical condition of the two groups was different in many aspects at ART initiation; cases had more advanced WHO clinical stage than control groups. Majority of cases; 78.4% (152) were in WHO clinical stage III or IV. In contrary, 55.5% (213) in control groups were in WHO clinical stage I or II. More individuals in control were able to perform usual work in or out of their house (working); 90.3% (355) than in cases; 41.7 % (75) at ART initiation. More than half of the cases had an opportunistic infection at ART initiation; 59.8% (110) but 23.6% (91) of patients in control group had opportunistic infection. During ART initiation 85 % of cases and 64.9 % of controls did not use INH preventive therapy.

The median and IQR for CD4 count in cases was 139 and 81-201 and the corresponding value in controls was 192 and 125-307 respectively. Of the total 183 patients in cases; three fourth, 73.2 % of patients had CD4+ cell count less than 200cells/µl. But nearly half, 53.6 % of patients in controls had CD4+ cell count less than 200cells/µl. Another important base line variable considered is Hgb level. The minimum and maxim Hgb level in cases was 3 mg /dl and 18.2 mg /dl with IQR 8-13 and mean of 10.68 mg /dl. While in controls the maximum and minimum Hgb level was 4 mg /dl 23.1 mg /dl respectively with IQR 11.8-14.4 and mean of 13 mg /dl. Among cases 39 % of them had Hgb level less than 10mg /dl. In contrary only 7.2 % of controls had Hgb level less than 10mg/dl.

At start of antiretroviral treatment, all patients were initiated with first line antiretroviral drugs; out of the total patients initiated with first line drugs; majority 52(26.5%) of cases started with drug type TDF-3TC-EFV followed by d4t-3TC-EFV; 74(23.0%). But in control groups 29 % and 27.5 % of patients started with ARV drug type of 1c=AZT-3TC-NVP and 1e=TDF-3TC-EFV respectively (Table 4).

Table 4**:** Baseline clinical and immunological characteristics of HIV and TB/HIV co infected patients at the ART initiation in Addis Ababa, 2012

Base line variables	Cases n (%)	Controls n(%)	Total n (%)
Who clinical stage	**(n=194)**	**(n=384)**	**(n=578)**
Stage I	9 (4.6)	100 (26.0)	109 (18.9)
Stage II	33 (17.0)	113 (29.4)	146 (25.3)
Stage III	113 (58.2)	150 (39.1)	263 (45.5)
Stage IV	39 (20.1)	21(5.5)	60 (10.4)
Isoniazid Preventive Therapy	**(n=180)**	**(n=390)**	**(n=570)**
Yes	27(15.0)	137(35.1)	164(28.8)
No	153 (85.0)	253 (64.9)	406 (71.2)
Cotrimoxazole preventive	**(n=185)**	**(n=395)**	**(n=580)**
Yes	164 (88.6)	380 (96.2)	544 (93.8)
No	21(11.4)	15 (3.8)	36(6.2)
Opportunistic infection	**(n=184)**	**(n=385)**	**(n=569)**
Yes	110 (59.8)	91 (23.6)	201 (35.3)
No	74 (40.2)	294 (76.4)	368 (64.7)
ART Regimen			
1a[1]	23 (11.7)	67 (16.9)	90 (15.2)
1b[2]	45 (23.0)	35 (8.8)	80 (13.5)
1c[3]	33(16.8)	115(29.0)	148(25.0)
1d[4]	38(19.4)	49(12.3)	87(14.7)
1e[5]	52(26.5)	109(27.5)	161(27.2)
1f[6]	5(2.6)	22(5.5)	27(4.6)
Functional status	**(n=187)**	**(n=393)**	**(n=580)**
Working	78(41.7)	355(90.3)	433(74.7)
Ambulatory	70(37.4)	18(4.6)	88(15.2)
Bedridden	39(20.9)	20(5.1)	59(10.2)
Hemoglobin level (mg/dl)	**(n=187)**	**(n=388)**	**(n=575)**
≤10	73(39)	28(7.2)	101(17.6)
10-12.49	54(28.9)	118(30.4)	172 (29.9)
≥12.5	60(32.1)	242(62.4)	302(52.5)
CD4 **count (cells/µL)**	**(n=187)**	**(n=392)**	**(n=579)**
≤50	26(13.9)	22(5.6)	48(8.3)
51-200	112(59.9)	187(47.7)	299(51.6)
201-349	33(17.6)	109(27.8)	142(24.5)
>=350	16(8.6)	74(18.9)	90(15.5)

[1] Stavudine , lamivudine , neverapine → d4t-3TC-NVP
[2] Stavudine , lamivudine , efavirenz → d4t-3TC-EFV
[3] Zidovudine , lamivudine , neverapine→AZT-3TC-NVP
[4] Zidovudine , lamivudine , efavirenz→ AZT-3TC-EFV
[5] TDF, lamivudine , efavirenz →TDF-3TC-EFV
[6] TDF, lamivudine , neverapine → TDF-3TC-NVP

5.4. Clinical Presentation (type) of Tuberculosis in HIV patients after ART initiation

Half; 50.5% (99) of the TB patients presented with smear negative PTB followed by extra pulmonary TB, 31.1 % (61) and the rest 18.4% (36) patients had smear positive pulmonary TB .

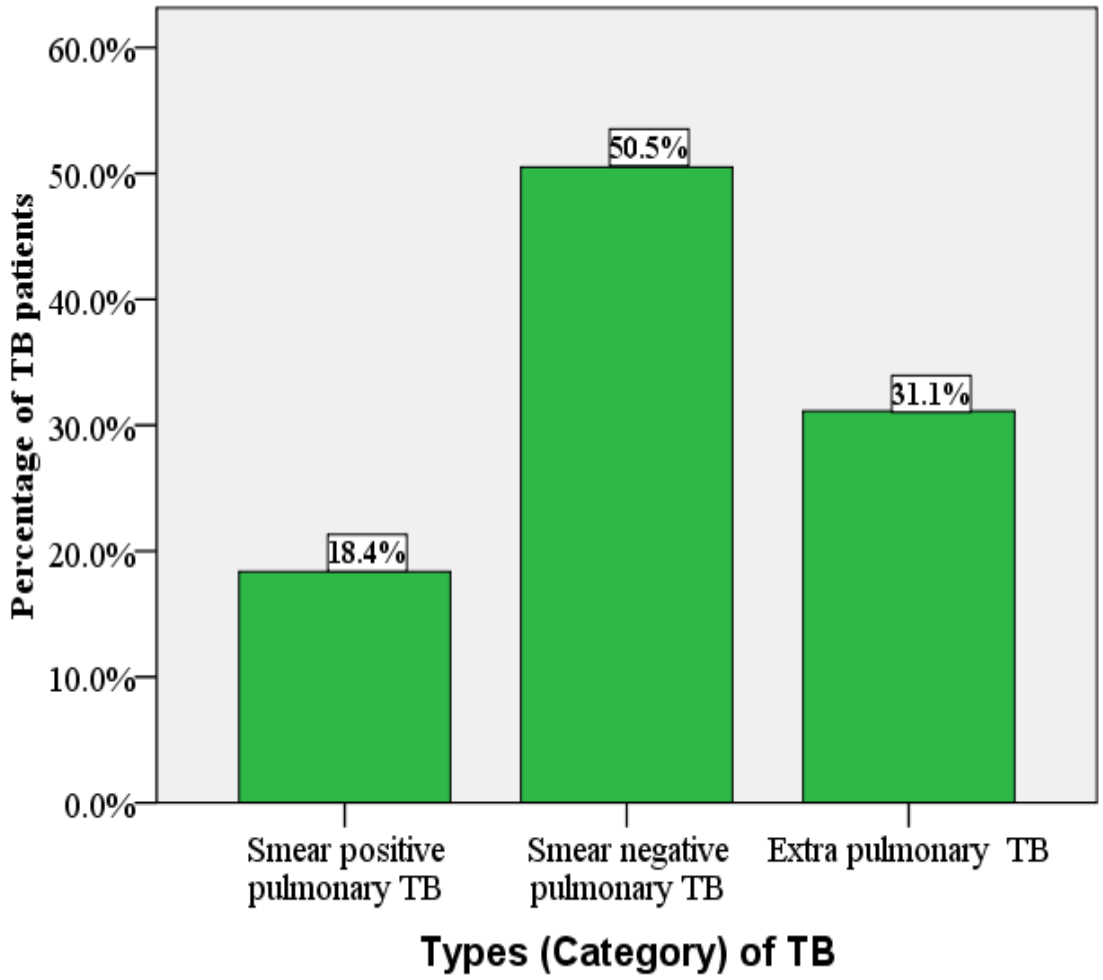

Figure 1: Clinical Presentation (type) of TB in HIV patients after ART initiation, Addis Ababa 2012

5.5. Determinant factors for the occurrence of TB in HIV positive patients after ART initiation

5.5.1. Bivariate analysis

Logistic regression model was used in bivariate analysis to assess the relationship between each independent variables and the occurrence of TB. The result showed that from socio demographic variables sex, occupation and marital status were statistically associated with occurrence of TB. Likewise history of chat chewing, history of smoking, history of alcohol intake, history of previous TB, history of asthma and Diabetes Mellitus, lack of available separate kitchen in the house hold, lived in other place at least 6 months in the last 5 year, lack of latrine in the compound, using gas as a source of energy in house hold also associated with occurrence of TB infection. Similarly baseline weight, WHO clinical stage, functional status, Isoniazid prophylaxis, cotrimoxazole prophylaxis, opportunistic infection, ART regimen, CD4 cell count, number of people living together in the house hold, hemoglobin level were significantly associated with occurrence of TB in HIV infected patients after ART initiation.

The bivariate logistic regression analysis showed that a higher proportion of male patients (COR=1.73; 95% CI: 1.23, 2.46) (p=0.003) develop TB Compared to female. In the study, the risk of new TB decreases for every 1kg increase in weight by 4%. The divorced or widowed (COR=0.560; 95% CI: 0.36, 0.87) patients were at the lower risk of developing TB compared with never married (single) individuals. But educational status and occupation were not associated with occurrence of Tuberculosis (Table 5).

Table 5: Socio demographic Determinant factors for occurrence of TB among people living with HIV after ART initiation: comparison of TB cases and controls by bivariate logistic regression analysis, Addis Ababa, 2012

Variables	Cases n (%)	Controls n(%)	COR	95% CI	p-value
Sex					
Male	85(43.4)	122(30.7)	1.73	1.21, 2.46	0.003*
Female	111(56.6)	275(69.3)	1		
Age					
18-29	53(27)	96(24.2)	1		
30-39	73(37.2)	181(45.6)	0.731	0.47, 1.13	0.15
≥40	70(35.)	120(30.2)	1.057	0.68, 1.65	0.81
Religion					
Muslim	30 (15.3)	43 (10.8)	1		
Orthodox tewahdo	14 1(71.9)	320 (80.6)	0.63	0.38, 1.05	0.075*
Protestant	24(12.2)	32(8.1)	1.075	0.531, 2.18	0.841
Other	1(0.5)	2(0.5)	0.72	0.062, 8.27	0.789
Ethnicity					
Amhara	90(45.9)	198(49.9)	1		
Oromo	51(26.0)	111(28.0)	1.01	0.67, 1.53	0.959
Tirgie	25(7.6)	30 (7.6)	1.83	1.02, 3.30	0.043
Gurage	23 (11.7)	43 (10.8)	1.18	0.669, 2.10	0.572
Other	7(3.6)	15(3.8)	1.03	0.405, 2.61	0.956
Education					
No education	33 (16.8)	76 (19.1)	1.02	0.508,2.06	0.952
Primary	85 (43.4)	159 (40.1)	1.26	0.673,2.35	0.472
Secondary	61 (31.1)	122 (30.7)	1.18	0.617,2.24	0.622
Tertiary	17 (8.7)	40 (10.1)	1		
Marital					
Single	63(32.1)	93(23.4)	1		
Married	78(39.8)	159(40.1)	0.72	0.48-1.10	0.131
Divorced/ Widowed	55(28.1)	145(36.5)	0.56	0.36, 0.87	0.011*
Occupation					
Merchant	24 (12.2)	21 (7.8)	1.106	0.46, 2.63	0.82
Gov't employed	23 (11.7)	26 (6.5)	1.264	0.52,3.06	0.60
Nongov't/privatorganization employee	34 (17.3)	99 (24.9)	0.49	0.22, 1.08	0.076
Day laborer	18 (9.2)	58 (14.6)	0.44	0.19,1.05	0.065
Jobless	52(26.5)	117 (29.5)	0.64	0.30,1.35	0.240
Driver	10 (5.1)	5 (1.3)	2.86	0.80,10.12	0.106
Private/self employed	21 (10.7)	41(10.3)	0.72	0.31, 1.73	0.478
Others	14 (7.1)	20 (5)	1		

* significant at $\alpha = 0.05$

A former episode of TB in the cases associated with TB. The risk of TB was also found to increase with smoking (COR =3.34; 95% CI: 2.087, 5.35), as well as with alcohol intake (COR=2.39; 95% CI: 1.63, 3.52) and chat use (COR=2.31; 95% CI: 1.57, 3.40). Tuberculosis also associated with diabetes and history of asthma. Patients who lived in other place for at least 6 months have about 1.7 times risk of developing TB after ART initiation (p=0.017). In addition, controls were more likely to have available separate kitchen (p=0.032) and latrine (p=0.02). More over using gas as a source of energy in house hold associated with increased risk of TB (COR=2.5; 95% CI: 1.74, 3.61). However, there was no significant difference between cases and controls concerning previous family history of TB, history of imprisoned, living in his/her own or family's house and house floor made of cement or mud. The number of persons in the household between 6-10 were more likely at increased risk of TB compared with the number of persons in the household between 1-5 (COR=1.914; 95% CI: 1.23, 2.99). Similarly the number of adults in the household between 6-10 have 1.89 times more likely to develop TB than adults in the household between 1-5 (*P*=0.043) although TB was not associated with the number of persons per room in the household and number of rooms in the house (Table 6).

Table 6: Host and Environmental determinant factors for occurrence of TB among HIV patients after ART initiation: comparison of cases and controls by logistic regression in bivariate analysis, Addis Ababa, 2012

Variables	Cases n (%)	Controls n %)	COR	95% CI	p-value
Chat chewing					
Yes	70 (35.7)	77 (19.4)	2.31	1.57, 3.40	<0.0001*
No	126 (64.3)	320 (80.6)	1		
Smoking					
Yes	49(25.0)	36(9.1)	3.34	2.087,5.35	< 0.0001*
No	147 (75.0)	361(90.9)	1		
Alcohol drinking					
Yes	71 (36.2)	76 (19.1)	2.39	1.63, 3.52	< 0.0001*
No	125 (63.8)	321 (80.9)	1		
TB history					
Yes	63 (32.1)	108 (27.2)	1.08	0.74,1.59	0.68
No	120 (61.2)	223(56.2)	1		
Idon't know	13(6.6)	66(16.6)	0.37	0.19,0.69	0.02*
Asthma					
Yes	11(5.6)	16(4.0)	1.303	0.59, 2.87	0.511
No	181(92.3)	343(86.4)	1		
Idon't know	4(2.0)	38(9.6)	0.19	0.07, 0.57	0.003*
Diabetes Mellitus					
Yes	5 (2.6)	5(1.3)	1.893	0.54, 6.62	0.318
No	187(95.4)	354(89.2)	1		
Idon't know	4(2.0)	38 (9.6)	0.199	0.07, 0.57	0.002*
Family history of TB					
Yes	33(16.8)	75(18.9)	0.847	0.54, 1.33	0.471
No	159(81.1)	306(77.1)	1		

* **significant at $\alpha = 0.05$**

Idon't know	33(16.8)	75(18.9)	0.847	0.54, 1.33	0.471
Imprisoned					
Yes	15(7.7)	39(9.8)	0.761	0.41, 1.42	0.389
No	181(92.3)	358 (90.2)	1		
Lived other place					
Yes	40(20.4)	51 (12.8)	1.74	1.10, 2.74	0.017*
No	156(79.6)	346(87.2)	1		
Have kitchen					
Yes	109(55.6)	257(64.7)	0.682	0.481, 0.97	0.032*
No	87(44.4%)	140(35.3)	1		
Owen house					
Yes	52 (26.5)	137 (34.5)	0.685	0.47,1.00	0.05*
No	144(73.5)	260(65.5)	1		
Latrine					
Yes	160(81.6)	352(88.7)	0.568	0.35, 0.94	0.02*
No	36 (18.4)	45 (11.3)	1		
Gas as source of energy in household					
Yes	139(70.9)	196(49.4)	2.501	1.74, 3.61	<0.0001*
No	57(29.1)	201(50.6)	1		
No. of people living in the household					
1-5	149(76.0)	337(84.9)	1		
6-10	44(22.4)	52(13.1)	1.914	1.23, 2.99	0.004*
>10	3(1.5)	8(2.0)	0.85	0.22, 3.24	0.81
No. of adult person living in the household					
1-5	172(87.8)	370(93.2)	1		
6-10	21(10.7)	24(6.0)	1.88	1.02, 3.47	0.043*
>10	3(1.5)	3(.8)	2.15	0.43, 10.77	0.35
Numbers of Room					
1-2	153(78.5)	299(75.3)	1.194	0.79, 1.80	0.397
>=3	42(21.5)	98(24.7)	1		

* **significant at $\alpha = 0.05$**

Other important predictors for the TB occurrence were base line clinical variables. Study subjects with baseline WHO clinical stage III or IV have about 4.5 times higher risk of developing TB than those in stage I or II (P<0.0001). The presence of INH prophylaxis (COR=0.32; 95% CI: 0.21, 0.52) and cotrimoxazole prophylaxis (COR=0.27; 95% CI: 0.14, 0.53) were associated with decreased risk of developing TB. Individuals with hemoglobin level <10mg/dl has increased risk of developing TB than individuals with Hemoglobin level ≥123.5 mg/dl (COR= 10.5; 95% CI: 6.26, 17.68). Patients who were bedridden (COR =8.87; 95% CI: 4.91, 16.05) and ambulatory (COR=17.7; 95% CI: 9.98, 31.39) by their functional status were at increased risk of developing TB compared to working status. Similarly patients whose CD4 cell count ≤ 50 cell/µL were more likely at risk for the occurrence TB compared to patients who had ≥ 350 cell/µL cd4 cell count (COR= 5.47; 95% CI: 2.56, 11.97) (Table7).

Table 7 : Clinical and immunological factors for occurrence of TB among HIV patients after ART initiation: comparison of cases and controls by bivariate analysis in logistic regression, Addis Ababa, 2012

Variables	Cases n(%)	Controls n(%)	COR	95% CI	p-value
WHO Clinical Stage					
Stage I or II	42(21.6)	213(55.5)	1		
Stage III or IV	152(78.4)	171(44.5)	4.51	3.032, 6.70	<0.0001*
INH prophylaxis					
Yes	27(15.0)	137(35.1)	0.33	0.21, 0.52	<0.0001*
No	153 (85.0)	253 (64.9)	1		
CTX prophylaxis					
Yes	164 (87.2)	380 (96.2)	0.27	0.14, 0.53	<0.0001*
No	24(12.8)	15(3.8)	1		
Functional status					
Working	78(41.7)	355(90.3)	1		
Ambulatory	70(37.4)	18(4.6)	17.70	9.98, 31.39	<0.0001*
Bed	39(20.9)	20(5.1)	8.87	4.91, 16.05	<0.0001*
Opportunistic infection					
Yes	110(59.8)	91(23.6)	4.80	3.29, 7.00	<0.0001*
No	74(40.2)	294(76.4)	1		
ART Regimen					
1a	23 (11.7)	67 (16.9)	1		
1b	45 (23.0)	35 (8.8)	3.75	1.96, 7.16	<0.0001*
1c	33(16.8)	115(29.0)	0.84	0.45, 1.54	0.566
1d	38(19.4)	49(12.3)	2.26	1.197, 4.26	0.012*
1e	52(26.5)	109(27.5)	1.39	0.78, 2.48	0.246
1f	5(2.6)	22(5.5)	0.66	0.23, 1.95	0.454
Hgb level (mg/dl)					
<10	73(39.0)	28(7.2)	10.52	6.26, 17.68	<0.0001*
10-12.49	54(28.9)	118(30.4)	1.85	1.20, 2.83	<0.0001
>=12.5	60(32.1)	242(62.4)	1		
CD4 cell count (cell/μL)					
≤50	26(13.9)	22(5.6)	5.47	2.56, 11.97	<0.0001*
51-200	112(59.9)	187(47.7)	2.77	1.54, 4.99	0.001*
201-349	33(17.6)	109(27.8)	1.400	0.72, 2.73	0.322
≥350	16(8.6)	74(18.9)	1		

* **significant at $\alpha = 0.05$**

5.5.2. Multivariate analysis

To identify independent predictors of developing tuberculosis, a multivariate logistic regression model was fitted with the variables having a P-value < 0.05 in the bivariate logistic regression analysis. Accordingly, some variables were remained independent predictors for the occurrence of TB after controlling for the other factors. From these factors, being widowed or divorced were at lower risk of TB compared to single individuals (AOR=0.36; 95% CI: 0.16, 0.82). Patents who had separate kitchen were associated with lower risk of TB (AOR=0.5; 95% CI: 0.26, 0.96; P<0.038). Similarly the presence of INH prophylaxis (AOR=0.35; 95% CI: 0.125, 0.69; P=0.005) and cotrimoxazole prophylaxis (AOR=0.19; 95% CI: 0.06, 0.62) had an independent protective benefit against risk of tuberculosis. That is the occurrence of TB in HIV patients decreased in patients who were on IPT and CPT. In contrary Study subjects who were bedridden (AOR=9.36; 95% CI: 3.39, 25.85) and ambulatory (AOR=19.4; 95% CI: 7.44, 50.78) by their functional status were at increased risk of developing TB compared to working status even though CI is wide and lack statistic power. Study subjects with baseline WHO clinical stage III or IV had higher risk of developing TB than those in stage I or II (AOR=3.4; 95% CI: 1.69, 6.87). As well individuals with hemoglobin level <10mg/dl has increased risk of developing TB than individuals with hemoglobin level ≥123.5 mg/dl (AOR=7.43; 95% CI: 3.04, 18.31). Likewise having opportunistic infection at ART initiation (AOR=5.22; 95% CI: 2.67, 10.27), the ART regimen initiated at base line and using gas (kerosene) as energy source in the house hold (AOR=2.67; 95% CI: 1.36, 5.2) were independently associated with increased risk of TB occurrence. But occupational status, smoking, alcohol intake, asthma, Diabetes Mellitus, family history of TB, sex, lived other place, number of people living in the house hold and CD4 cell count lost their statistical significance in the multivariate analysis (Table 8).

Table 8: Multivariate analysis (Logistic regression model) of determinants associated with developing TB among HIV infected patients after ART initiation, Addis Ababa, 2012.

Variables	COR(95% CI)	p-value	AOR(95% CI)	p-value
Gas(kerosene) as source of energy in household				
Yes	2.5(1.7, 3.6)	<0.0001	2.67 (1.36, 5.2)	0.004
No	1		1	
Have kitchen				
Yes	0.68 (0.48, 0.95)	0.032	0.50 (0.26,0.96)	0.038
No	1		1	
WHO clinical stage				
Stage I&II	1		1	
Stage III&IV	4.508 (3.03,6.7)	<0.0001	3.40 (1.69, 6.87)	0.001
Isoniazid preventive therapy				
Yes	0.326(0.21, 0.52)	<0.0001	0.35 (0.125, 0.69)	0.005
No	1		1	
CTX preventive therapy				
Yes	0.27(0.14, 0.53)	<0.0001	0.19 (0.06, 0.62)	0.006
No	1		1	
Functional status				
Working	1		1	
Ambulatory	17.8 (10,31.4)	<0.0001	19.44 (7.44, 50.78)	<0.0001
Bed	8.88(4.91,16.05)	<0.0001	9.36(3.39, 25.85)	<0.0001
Opportunistic infection				
Yes	4.80(3.29, 7.0)	<0.0001	5.22 (2.67, 10.27)	<0.0001
No	1		1	
Hgb level				
<10	10.52(6.26,17.7)	<0.0001	7.43 (3.04, 18.31)	<0.0001
10-12.49	1.85 (1.2, 2.83)	<0.0001	1.34 (0.65, 2.77)	0.430
≥12.5	1		1	
Marital status				
Single	1		1	
Married	0.72 (0.48,1.1)	0.131	0.99 (0.48, 2.0)	0.985
Divorced or widowed	0.56(0.36,0.87)	0.011	0.36 (0.16, 0.82)	0.015

6. Discussion

This case-control study has identified several determinant factors for the occurrence of TB among HIV infected people enrolled on ART in Addis Ababa. Housing condition and living standard and isoniazid preventive therapy were risk factors for TB in this setting. Patients who have advanced condition (WHO clinical stage III or IV disease, being bedridden and having hemoglobin level less than 10mg/dl) were also associated with development of new TB infection.

In this study among determinants factors, marital status was significantly associated with TB. Patients who were divorced or widowed have decreased risk of developing TB compared to never married (single) which is consistent with other reports in west Africa and Ethiopia (22, 40). It might be explained by never married (single) persons are usually younger than married persons and have a different lifestyle, especially males, who often migrate to towns in search of a job where they frequently live alone or with friends.

In this study low level of education was not significantly associated with TB. But it is not consistent with the study from south west Ethiopia (23). This could be probably due to the high prevalence of literate in our study population as it was from the capital of the country.

Smoking was identified as risk factor for the development of TB in clinic-based case-control study in West Africa (22). But in a Case control study in Gambia, smoking was not associated with active TB (24). Similarly in this study smoking was not significantly associated with TB occurrence in multivariate analysis. This could be due to the low prevalence of smoking in our study population. There could also be a social desirability bias whereby smokers denied their smoking status.

In a case control study from West Africa, history of asthma appeared strongly protective against TB (22). However in this study history of asthma was not statically associated with TB. This is consistent with the case control study in Gambia (24).

Studies demonstrated that contact with TB patients in the family associated with increased the risk of TB occurrence (22-24). But in this study family history of TB showed some degree of association with TB in bivariate analysis, but it did not have an independent effect on the risk of TB in multivariate analysis when adjusting on other variables.

Other independent predictors of tuberculosis were WHO stage 3 or 4; patients with WHO stage 3 or 4 have higher risk of developing TB than those with WHO stage 1 or 2. It is consistent with other study done in South Africa and South west Ethiopia (12, 23). This suggests that those who developed TB may have been more immune-compromised and different opportunistic infections have been developed at baseline.

Patients who were bedridden at the initiation of ART have 8.87 times higher risk of developing TB than working patients. This is consistent with the retrospective cohort study in Ethiopia (40). This might be due to being seriously sick secondary to deteriorated clinical and immunological condition.

Availability of separate kitchen in the household associated with decreased risk of TB development which is consistent with a study from south west Ethiopia (23). It might be explained by increased indoor air pollution if there is no separate cooking kitchen in the house. Likewise using gas (kerosene) as energy source in the household significantly associated with TB as it was commonly used cooking fuels in urban areas.

Studies have shown that risk of TB was associated with the number of people living together in the household (over Crowding) (24, 25, 41). However, this study did not find the association between TB and number of people in the household. This might be related to high proportions of unmarried persons in the study population resulted in low number of family size in the house hold. The other reason may be that TB development represents a reactivation of an infection acquired years ago due to HIV infection, with no relation to current living and crowding conditions.

Patients having a hemoglobin level of ≤10mg/dl have 2.4 times higher risk of developing TB than those patients having hemoglobin level ≥12.5mg/dl, similar to other study findings in south west Ethiopia (23). This shows that patients having higher hemoglobin level have a low risk of developing TB than those with low hemoglobin level. TB and hemoglobin level might be indirectly associated with advanced stage of HIV disease, when HIV positive patients have chronic disease and high viral load it resulted in immune-suppression and suppression of red blood production in bone marrow. This might lead to both TB due to deteriorated immunity and Anemia due to supersession of RBC production.

Different studies have shown that ionized preventive therapy reduces the risk of TB infection in people living with HIV (34-37). Similarly in this study significant difference was observed between patients who were on INH preventive therapy and not on preventive therapy. Patients who were on INH preventive therapy were at the lower risk of developing TB compared to patients who were not on INH preventive treatment. A Study from West Africa showed that ownership of the house by the TB patient's family associated with lower risk for TB (22). However, this study did not show statistical difference between those who had house and those who had not. This inconsistency might be due to source population difference, as the source population of this study was from the capital of the country.

7. Strengths and Limitations

7.1. Strength

1. Wide scope of the study setting and population being from 2 hospitals and 13 health centers set up and population in the study makes it more representative
2. Strong power

7.2. Limitation

- Use of case control study design could not establish temporal relation ships
- Case control study can only identify associations, could not proof causations.
- Recall bias might have affected the accuracy of information related to substance use such as cigarette smoking and alcohol consumption.
- Challenges to diagnosis of tuberculosis in HIV patients

8. Conclusion and Recommendations

8.1. Conclusion

Being divorced and widowed, cotrimoxazole preventive therapy & having separate kitchen were independent predictors of decreased occurrence TB after ATR initiation. Whereas having WHO clinical stage III or IV disease, being bedridden and having hemoglobin level less than 10mg/dl, using kerosene gas as source of energy in the house hold and having opportunistic infection were factors associated with increased risk of TB occurrence at multivariate analysis.

8.2. Recommendations

- The continuous assessment of patients for signs and symptoms of TB after starting ART particularly among patients that have risk factors mentioned in this paper will lead to an earlier TB diagnosis and ultimately to reduced morbidity.
- The improvement of TB control with enhanced health education on TB and its risk factors is important thorough model households, community health agents extension health workers and health professionals
- Increasing coverage of INH and cotrimoxazole preventive therapy is necessary to reduce the overall risk of TB among HIV patients who instantiated treatment.
- Due attention should be given to patients who have advanced clinical condition at ART (WHO clinical stage III or IV), being bedridden and having hemoglobin level less than 10mg/dl) to reduce the risk of development of new TB infection.
- Improving housing condition and living standard is also recommended.
- Moreover it is recommended that further prospective cohort study should be conducted to make clear relation b/n marital status and risk of TB and other risk factors such as social and economic status including smoking and alcoholism and TB contact history in order to evaluate their effect in the development of TB among HIV infected patients after ART initiation

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Appendix

Annex-I Conceptual Frame Work

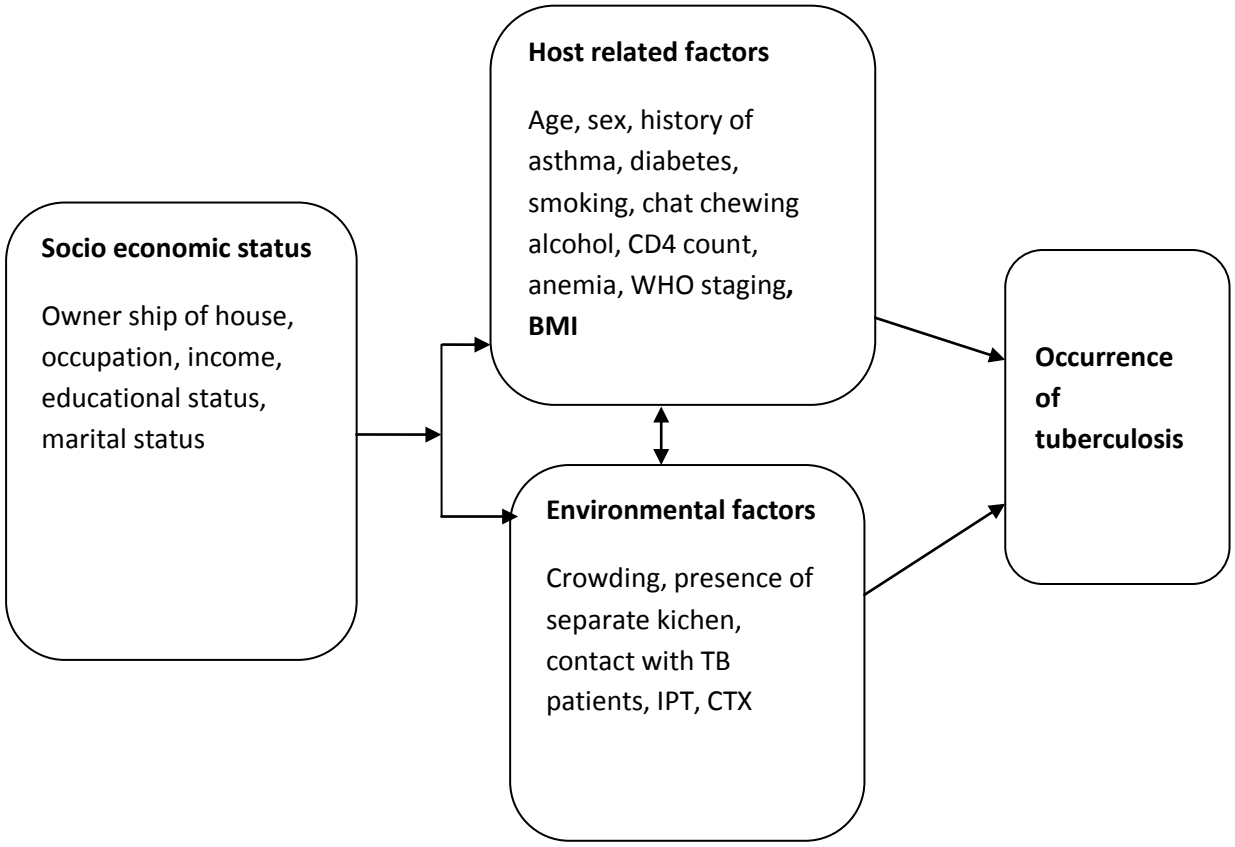

Figure 2: Determinants factors for TB development in HIV Patients after ART

Annex-II Questionnaire (English Version)

Introduction:

This patient information collection questionnaire is intended to assess determinant factors of TB occurrence in HIV/AIDS patients after the ART initiation in selected public Hospitals and health centers in Addis Ababa, Ethiopia. The study will be conducted through face to face interview of patients during the ART/TB follow up visit and reviewing ART /TB log books. The study is aimed to fill the information gap and provide empirical evidence for program planner, decision makers and TB-ART program implementer at the different level by enabling them to access a base line data on determinant factors of TB occurrence during HAART.

Name and signature of interviewer _____

Date_____

Patient's card No _____

No.	Variables	Descriptions / categories
Part I: Socio-demographic Characteristics		
1	Age	_____years
2	Sex	1. Male 2. Female
3	Religion	1. Muslim 2. Orthodox 3. Protestant 4. Catholic 99. Other (specify)----------
4	Ethnicity	1. Amhara 2. Oromo 3. Tigirie 4. Gurage 99. Other(specify) _____
5	Educational status	1. No education 2.primary 3. Secondary 4. Tertiary
6	Marital status	1. Never married 2. Married 3. Divorced 4. Widowed
7	Occupational status	1. Farmer 2. Merchant 3. Governmental employee 4. Non-governmental employee 5. Day laborer 6. Jobless 7. Driver 8. Private 99. Others (specify)_____
	Substance use	
8	Have you ever tried to chewing chat?	1. Yes 2. No
9	If you say yes for question number "8", how long do you chew	_____years _____months
10	Have you ever smoked cigarette,	1. Yes 2. No

	even one or two puffs?	
11	If you say yes for question number "10" , for how long	_____years _____months
12	Have you ever drunk alcohol?	1. Yes 2. No
13	If you say yes for question number "12" for how long	_____years _____months
14	Have you any history of tuberculosis?	1. Yes 2. No 3. I don't know
15	Have you history of Bronchial Asthma	1. Yes 2. No 3. I don't know
16	Have you History of Diabetes Mellitus	1. Yes 2. No 3. I don't know
17	Is there any member in your family who suffered from TB?	1. Yes 2. No 3. I don't know/ not sure
18	Have you ever in imprisoned	1. Yes 2. No
19	Have you ever lived anywhere else for more than six months in the last five years	1. Yes 2. No
20	Number of people in house hold	
21	Number of adults in house hold (>= 15 years of age)	
22	Number of room	
23	Is there any Available separate kitchen?	1. Yes 2. No
24	Do you have your own house?	1. Yes 2. No
25	Do you have latrine in your home?	1. Yes 2. No
26	Monthly income	
27	By what material do your house floor is made?	1. Mud 2. cement
28	Do you have water at your home?	1. Yes 2. No
29	Type of fuel for energy source	Firewood yes no Gas/kerosene yes no

		Electricity yes no Charcoal yes no

Part-II Base line (at ART initiation) clinical, laboratory and ART information (Filed from ART registration book)

1	Weight	
2	Height	
3	CD4 count	
4	Hemoglobin level	
5	WHO clinical staging	1. Stage I 2. Stage II 2. Stage III 3. Stage IV
6	Isoniazid preventive therapy	1. Yes 2. No
7	Cotrimozazole preventive therapy	1. Yes 2. No
8		
9	Functional status	1. Working 2. Ambulatory 3. Bedridden
10	ART Regimen	1)1a (30) =d4t (30)-3TC-NVP 2)1a (40) =d4t (40)-3TC-NVP 3) 1b (30) =d4t (30)-3TC-EFV 4) 1b (40) =d4t (40)-3TC-EFV 5) 1c= AZT-3TC-NVP 6) 1d=AZT-3TC-EFV 7) 2nd line regimens(2a/2b/2c/2d)
11	Opportunistic infection	1. Yes 2. No
12	Viral load	
13	WBC count	
14	Types of TB	1. Smear positive pulmonary TB 2. Smear Negative pulmonary TB 3. Extra pulmonary TB

Annex-III Questionnaire (Amharic Version)

(የአማርኛ መረጃ መጠይቅ)

መግቢያ

ይህ የመረጃ መሰብሰቢያ መጠይቅ አላማው አዲስ አበባ ከሚገኙ የህዝብ ሆስፒታሎች ና ጤና ጣቢያዎች ውስጥ ፀረ-ኤችአይቪ መድሃኒት ከጀመሩ በኋላ ለቲቪ በሽታ መከሰት ምክንያት/መንስኤ የሆኑትን ነገሮችን ለመለየት ሲሆን ጥናቱ የሚከናወነው በቃለመጠይቅና ከህክምና መዝገብ ላይ የህክምና መረጃዎችን በመውሰድ ይሆናል ። ይህ ጥናት የመረጃ ክፍተት ለመሙላትና መሰረታዊ መረጃ ፥ ለፕሮግግራም አውጭዎች ፣ ለውሳኔ ሰጭዎች እና ለቲቪ-ኤችአይቪ ህክምና ፈፃሚዎች ለቲቪ በሽታ መከሰት ምክንያቶች ላይ መረጃ እንዲያገኙ ያሥችላል ።

ይህንን ቃለ መጠይቅ ያከናወነው ሰው ስምና ፊርማ _____

ቀን _____

የበሽተኛው መለያ ቁጥር _____

ተ.ቁ		**ዝርዝር**
ክፍል አንድ : የማህበራዊና ግለሰባዊ መግለጫ		
1	**ዕድሜ**	**_____ዓመት**
2	**ፆታ**	**1. ወንድ 2. ሴት**
3	**ሃይማኖት**	**1. ሙስሊም 2. ኦርቶዶክስ ተዋህዶ 3. ፕሮቴስታንት 4. ካቶሊክ 99. ሌላ (ይጠቀስ)_____**
4	**ብሔር**	**1. አማራ 2. ኦሮሞ 3. ትግሬ 4. ጉራጌ 99. ሌላ (ይጠቀስ)_____**
5	**የትምህርት ደረጃ**	**1. ምንም ያልተማረ 2. መጀመሪያ ደረጃ 3. ሁለተኛ ደረጃ 4. ከፍተኛ ደረጃ (12+)**
6	**የጋብቻ ሁኔታ**	**1. ያላገባ/ች 2. ያገባ/ች 3. አግብቶ የፈታ/ች 4. የሞተበት/ባት**
7	**የሥራ ሁኔታ**	**1. ገበሬ 2. ነጋዴ 3. የመንግስት ሰራተኛ 4. የግል መ/ቤት ሰራተኛ 5. የቀን ሰራተኛ 6. ሥራ የሌለው 7. ሹፌር 8. የግል ስራ 99. ሌላ (ይጠቀስ)_____**
አደንዛዥ እፅ መጠቀም በተመለከተ		
8	**ጫት ቅመህ ታውቃለህ/ሽ?**	**1. አዎ 2. ቅሜ አላውቅም**

9	ለተራ ቁጥር “8” መልስዎ አዎ ከሆነ መቃም ከጀመሩ ምን ያህል ጊዜ ሆነዎት ?	_____ዓመት _____ ወር
10	ሲጋራ ታጨሳለህ/ሽ?	1. አዎ 2. አላጨስም
11	ለተራ ቁጥር “10” መልስዎ አዎ ከሆነ ማጨስ ከጀመሩ ምን ያህል ጊዜ ሆነዎት ?	_____ዓመት _____ ወር
12	አልኮል ትጠጣለህ/ጫለሽ?	1. አዎ 2. አልጠጣም
13	ለተራ ቁጥር “12” መልስዎ አዎ ከሆነ መጠጣት ከጀመሩ ምን ያህል ጊዜ ሆነዎት?	_____ዓመት _____ ወር
14	ካሁን በፊት ለቲቢ በሽታ ታክመው ያውቃሉ?	1.አዎ 2. ታክሜ አላውቅም 3. አላውቀውም
15	የቆየ የአስም በሽታ አለብዎት ?	1. አዎ 2. የለብኝም 3. አላውቅም
16	የቆየ የስኳር በሽታ አለብዎት ?	1. አዎ 2. የለብኝም 3. አላውቅም
17	በቤተሰቡ ውስጥ በቲቪ በሽታ የተያዘ ሰው ነበረ?	1. አዎ 2. የለም 3. አላውቅም
18	ካሁን በፊት በማረሚ ያ ቤት ታስረው ያውቃሉ?	1. አዎ 2. የለም
19	ባለፉት 5 አመታት ሌላ ቦታ ሄደው ከ6 ወርበላይ ኖረው ያውቃሉ	1. አዎ 2. የለም
20	በቤት ውስጥ በአንድ ላይ የሚኖሩ ሰዎች ስንት ናቸው ?	
21	በቤቱ ውስጥ ትላለቅ ሰዎች(15 አመት በላይ) ስንት ናቸው ?	
22	መኖሪያ ቤትዎ ስንት ክፍሎች አሉት?	
23	መኖሪያ ቤትዎ የተለየ ኩሽና ቤት አለው?	1. አዎ 2. የለም
24	የቤተሰብ ወይ የራስዎ መኖሪያ ቤት አለዎት ?	1. አዎ 2. የለኝም
25	መፀዳጃ ቤት በግቢ ውስጥ አለ ?	1. አዎ 2. የለም
26	ወርሃዊ ገቢዎ ስንት ነው	
27	የሚኖሩበት የቤት ወለል የተሰራው ከምንድ ነው ?	1. ከጭቃ 2. ከሲሚንቶ
28	ውሃ በግቢ ውስጥ አለ ?	1. አዎ 2. የለም

29	በቤት ውስጥ የሃይል ምንጭ ምንድ ነው?	እንጨት ሀ. አዎ ለ. አይደለም ጋዝ ሀ. አዎ ለ. አይደለም ኤሌክትሪክ ሀ. አዎ ለ. አይደለም ከሰል ሀ. አዎ ለ. አይደለም ሁሉም

ክፍል 2 ሁለት፣ መነሻ(የፀረ-ኤች አይቪ መድሃኒተት ሲጀምሩ) የነበሩ የላብራቶሪና የህክምና መረጃዎች (ከፀረ- ኤች አይቪ መድሃኒተት መከታተያ መዝገብ ላይ የሚሞላ)		
1	ክብደት	
2	ቁመት	
3	የ CD4 ቁጥር	
4	የሄሞግሎቢን መጠን	
5	WHO ክሊኒካል ደረጃ	1. ደረጃ I 2. ደረጃ II 3. ደረጃ III 4. ደረጃ IV
6	የቲቢ መከላከያ መድሃት (INH) ይወስዱ ነበር?	1. አዎ 2. አልወሰዱም
7	ኮትሪሞክዛዞል ይወስዱ ነበር ?	1. አዎ 2. አልወሰዱም
8	የፀረ ኤችአይቪ መድሀኒት በትክክል ሳያቋርጡ የመውሰድ ደረጃ	1. ጥሩ 2. ተመጣጣኝ 3. ደካማ
9	የበሽተኛው አጠቃላይ ሁኔታ	1. ሥራ መስራት የሚችል 2. መንቀሳቀስ የሚችል 3.ያልጋ ቁራኛ
10	በሽተኛው የወሰዳቸው የፀረ ኤችአይቪ መድሀኒት ዓይነቶች	1) 1a (30) =d4t (30)-3TC-NVP 2) 1a (40) =d4t (40)-3TC-NVP 3) 1b (30) =d4t (30)-3TC-EFV 4) 1b (40) =d4t (40)-3TC-EFV 5) 1c= AZT-3TC-NVP 6) 1d=AZT-3TC-EFV 7) 2nd line regimens(2a/2b/2c/2d)
11	ተጓዳኝ ህመሞች (IOs)	1. አለ/ሉ 2. የለም/ሉም
12	የቫይረስ መጠን (Viral load)	
13	የነጭ ደም ህዋስ መጠን (WBC count)	
14	የቲቢው ዓይነት	1. ስሚር ነጋቲቭፑልሞናሪቲቢ 2. ፖዝቲቭፑልሞናሪ ቲቢ 3. ኤክስትራ ፑልሞናሪ ቲቢ

Annex-IV Patient Information Sheet and Consent Form (English Version)

This questionnaire and patient information collection sheet is intended to assess determinant factors associated with active TB developments in patients living with HIV/AIDS and started ART treatment in Addis Ababa. The study will be conducted through face to face interview and reviewing secondary data (patients ART /TB log book). This study can give some evidence and information for governmental and non - governmental organizations which work in the area of HIV/AIDS specifically on TB/HIV at national, regional and district level by providing basic information on predicting factors of TB in PLWHA after ART treatment. This research being conducted by Ato Kelemu Tilahun who is the Master of public health student in Addis Ababa University. You are selected as one of study subject by chance.

Information which is necessary for the study will be taken from your ART log book and interviewing you. The study will not cause any harm as far as the confidentiality is kept. The information will be taken when you give permission, participation is totally voluntary. Your willingness for interview your ART record information to be utilized in this study will help to achieve the stated benefits of the study. Your name and other personal identifiers will not be recorded questionnaire and the information that you give us will be kept confidential and will also be used for this study purpose only. You have full right not to give your information for this study. But the information that would be taken will be quite useful for the study. You will not face any problem if you do not allow the information to be taken from your records and you will not also be denied of getting any medical services from the hospital. If you participated in the study, there is no special benefit given for you.

Are you willing to give information for this study?

1. Yes 2. No

Signature of the interviewer which shows that the respondent has consented (verbally) to take part in the study _____

Annex-V Patient Information Sheet and Consent Form (Amharic Version)

(ለጥናቱ ተሳታፊዎች መረጃ የመስጫ እና የፈቃደኝነት መጠየቂያ ቅጽ)

ይህ መጠይቅ የተዘጋጀው የፀረ-ኤችአይቪ መድሃኒት በሚወስዱ ሰዎች ላይ ለቲቪ በሽታ መከሰት አስተዋፅኦ የሚያደርጉ ነገሮችን ለመለየት ነው ። ጥናቱ የሚከናወነው በሽተኞችን ቃለ መጠይቅ በማድረግ ና አንዳንድ የላብራቶሪ ና የህክምና መረጃዎችን ከ በሽተኛው መዝገብ ላይ በመውሰድ ነው። ይህ ጥናት ሳይንሳዊ ሂደትን የተከተለ ሲሆን በቲቪ/ ኤች አይቪ ዙሪያ በተለያየ ደረጃ ላይ ለሚሰሩ መንግስታዊ ና መንግስታዊ ላልሆኑ ተቋማት ፣ ፀረ ኤችአይቪ መድሃኒት በሚወስዱ ሰዎች ላይ ለ ቲቢ በሽታ መከሰት ምክንያት ሊሆኑ በሚችሉ ነገሮች ላይ መሰረታዊ ና ተመጣጣኝ የሆነ መረጃ በማቅረብ ለቲቢ/ኤች.አይ.ቪ ታካሚዎች የተለየ ጥንቃቄ እንዲደረግ አስተዋጽኦ የጐላ እንደሚሆን ይታመናል ።

ይህ ጥናት የሚካሄደው በ አቶ ቀለሙ ጥላሁን የ አዲስ አበባ ዩኒቨርሲቲ የሁለተኛ ድግሪ ተማሪ ሲሆን ፣ እርስዎ በእጣ አንዱ የጥናቱ ተሳታፊ ሆነው ተመርጠዋል። ለዚህ ጥናት መሳካት የሚያስፈልገው መረጃ ከእርስዎ ቃለ መጠይቅ ና ከፀረ-ኤች አይቪ /ቲቢ መዝገብዎ ላይ በመውሰድ ነው ። ከእርስዎ የሚወሰደው መረጃ ሚስጢራዊነቱ በደንብ ስለሚጠበቅ ምንም አይነት ጉዳት በእርስዎ ላይ አይመጣም ። መረጃ ከእርስዎ የሚወሰደው በእርስዎ ፈቃድ ብቻ ነው።

እርስዎ የሚሰጡት መረጃ ለተጠቀሰው የጥናቱ ዓላማ መሳካት የጐላ አስተዋጽኦ ይኖረዋል፡ የእርስዎን ማንነት የሚገልጽ ስም እና ሌላ ምንም ዓይነት ነገር ወደ መጠይቁ አይሞላም። የተወሰደውም መረጃ ምስጢራዊነቱ ተጠብቆ ሙሉ በሙሉ ለምርምር ሥራ ብቻ ይሆናል። የሕክምና መረጃዎ ለምርምር ሥራ እንዳይውል የማድረግ መብት አለዎት። ነገር ግን መረጃዎ ለምርምር ሥራው ቢውል ጠቀሜታው የጐላ ነው። በጥናቱ ለመሳተፍ ፈቃደኛ ባይሆኑ በሕክምናዎት ላይ ምንም ዓይነት ጉዳት አይፈጠርም። በሌላ በኩል መረጃዎን በመስጠትዎ የሚያገኙት የተለየ ጥቅም አይኖርም።

ለ ዚህ ጥናት መረጃ ለመስጥተ ፈቃደኛ ነዎት ?

1. አዎ 2. አይደለሁም

ግለሰቡ ለዚህ ጥናት መረጃ ለመስጠት ፈቃደኛ ሆነዋል ። የመረጃ ሰብሳቢው ስምና ፊርማ

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DECLARATION

I, the undersigned, declare that this thesis is my original work and has not been presented for a degree in this or another university and all the sources of materials used for the thesis have been fully acknowledged.

Name: **Kelemu Tilahun (Bsc in PH)**

Signature: _____

Date _____

This thesis work has been submitted for the examination with my approval as a university advisor

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Date: _____