Prevalence and associated factors of TB/HIV co-infection among HIV Infected patients in Amhara region, Ethiopia.

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Abstract

Background: Tuberculosis is one of the world's most common causes of death in the era of Human immunodeficiency virus. The purpose of this study was to determine the prevalence and associated factors of TB/HIV co-infection.

Methods: Hospital based retrospective studies were conducted among adult HIV-positive patients. Logistic regression method and Chi square test were applied.

Results: A total of 571 HIV positive study participants were enrolled. Of these, 158 (27.7%) were found to have pulmonary tuberculosis. Lower baseline CD4 count<200cell/µl, patients who drunk alcohol, patients who were ambulatory at the initiation of ART, patients whose marital status was single were significant predictors for increased risk of tuberculosis in PLWHIV (P <0.05). Non smoker patients, patients in WHO clinical stage I, patients in WHO clinical stage II and ownership of the house had significant protective benefit against risk of TB (P <0.05).

Conclusion: The prevalence of TB/HIV co-infection in adults on ART in our study was moderately high. Having advanced clinical status and presence of risk factors were found to be the predicting factors for co-infection. The health office should open TB/HIV co-infection units in the hospitals and health workers should be cautious when a patient has an advanced disease.

Keywords: Tuberculosis, co-infection, HIV/AIDS, risk factors

Background

Tuberculosis (TB) is one of the world's most common causes of death in the era of Human Immunodeficiency Virus (HIV). It is among the leading causes of death for people living with HIV (PLWHIV) which shares about twenty-five percent of all causes of the deaths[1]. HIV promotes progression of latent or recent infections of Mycobacterium tuberculosis to active disease and also increases the rate of occurrence of TB[2]. PLWHIV may also be more susceptible to TB infection[3]. HIV is the first and TB is the second leading cause of death from infectious disease worldwide[4]. Globally, there were an estimated 9 million incident cases of TB in 2013 with 13% co-infected with HIV. There were an estimated 1.5 million TB deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people)[5]. Hospital data indicated that TB is the leading cause of morbidity and the third cause of hospital admissions in the country[6]. According to World Health Organization report Ethiopia ranks 7th among the 22 high burden countries with TB and HIV infection in the world[7].

TB/HIV co-infection is associated with special diagnostic and therapeutic challenges and constitutes an immense burden on healthcare systems of heavily infected countries like Ethiopia[8]. Studies indicated that certain HIV-infected people develop TB, while others do not. This phenomenon iterates that being HIV positive is not the only factor for being infected with TB, and there are various determinant factors that contribute to the TB/HIV co-infection[9-11]. Understanding the predictors of TB/HIV co-infections in the local context is critical for Ethiopia to improve TB/HIV co-infected patients' co-management. Therefore, the main goal of this study was

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to determine prevalence and associated factors of TB co-infection among HIV patients in the HIV clinics in Amhara Region, Ethiopia. It is anticipated that findings from this study will contribute to the body of knowledge that informs TB/HIV program planners, decision makers, and project implementers by providing predictors of TB/HIV co-infection.

Methods
Study design and area
Hospital based retrospective studies were conducted among adult HIV-positive patients attending HIV clinic between June 2006 and January 2014 in Amhara Region, Ethiopia. The Amhara Region is located in the North-Western and North Central parts of Ethiopia and lies within 9^0 and 23^045'N and 36^0 and 40^030'E. Elevation ranges from 700m in the Eastern parts to over 4620m in the NorthWest. It has a total area of 170,000km^2, which is divided in to 11 administrative Zones and 105 Weredas. In this region, there are 5 referral hospitals. The sources of data for this study were Felege Hiwot, Gonder University, Dessie, Debere Berihan and Debere Markos referral Hospitals. The sampling frame consisted of 65000 HIV/AIDS patients who have visited these referral hospitals since the initiation of ART.

Sample size and sampling procedure
Sample size was calculated using single population proportion formula using 95% confidence level, 4% degree of precision and 33% proportion of TB/HIV co-infection[17]. The sample size was 520 which after adding 10% for non-response gave an overall sample size of 572. A stratified random sampling method was adopted for selecting a representative sample. The sample size was allocated proportionally based on the number of patients in each referral hospital. Patients were selected randomly using their ART unique identification number. The study considered all HIV infected patients on ART, whose age was >15 years regardless of their treatment category during the study period in the referral hospitals.

Measurements
The response variable for this study was the occurrence of TB/HIV co-infection. The predictor variables included socio-demographic and economic characteristics (age, sex, income, employment status, residence, educational status, and marital status) and clinical related characteristics (WHO clinical stage, baseline CD4 count, month on ART, functional status, and smoking status).
Functional status was measured at baseline, and a person was categorized as working if "he/she was able to perform usual work in or out of the house"; ambulatory if "he/she was able to perform activities of daily living" and bedridden if "he/she was not able to perform activities of daily living". Alcohol use was categorized as "yes" if a person was currently or previously an alcoholic beverages consumer and "no" if he/she had never been an alcoholic beverages consumer.

Data collection
Nurses who worked in ART clinics were selected to collect data from January, 2013 to January, 2014. A structured questionnaire was used to collect data on socio demographic, behavioral and economic factors. All records of HIV/AIDS patients between June 2006 and September 2014 were considered for data collection. Lab requests, follow-up forms, anti-TB record forms, ART intake forms, and patient cards were reviewed. Laboratory results recorded before starting ART were used as base line values. If there was no pre-treatment laboratory test, however, results obtained within one month of ART initiation were considered as baseline values. Data quality was assured by using a pre-tested data collection tool and trained data collectors. Two professionals were engaged in continuous supervision and monitoring. Completeness and consistency of data was checked by supervisors, data clerks and investigators before and after data entry.

Ethics statement
This investigation was conducted according to the principles expressed in the Declaration of Bahir Dar University, Ethiopia. It was approved by the research ethics committee at Bahir Dar University and all participants who agreed to participate in this study signed a consent form.

Data analysis
The data was coded and entered to Epi Info 3.14 for Windows. Statistical package for social science (SPSS) version 20 and STATA version 12.0 were used for analysis. Descriptive statistics were used to assess normality, outliers and identify missing values. Chi square test and independent t-test were used to test the relationship between each covariate and TB/HIV co-infection status. Multi covariate logistic regression was done by entering all variables

with *P* value less than 0.25 in the bivariate analysis. Finally, logistic regression with forward likelihood selection method with *P* value less than 0.05 was used to identify the determinant factors associated with TB/HIV co-infection. The crude and adjusted odds ratio (OR) and its 95% confidence interval (CI) were estimated.

Results
Descriptive statistics for socio-demographic and economic factors
There were 571 respondents in the study. Of these, 413 (72.3%) were not found to have TB/HIV-co infection while 158(27.7%) had TB/HIV co-infection. The proportion of female respondents who had TB/HIV-co infection accounted for a larger proportion in the sample 107(69%) compared to male respondents 48(31%). Patients with primary education accounted for the larger proportion 64(40%) of having TB/HIV co-infection compared to those with no education 39(24.8%), secondary education 33(21%), and certificate and above 21(13.4%).

In addition, majority of TB/HIV patients 130(82.8%) were urban residents while 27(17.2%) were residing in rural areas. Among TB/HIV co-infected patients, 149(96.8%) were non smokers 123(79.9%) of TB/HIV co-infected patients were nonalcoholics. The majority of participants who had TB/HIV co-infection, 104(67.5%) were in WHO clinical stage of III followed by WHO clinical stage IV 23(14.9%) and WHO clinical stage II 19(12.3%). Only 8(5.2%) study participants who have TB/HIV-co infection were found to be in WHO clinical stage I.

Chi-square test shows that the TB/HIV co infection is significantly associated with marital status, alcohol intake, baseline CD4 count, baseline WHO clinical stage, baseline functional status, TB Smear type (p-value < 0.05) (Table 1).
The mean monthly income of HIV infected participants was 948.99±800 birr and TB/HIV co-infected patients had mean monthly income of 900+707.11 birr. The mean age of HIV mono infected participants was

33.00+2.83 and TB/HIV co-infected patients had mean age of 35.83+8.4 (Table 1).
Multivariate analysis for predicting TB/HIV co-infection
One problem of single covariate approach is that it ignores the possibility that a collection of variables, each of which is weakly associated with the outcome, can become an important predictor of the outcome when taken together. It is therefore important to reduce the possibility of excluding variables at the univariable analysis stage. It is for this reason that a univariate test p-value of 0.25 or less was used for selection of variables for the multi covariate analysis from single covariate findings. Based on this marital status, alcohol intake, smoking status, baseline CD4 count, baseline functional status, home ownership and baseline WHO stage were selected with forward likelihood logistic regression method.

After adjusting other covariates, a patient whose marital status was single was 2.17 times more likely to develop TB than those patients whose marital status was divorced and widowed (Adjusted OR=2.17, 95% CI=1.19-3.96). A non smoker was about 69% less likely to develop TB than those who were smokers (Adjusted OR=0.31, 95% CI= 0.10-0.96).
Low CD4 T-lymphocytes count was the strongest clinical predictor of TB/HIV co-infection. Patients with CD4 T-lymphocytes count less than 200 cells/μl were 1.71 times more likely to develop TB as compared to patients with CD4 T-lymphocytes count of more than 200 cells/μl (Adjusted OR=1.71, 95%CI=1.09-2.68). Patients in WHO clinical stage I were 78% less likely to develop TB than that of the patient in WHO clinical stage IV (Adjusted OR=0.22, 95%CI=0.08-0.58). Similarly, patients in WHO clinical stage II were about 70% less likely to develop TB than those patient in WHO clinical stage IV (Adjusted OR=0.30, 95%CI=0.14-0.66). Patients with ambulatory baseline functional status (Adjusted OR=1.73, 95%CI=1.10-2.78) had an increased risk to develop TB. A patient who had a home was about 41% less likely to develop TB as compared to those patients who did not have their own home (Adjusted OR=0.59, 95%CI=0.39-0.92). Furthermore, patients who drunk alcohol were 2.26 times more likely to develop TB than those who did not drink (adjusted OR=2.26, 95%CI=1.29-4.02) (Table 2).

Table 1 Summary result of TB/HIV co-infection vs. socio-demographic, economic and clinical, and risk variables in Amhara Region, Ethiopia.

Variables	TB/HIV Co infection		Chi-square p-value
	No, n(%)	Yes, n(%)	
Sex			
Male	112(27.8)	48(31)	0.457
Female	291(72.2)	107(69)	
Age			
Mean±SD	33.00+2.83	35.83+8.4	0.894
Monthly Income			
Mean±SD	948.99±800	900+707.11	0.058
Educational Status			
No Education	106(26.2)	39(24.8)	
Primary	168(41.6)	64(40.8)	
Secondary	81(20)	33(21)	0.961
Certificate and above	49(12.1)	21(13.4)	
Marital Status			
Single	48(11.8)	34(21.7)	
Married	204(50.1)	67(42.7)	
Divorced/separated	90(22)	37(23.6)	0.017*
Widowed	65(16)	19(12.1)	
Employment status			
Employed	209(51.9)	70(44.9)	
Unemployed	94(23.3)	39(25)	0.295
Retired	100(24.8)	47(30.1)	
Residence			
Urban	350(86.8)	130(82.8)	
Rural	53(13.2)	27(17.2)	0.219
Smoking Status			
Smoker	19(4.7)	5(3.2)	
Non smoker	388(95.3)	149(96.8)	0.758
Alcohol Intake			
Yes	49(12.3)	31(20.1)	
No	351(87.8)	123(79.9)	0.005*
Baseline CD4 count			
≤200	254(61.5)	121(76.6)	
>200	159(38.5)	37(23.4)	0.001*
Baseline WHO stage			
Stage I	53(13.1)	8(5.2)	
Stage II	94(23.2)	19(12.3)	
Stage III	226(55.7)	104(67.5)	0.000*
Stage IV	33(8.1)	23(14.9)	
Missed to take HIV medication			
Yes	3(18.8)	6(3.9)	
No	13(81.2)	147(96.1)	0.012*
Baseline functional status			
Bed driven	25(6.3)	16(10.5)	
Ambulatory	85(21.4)	47(30.7)	0.009*
Working	287(72.3)	90(58.8)	
TB Smear type			
Positive	5(9.3)	21(44.7)	
Negative	48(88.9)	25(53.2)	0.000*

*The relationship is a significant at α=0.05

Table 2 Multi-Covariate and Bivariate Analysis result for different socio-economic, demographic, clinical and risk variables that affect TB/HIV Co-infection, Amahra region, Ethiopia.

Variables	COR(95%CI)	COR P-value	AOR(95% CI)	AOR P-value
Marital Status				
Single	1.96(1.15-3.35)	0.014*	2.17(1.19-3.96)	0.012*
Married	0.91(0.60-1.37)	0.650	1.01(0.64-1.59)	0.971
Divorce and others	1		1	
Smoking status				
Non smoker	0.69(0.25-1.87)	0.247	0.31(0.10-0.96)	0.042*
Smoker	1		1	
Alcohol Intake				
Yes	1.81(1.10-2.96)	0.005*	2.26(1.29-4.02)	0.005*
No	1		1	
Baseline CD4 Count				
≤200 cells/μl	2.05(1.35-3.11)	0.001*	1.71(1.09-2.68)	0.019*
>200 cells/μl	1		1	
Baseline WHO Stage				
Stage I	0.22(0.09-0.54)	0.002*	0.22(0.08-0.58)	0.002*
Stage II	0.29(0.14-0.59)	0.001*	0.30(0.14-0.66)	0.003*
Stage III	0.66(0.37-1.18)	0.108	0.63(0.33-1.18)	0.147
Stage IV	1		1	
Baseline Functional Status				
Bed driven	2.04(1.04-3.99)	0.037*	1.69(0.83-3.49)	0.150
Ambulatory	1.76(1.15-2.71)	0.009*	1.73(1.10-2.78)	0.020*
Working	1		1	
Home Ownership				
Yes	0.60(0.41-0.89)	0.012*	0.59(0.39-0.92)	0.018*
No	1		1	
Residence				
Urban	0.73(0.44-1.21)	0.220		
Rural	1			
Missed to take HIV Medication				
Yes	0.18(0.04-0.79)	0.023*		
No	1			

Keys: COR (Crude odds ratio)
AOR (Adjusted Odds Ratio)
CI (Confidence Interval)
[1] (Reference Category)
*Odds Ratio is a significant at α=0.05

Discussion

The prevalence of TB/HIV co-infection in adults on ART in our study was moderately high at 27.7%. This is in line with other studies[12-15]. It was slightly lower than 32.8% reported from Nigeria[16] and 33% reported from Ethiopia[17]. However, the findings of this study were higher compared to studies conducted in Ethiopia (7.5%), Nigeria (7.8%) and Tanzania (8.5%)[2,19-20]. These wide variations in the co-infection rates of TB/HIV across the globe, as reported, can partly be accounted for by the following reasons: coverage level of highly active antiretroviral treatment (HAART), under-reporting, diagnostic procedures used, difference in TB diagnosis, epidemiology of TB in different countries and study methodology applied.

Our study also revealed the determinants of TB/HIV co-infection among HIV-positive adults attending clinical care in Amhara region, Ethiopia. Baseline functional status, CD4 count, WHO clinical stage, alcohol use, smoking status and home ownership status were independent predictors of TB/HIV co-infection among HIV-positive adults.

As CD4+ lymphocyte count decreased the body defence mechanism will be overwhelmed by various opportunistic infections. The results showed that, patients with CD4 T- lymphocytes count less than 200 cells/μl were about 2 times more likely to develop TB as compared to CD4 T-lymphocytes count more than 200 cells/μl. A study conducted in Nigeria revealed similar finding where lower CD4+ lymphocyte count was observed in co-infected patients than mono infected patients[21]. Substance use such as cigarette smoking and alcohol consumption were the predictors of TB/HIV co-infection in HIV positive in the current study. A study conducted in West Africa revealed similar finding where cigarette smoking and alcohol consumption were the risk factors for the development of TB[22]. In contrast, a study from the Gambia found that cigarette smoking and alcohol consumption were not associated with TB[23].

In our study we found that marital status was significantly associated with TB. Divorced or widowed Patients were less likely to develop TB compared to unmarried (single), which is consistent with other reports in West Africa and Ethiopia24. It might be explained as unmarried (single) persons are younger than married persons and have a different lifestyle, especially males, who often migrate to towns in search of a job where they live alone or with friends. Similarly, education was not the predictor of TB/HIV co-infection in HIV clinic. This result is consistent with Kiberet et al.[17] and Wondimeneh et al.[20] in Ethiopia. In contrast, studies from south west Ethiopia[9,25] have showed that low level of education was associated with TB. This could be due to the high prevalence of literates in our study population.

The other important finding identified was association of patient's WHO clinical stage with TB-co infection. Those patients in first and second WHO clinical stages were about 78% and 70% less likely to develop TB compared with those in WHO clinical stages IV, respectively. Congruent findings have been reported from in-country and outside of the country[10,26,27]. This could be explained as once the patients get into late stages, the immunity protective capacity will be minimal which would make them prone to tuberculosis infection. A worth to mention as well is that TB is one of the AIDS defining criteria to categorize the patients in to the late WHO clinical staging which was also used as a criteria in HIV/AIDS clinics in Ethiopia.

Patients who were ambulatory at the initiation of ART were about 2 times more likely to develop TB than those who were working at the initiation of ART. This is consistent with the retrospective cohort study in Ethiopia[17-18]. Furthermore, ownership of the house by the TB patient's family was a predictor of TB/HIV co-infection among HIV positive. A study conducted in West Africa revealed similar finding where ownership of the house by the TB patient's family was associated with lower risk for developing TB[22].

Conclusion and recommendations
The study identified marital status, functional status, WHO clinical staging, baseline CD4 count, smoking status, alcohol intake, and home ownership were associated with TB/HIV co-infection among adult HIV positives. In general, advanced clinical disease, smoking and alcohol consumption were found to be the main predictors for TB/HIV co-infection. All PLWHIV should be screened for TB, but for substance abusers and patients with advanced disease (WHO clinical stage IV, being ambulatory and CD4 count<200cell/μl) intensified screening is highly recommended during treatment follow up.

Since the results of the study underlined risk factors (alcohol use and smoking status) as the predictors of TB/HIV co-infection in HIV positive, physicians are expected to work hard to bring about behavioural changes towards substance use. According to the results of this study, the main factors associated with TB/HIV co-infection are clinical variables. So, health workers should be cautious when a patient has lower CD4 counts, is ambulatory at the initiation of ART and in WHO clinical stage IV. Furthermore, the health office should open TB/HIV co-infection units in the Hospitals.

Competing interest
The authors declare that they have no competing interests.

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