

## Brief Original Article

# Prevalence and determinants of Tuberculosis among HIV infected patients in south Ethiopia

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### Abstract

**Introduction:** Tuberculosis (TB) is a chronic infectious disease that has represented a major health problem over the centuries. The human immune deficiency virus (HIV)/AIDS has substantially altered the epidemiology of TB by increasing the risk of reactivating latent TB, increasing chance of TB infection once exposed to tubercle bacilli (re-infection) and by increasing the risk of rapid progression soon after infection.

**Methodology:** This study employs a retrospective review analysis of patient medical records. A total of 499 HIV/AIDS patient cards were reviewed and variables were recorded. Frequencies and odds ratio were calculated to determine prevalence and associated risk factors respectively.

**Results:** A total of 499 HIV/AIDS positive patient cards were reviewed. Ninety one (18.2%) of the study participants were found to have tuberculosis of which 20 (22%), 58 (64%) and 13 (14%) were smear positive, smear negative and extra-pulmonary tuberculosis cases, respectively. In multivariate logistic regression being female (AOR=0.39; 95% CI:0.20-0.77), WHO clinical stage 3 (AOR=5.66; 95%CI:1.79-17.94); WHO clinical stage 4 (AOR=7.89;95%CI:2.01-30.96); and functional status being ambulatory (AOR=2.22; 95%CI:1.06-4.64) were independently associated with tuberculosis-HIV co-infection with p value <0.05.

**Conclusion:** Prevalence of tuberculosis was high. Among tuberculosis positive cases, the proportion of smear negative cases was also high which requires strengthening of TB diagnostic techniques. Tuberculosis was associated with some social demographic characteristics and clinical variables.

**Key words:** HIV; AIDS; Tuberculosis; TB/HIV; south Ethiopia.

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### Introduction

Tuberculosis (TB) is a chronic infectious disease that has represented a major health problem over the centuries and it has accounted for more human misery, suffering and loss of earning and failure of economic and social development than any other disease. According to the World Health Organization (WHO) estimation, about one third of the world's population is infected with tuberculosis bacteria, about ten million cases of active disease are estimated to occur each year, and annually three million people die of tuberculosis.

The human immune deficiency virus (HIV)/AIDS has substantially altered the epidemiology of TB by increasing the risk of reactivating latent TB, increasing chance of TB infection once exposed to tubercle

bacilli (re-infection) and by increasing the risk of rapid progression soon after infection. Several studies documented that the person infected with *Mycobacterium tuberculosis* (MTB) only has a 10% risk of developing TB during life time but for persons co- infected with both TB and HIV the annual risk of developing active TB disease exceeds 10%.

HIV does not only increase the prevalence but also complicates the follow up and compromises the response to anti-TB treatment. The complication of treatment outcomes of both diseases due to the TB-HIV co-infection results particularly from the concomitant use of anti-retroviral treatment (ART) and intensive phase of TB treatment; additionally, it leads to drug-drug interaction, side effects of multiple drugs, increased pill burden, decreased adherence and

development of higher rate of drug resistant organisms due to the combination of the above factors. HIV also causes difficulties in diagnosis and treatment of TB due to unusual clinical picture with increased smear negative Acid Fast Bacilli (AFB) pulmonary TB, atypical finding on chest radiography and increased prevalence of extra pulmonary TB.

Epidemiology of tuberculosis transmission and emergency of drug resistant tuberculosis are complicating the tuberculosis disease control effort. Therefore, proper diagnosis and treatment of tuberculosis helps to reduce the burden of TB, provided that infectious cases are detected and treated successfully. Thus, the knowledge of the prevalence of the disease and its determinant factors among HIV infected population in a local context will also help to reduce the burden of the disease by facilitating the early detection of at-risk patients and urging the responsible authority for devising surveillance and proper follow-up activities in the area of TB/HIV collaborative activities.

TB/HIV co-infection rate of the national report in Ethiopia revealed 40%-50%. The prevalence of TB among HIV sero-positive individuals at Hawassa University referral hospital is probably higher than in other sites in the region due to the large number of patients treated in the TB-HIV care unit. Moreover, there are only few of such studies in the area of TB/HIV co-infection, which do not represent our study area population. Therefore, the study will help to design regular surveillance techniques of TB infection in HIV patients thus assisting physicians in identifying major determinants of TB in HIV patients and expect these disease infectious trends ahead of time to manage them. Our study also provides information for health authority on the prevalence of TB in HIV patients at Hawassa University Referral Hospital, so that it would give a better emphasis to TB/HIV collaborative activities and serve as reference document for further studies in the area.

## Methodology

### Setting

Hawassa University Referral Hospital (HURH) is located in Hawassa town Sidama zone, Southern Nations and Nationalities Peoples Region (SNNPR), located 275km south from Addis Ababa, the capital of Ethiopia. The services delivered by the hospital are organized into four major departments; namely medical, surgical, pediatrics, and gynecology and obstetrics departments, together with clinics and care units such as TB-HIV, ART, Voluntary Counseling

and Testing (VCT), Ophthalmology and Emergency units, among others. A total of 5,000 pre-ART patients were registered at the ART clinic since July 2006 till now, of these 2,600 started ART.

### Study design and ethics

The current study was a facility based retrospective study to assess the prevalence and determinants of TB in HIV/AIDS patients using patient case files from the TB-HIV care unit of Hawassa University Referral Hospital. HIV/AIDS patients' files between January-May 2013 were reviewed. This research project was approved by the Institutional Review Board of Hawassa University and a support letter was obtained from the medical director of the hospital before actual data collection.

### Data management

Data was entered, cleaned and analyzed using SPSS v16.0. Frequencies were calculated for descriptive analysis of socio-demographic variables (age, sex, marital status, educational status, occupation, and residence area), TB status, CD4 count at TB diagnosis, at HIV Diagnosis, at ART initiation, status of ART, Isoniazid (INH) prophylaxis, adherence to ART, nutritional status and functional status of the patient. Odds ratios were used for comparative association between TB status and socio-demographic variables, INH prophylaxis, WHO staging, CD4 count at HIV diagnosis, ART status, adherence to ART medications and nutritional state. Bivariate and multivariate logistic regression analysis was used to calculate the unadjusted and adjusted odds ratios. The statistical tests were performed with a type I error of 0.05.

## Results

A total of 499 HIV/AIDS positive patient medical records containing required information were reviewed, although some of the variables were not properly recorded or were missing. Out of 499 people living with AIDS (PLWA), 36.1% were males and 63.7% were females; most of them were in the age range 16-45years (87%). Table 1 shows sociodemographic characteristics of study participants.

Ninety one (18.2%) of the study participants were found to have tuberculosis of which, 20 (22%), 58(64%) and 13 (14%) were smear positive, smear negative and extra-pulmonary tuberculosis cases, respectively. Other clinical and laboratory profiles of the patients are displayed in Table 2.

**Table 1.** Sociodemographic characteristics of study participants at Hawassa University Teaching and Referral Hospital, 2013

Characteristics	Frequency	Percent	
Age	18m-5yrs	8	1.6%
	6-15yrs	16	3.2%
	16-45yrs	434	87.0%
	46-64 yrs	36	7.2%
	≥ 65yrs	1	0.2%
	Missing	4	0.8%
Sex	Male	180	36.1%
	Female	318	63.7%
	Total	498	99.8%
	Missing	1	0.2%
Marital Status	Never married	116	23.2%
	Married	260	52.1%
	Divorce	87	17.4%
	Widow	33	6.6%
	Total	496	99.4%
	missing	3	0.6%
	Total	499	100%
Educational Background	Illiterate	73	14.6%
	Primary School	174	34.9%
	Secondary School	190	38.1%
	Tertiary	58	11.6%
	Total	495	99.2%
	Missing	4	0.8%
Occupation	Government employee	44	8.8%
	Merchant	41	8.2%
	Farmer	8	1.6%
	Student	12	2.4%
	House wife	43	8.6%
	Driver	8	1.6%
	Unemployed	95	19.0%
	Soldier	7	1.4%
	Others	228	45.7%
	Total	486	97.4%
missing	13	2.6%	
Religion	Muslim	47	9.4%
	Orthodox	283	56.7%
	Protestant	139	27.9%
	Catholic	5	1.0%
	Others	18	3.6%
	Total	492	98.6%
missing	7	1.4%	
Residence	Rural	28	5.6%
	Urban	471	94.4%
	Total	499	100.0%

**Table 2.** Frequency of clinical and laboratory profile of study participants at Hawassa University Teaching and Referral Hospital, 2013

Clinical Data		Frequency	Percent
TB Diagnosed	Positive	91	18.2%
	Negative	408	81.8%
TB Category	Smear positive	20	22%
	Smear negative	58	64%
	Extra pulmonary	13	14%
INH prophylaxis	Yes	13	2.6%
	No	484	97.0%
Method of Diagnosis	AFB (Microscopy)	20	22%
	Chest X- ray	58	64%
	Biopsy	13	14%
WHO stage	Stage1	156	31.3%
	Stage 2	89	17.8%
	Stage 3	173	34.7%
	Stage 4	43	8.6%
	Total	461	92.4%
	missing	38	7.6%
Functional Status	Working	374	74.9%
	Ambulatory	95	19.0%
	Bedridden	19	3.8%
	Total	488	97.8%
	missing	11	2.2%
ART Status	Pre- ART	173	34.7%
	ART	325	65.1%
	Total	498	99.8%
	missing	1	0.2%
CD4 at HIV Diagnosis	>500	91	18.2%
	200-500	145	29.1%
	<200	261	52.3%
	Total	497	99.6%
	missing	2	0.4%
CD4 at ART Initiation	>350	65	13.0%
	200-350	107	21.4%
	<200	161	32.3%
	Total	333	66.7%
	missing	166	33.3%
Drug Adherence	Good	290	58.1%
	Fair	4	0.8%
	Poor	31	6.2%
	Total	325	65.1%
	missing	174	34.9%

**Table 3.** Determinants of tuberculosis among HIV/AIDS positive patients at Hawassa University Teaching and Referral Hospital, 2012

Predictors		TB Disease		Odds Ratio (OR)	
		Yes	No	Crude OR	Adjusted OR
Age	18m-5yr	2 (25%)	6 (75%)	1	
	16-45yr	79 (18.2%)	355 (81.8%)	0.67 (0.13, 3.37)	
	46-65yr	7 (19.4%)	29 (80.6%)	0.72 (0.12, 4.38)	
Sex	Male	48 (26.7%)	132 (73.3%)	1	
	Female	43 (13.5%)	275 (86.5%)	0.43 (0.27, 0.68)*	0.39 (0.20, 0.77) *
Residence	Rural	9 (32.1%)	19 (67.9%)	1	
	Urban	82 (17.4%)	389 (82.6%)	0.45 (0.19, 1.02)	
Literacy	Illiterate	12 (16.4%)	61 (83.6%)	1	
	Primary	32 (18.4%)	142 (81.6%)	1.15 (0.55, 2.37)	
	Secondary	36 (18.9%)	154 (81.1%)	1.19 (0.58, 2.44)	
	Tertiary	9 (15.5%)	49 (84.5%)	0.93 (0.36, 2.40)	
Marital status	Never married	29(25%)	87(75%)	1	1
	Married	41 (15.8%)	219 (84.2%)	0.56 (0.33, 0.96) *	0.74 (0.35, 1.56)
	Divorce	17 (19.5%)	70 (80.5%)	0.73 (0.37, 1.43)	0.54 (0.19, 1.56)
	Widow	4 (12.1%)	29 (87.9%)	0.41 (0.13, 1.28)	0.53 (0.12, 2.29)
Religion	Muslim	8 (17%)	39 (83%)	1	
	Orthodox	51 (18%)	232 (82%)	1.07 (0.47, 2.43)	
	Protestant	28 (20.1%)	111 (79.9%)	1.23 (0.52, 2.92)	
	Catholic	1 (20%)	4 (80%)	1.22 (0.12, 12.40)	
	Others	3 (16.7%)	15 (83.3%)	0.98 (0.23, 4.18)	
Occupational status	Government Employee	8 (18.2%)	36 (81.8%)	1	
	Merchant	10 (24.4%)	31 (75.6%)	1.45 (0.51, 4.13)	
	Farmer	2 (25%)	6 (75%)	1.5 (0.25, 8.84)	
	Student	1 (8.3%)	11 (91.7%)	0.41 (0.05, 3.64)	
	House wife	9 (20.9%)	34 (79.1%)	1.19 (0.41, 3.44)	
	Driver	4 (50%)	4 (50%)	4.5 (0.92, 21.92)	
	Unemployed	22 (23.2%)	73 (76.8%)	1.36 (0.55, 3.34)	
	Soldier	2 (28.6%)	5 (71.4%)	1.8 (0.29, 10.99)	
ART status	Others	32 (14%)	196 (86%)	0.74 (0.31, 1.72)	
	Pre-ART	29 (16.8%)	144 (83.2%)	1	
WHO staging	ART	62 (19.1%)	263 (80.9%)	1.17 (0.72, 1.90)	
	Stage1	5 (3.2%)	151 (96.8%)	1	1
	Stage2	7 (7.9%)	82 (92.1%)	2.58 (0.80, 8.38)	1.40 (0.32, 6.23)
	Stage3	55 (31.8%)	118 (68.2%)	14.10 (5.46, 36.28) *	5.66 (1.79, 17.94) *
	Stage4	18 (41.9%)	25 (58.1%)	21.74 (7.40, 63.86) *	7.89 (2.01, 30.96) *
Functional status	Working	45 (12%)	329 (88%)	1	1
	Ambulatory	33 (34.7%)	62 (65.3%)	3.89 (2.30, 6.58) *	2.22 (1.06, 4.64) *
	Bedridden	10 (52.6%)	9 (47.4%)	8.12 (3.13, 21.07) *	3.26 (0.96, 11.09)
CD4 at HIV diagnosis	>500	10 (11%)	81 (89%)	1	
	200-500	25 (17.2%)	120 (82.8%)	1.69 (0.77,3.70)	
	<200	56 (21.5%)	205 (78.5%)	2.21 (1.08,4.55)	
CD4 at ART initiation	>500	5 (7.7%)	60 (92.3%)	1	1
	200-500	23 (21.5%)	84 (78.5%)	3.29 (1.18, 9.13) *	1.78 (0.56, 5.66)
	<200	37 (23%)	124 (77%)	3.58 (1.34, 9.57) *	1.59 (0.52, 4.88)
Adherence	Good	54 (18.6%)	236 (81.4%)	1	
	Fair	1 (25%)	3 (75%)	1.46 (0.15, 14.28)	
	Poor	8 (25.8%)	23 (74.2%)	1.52 (0.65, 3.58)	
INH prophylaxis	Yes	1 (7.7%)	12 (92.3%)	1	1
	No	90 (18.6%)	394 (81.4%)	2.74 (0.35, 21.35)	0.53 (0.04, 7.04)

\*Statistically significant (p value &lt;0.05)

In multivariate logistic regression being female (AOR=0.39; 95% CI:0.20-0.77), WHO clinical stage 3 (AOR=5.66; 95% CI:1.79-17.94); WHO clinical stage 4 (AOR=7.89; 95% CI:2.01-30.96); and functional status being ambulatory (AOR=2.22; 95% CI:1.06-4.64) were independently associated with TB-HIV co-infection. Table 3 shows the findings of the association of TB with other variables.

## Discussion

HIV infection is the single most important fueling agent for ever-increasing prevalence of tuberculosis in Ethiopia. Moreover, TB is a well-recognized opportunistic infection in patients with HIV/AIDS. In this study, we found that TB-HIV co-infection was 18.2%. This finding was in line with studies conducted in India (17%), Nigeria (16.8%, 14.4%, 9.6% [1-4]. However, relatively higher prevalence has been reported from Nepal (27.3%) and Nigeria (22.7%) [5,6], and lower results were reported from Northern Tanzania (8.3%) [7]. Slight variation on the magnitude of tuberculosis in HIV/AIDS patients may be due to differences of HIV infection rate in the population, TB- diagnostic facilities available, health care awareness of the community to seek health care for both TB and HIV.

Of 91 TB-HIV co-infected cases, 58 (64%) were smear negative indicating the importance of TB diagnostic techniques other than AFB microscopy. Clinical data supplemented with chest radiography were employed to diagnose suspicious smear negative cases.

Regarding social demographic and clinical characteristic of the study participants, the proportion of tuberculosis was high among bedridden (52.6%), followed by WHO stage 4 clinical disease (41.9%), being rural resident (32.1%), male (26.7%), poor drug adherent (25.8%), single (25%), drivers (25%), having CD4 level less than 200 cells/mm<sup>3</sup> blood at ART initiation (23%), patients taking ART medication(19.1%). These findings were again in line with studies conducted in Nepal and Ethiopia [5,8].

The most important determinant factor for development of TB in HIV/AIDS patients as it is frequently reported in literature is the immunological state of the person. Maintaining the CD4 positive cell level as high as possible in patients with advanced disease helps the person to have low risk of infection or re-activation of tubercle bacilli. In our study, those HIV/AIDS patients who had started ART medication with CD4 level of less than 200cell/mm<sup>3</sup> blood had higher TB prevalence (23%). And this finding was

concurrent with studies conducted elsewhere. For instance, an observational community-based ART cohort study conducted in South Africa to show short-term and long-term risk of tuberculosis associated with CD4 cells recovery during antiretroviral therapy revealed that unadjusted TB incidence rates were 16.8, 9.3, 5.5, 4.6, 4.2 and 1.5 cases/100 person-years, respectively (P < 0.001) [14], during person-time accrued within CD4 cell strata 0–100, 101–200, 201–300, 301–400, 401–500 and more than 500 cells/μl. Similarly, low level of CD4 count was reported as risk factor for development of tuberculosis in HIV/AIDS patients from Tanzania [7] and Ethiopia [8-10].

Our study revealed a poor INH prophylactic management for participants, indicating higher proportion of tuberculosis (18.6%) among non-prophylactic compared with prophylactic (7.7%). The roll of INH prophylaxis in reduction of incidence of tuberculosis has been reported in many clinical trials and found to be important [13]. Meta-analysis study conducted on randomized controlled trials of Isoniazide prophylaxis for tuberculosis in HIV infected patients revealed that the risk of developing tuberculosis in the non-prophylactic group was 1.72 times higher than for the prophylactic group [11]. In another randomized controlled trial study to show the effect of isoniazid prophylaxis on mortality and incidence of tuberculosis in children with HIV, the incidence of tuberculosis was lower in the isoniazid group (5 cases, 3.8%) than in the placebo group (13 cases, 9.9%) (Hazard ratio 0.28, 0.10 to 0.78, p = 0.005) [12].

## Conclusions

We conclude that prevalence of tuberculosis in this study was high. The proportion of smear negative cases among tuberculosis cases was also high which requires special attention for confirming clinically suspected TB cases. Tuberculosis was associated with some social demographic characteristics and clinical variables. Working age group patients were the most affected by both HIV and tuberculosis. There were also statistically significant differences on the prevalence of tuberculosis between males and females, males being more affected. In addition, being deriver and single was also positively associated.

As expected, TB was found to be high among patients on ART, WHO clinical stage III and IV, CD4 cell count <200/ml during ART initiation and patients who had not received INH prophylaxis. An overall diagnostic approach as well as INH prophylactic

preventive measures should be strengthened to manage cases as early as possible to reduce TB incidence.

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### Authors' contributions

SF conceived the research idea, developed the research proposal and wrote the research paper; WT carried out data entry, analysis and also involved in the manuscript write up. GA involved in protocol development. All authors approved the final version for publication.

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