

Acquired Immuno Deficiency Syndrome

Research Article

Incidence and Predictors of Tuberculosis among Adult People Living with HIV/AIDS in Afar Public Health Facilities, Northeast Ethiopia

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Abstract

Introduction: Tuberculosis is the leading cause of morbidity and mortality among HIV-infected individuals. Tuberculosis and human immune deficiency virus infections are two major public health problems in many parts of the world. Globally tuberculosis is a leading cause of death among people living with HIV and it is the most potent risk factor for the development of tuberculosis. There for the aim of this study assess incidence and predictors of tuberculosis among adult people living with HIV in Afar health facilities, Northeast Ethiopia.

Method: A five year retrospective follow up study was conducted among 503 adult HIV infected individuals who enrolled in HIV care clinic from July, 2010 to June, 2011. All adult HIV infected persons who enrolled newly in to chronic adult HIV care clinic from July 1, 2010 to June 30, 2011 were included in the study and those with incomplete baseline information (WHO stage, CD4 count and Hgb level) were excluded. Data were entered to EPI-INFO version 7 then exported to SPSS version 20 for further analysis. Bivariate and multivariate Cox proportional hazards model were used to identify predictors.

Result: A total of 451 charts were included and followed for a total of 1377.303 Person Years (PY) of observation, the overall incidence density of tuberculosis was 8.6 per 100person-year. More than half 68 (57.14%) of HIV infected persons developed TB at the first year of follow up. The cumulative proportion of TB free survival was 79%, 76%, 74%and 71% at the end of one year, two, three and four year respectively. Having past TB history (AHR=2.32, 95%CI=1.511-3.573); Ambulatory and bedridden functional status at baseline (AHR=2.42, 95%CI (1.05-5.59), (AHR=2.42, 95%CI=1.56-3.75); Baseline BMI<18.5kg/m² (AHR=1.621, 95 %CI =1.09-2.40); Not taking IP (Isoniazid prophylaxis therapy) (AHR= 6.96, 95%CI=2.53-19.08); Baseline Hgb <12.5g/dl (AHR=2.00, 95% CI=1.08-3.71), and Hgb <10 g/dl (AHR= 2.54, 95%CI=1.57-4.11) were predictors that associated for TB incidence.

Conclusion and recommendation: TB incidence rate is high among adults living with HIV. TB was high in the first year of follow up. Past history TB, not receiving IPT, low BMI, low Hgb and unable to work were the most significant predictors for occurrence of TB. Therefore the result of the study recommends for an improved TB/HIV collaboration activity and scale up of IPT in the setup to reduce risk of TB.

Keywords

 $Incidence\ and\ predictors,\ Tuberculosis,\ Adult\ people\ living\ with\ HIV/AIDS,\ Afar\ health\ facilities,;\ Northeast,\ Ethiopia$

Background

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium Tuberculosis (MTB). It is typically affects the lung but also can affect other parts of the body as well [1]. tuberculosis and Human Immune Deficiency Virus (HIV) infections are two major public health problems in many parts of the world [2,3]. Since the beginning of the later pandemic, nearly 78 million people have contracted HIV and close to 39 million have died of AIDS causes [2].

Worldwide, TB is a leading cause of death among people living with HIV and HIV is the most potent risk factor for the development of tuberculosis. According to WHO report 2014, 1.1 million incident TB cases are among people living with HIV. The prevalence of TB-HIV Co-infection is higher worldwide and 90% of these co-infected cases live in developing nations [4,5].

Sub-Saharan Africa accounted for 79% of the burden of TB-HIV co infections,



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followed by South-East Asia (11%). In the African region that has the highest TB/HIV burden, three out of four TB patients knew their HIV status globally, and 70% of the TB patients known to be living with HIV in 2013 were started on antiretroviral therapy (ART).

Even though tuberculosis is the most commonly diagnosed opportunistic infection and disease in HIV infected individuals which can be curable and reduced with appropriate measure of therapy but hidden TB can hasten the progression of HIV. The presence of TB may affect individuals with HIV infection in numerous ways. TB increase T-cell replication and it increases HIV replication and it leads to increased viral load. Tuberculosis facilitate occurrence of other opportunistic infections and become a challenging to diagnose TB with HIV because the clinical manifestations of TB in HIV infected individuals are somewhat different. The life time risk of HIV infected individuals to develop TB is 20-37 times greater than HIV negative individuals to develop active TB from the latent infection of mycobacterium tuberculosis [1,3,6]. The dangerous synergy affects all aspects of both diseases, from pathogenesis and the epidemiologic profile, to clinical presentation, treatment, and prevention [7]. This synergy also impacts largely the management of individuals co-infected with this deadly disease related to pill burden, drug to drug interaction, increased adverse effect and immune reconstitution inflammatory syndrome(IRIS) [7-9]. As a result, TB became the leading opportunistic infection that cause of death among HIV infected people. This factors and late diagnosis of TB highly contribute to keep the mortality rate of TB very high among the co-infected people [9].

Several studies conducted in different places of the world showed the synergic effect of TB and HIV among HIV infected patients. A large review conducted on syndemic interaction between HIV and TB epidemics showed that HIV-associated TB contributes substantially to the burden of TB-associated morbidity and mortality [10]. HIV infection is the strongest known risk factor for TB. High HIV prevalence rates are significantly correlated with high TB incidence rates [11]. Similarly, HIV increases the risk of progression to active TB in both primary and latent TB [12].

In developed nations the incident cases of TB was increased with the HIV epidemic on HIV infected patients [13]. In developing country the synergic effect is worse than the developed nations. HIV affects and alters TB transmission, duration of infectiousness and progression of disease

Among predictors for the incidence of tuberculosis among HIV infected individuals low CD4 count [14-18], diabetes mellitus, chronic kidney disease, functional status and presence of other opportunistic were significantly associated with reactivation and development of active TB among HIV infected people [18-21], a low BMI is a risk for development of TB among HIV patients, hemoglobin of $\leq \! 10$ mg/dl, BMI $\leq \! 15.5$ kg/m², and opportunistic infections other than TB were significant risk factors for the development of TB among this group [22]. INH preventive therapy (IPT) treatment, ART and CPT reduces the risk of active TB in HIV-infected individuals [23,24]. Therefore the study aimed to assess predictors for incidence of tuberculosis among HIV infected individuals in Afar public health facilities.

Methods

Study design and period

A five year Institution based retrospective follow-up study was employed to assess the incidence and predictors of tuberculosis among adult people living with HIV in Afar public health facilities from May to Jun, 2015.

Study area

The study was conducted in Afar regional state selected health facilities which is located in the North-eastern part of Ethiopia. The region has a population of 1,678,000 only 289,000 population live in urban and semi urban area [25]. Administratively the region consists of five administrative zones with 32 districts. The capital city of the region (Samara) is located 536 km away from Addis Ababa. In Afar there are four hospitals, 40 health centers, 270 health posts and 15 private clinics delivering health services for the people living in the region. Since 2006/7 when HIV care service introduced in the region 15 public health institutions provides HIV chronic care and support service for around 4,000 PLHIV. The study sites selected based on their number of client follow and presence of TB and HIV follow up clinic. Based on this, the study was focused on two health centers (Awash, and Samara), Asayta hospital, Abala hospital and the only general hospital (Dubti) in the region. These health institutions provide chronic HIV care and follow up for about 70% of patients living with HIV in the region.

Study participants were all (503) adult people infected with HIV enrolled to chronic HIV care from July 2010 to May 2015 in selected Afar public health facilities (Dubti hospital, Asayta Hospital, Abala hospital, Awash and Samara health centers). Those adult HIV infected individuals enrolled to chronic care clinic from July 2010 to June 2011 were followed till May 2015 and those with incomplete information like date of enrollment, baseline CD4 count and transfer in patients and TB patients in the last 3 month; were excluded in the study.

Data collection instrument and procedure

Registered patient chart was observed and suitable data extraction format was prepared in English. Subsequently, the data were collected by four diploma nurses and two BSc nurses who had ART training using the data collection format from the patient records. Data clerk and case managers assisted the data collators by identifying the charts. Charts were retrieved by using the patient medical record number and ART registration number which is found on the data base of the health facilities.

Data processing and analysis

Extracted data were checked for completeness, coded, and entered to EPI-INFO version 7 and exported to SPSS version 20 for further analysis. Statistical summary was applied to describe socio demographic, clinical and follow up variables. Magnitude was calculated and described by frequency and tables. Incidence density rate was calculated for the study period. Life table and long rank test was used to estimate TB free survival among study participants and to compare different categories of survival probability respectively.



Bi-variable and multivariate Cox regression model was used to identify the predictors. Variables with value of p < 0.2 in the bi-variable analysis was candidate for multivariate proportional hazard model. 95% CI of hazard ratio was computed and variables having p-value <0.05 in the multivariate Cox proportional hazards model was taken as significant predictors with the outcome variable.

Ethical Clearance was obtained from the IRB office of the institute of school of medicine, university of Gondar. Permission was obtained from the Afar regional health office (ARHO) and written permission letter was sent to each health facilities to conduct this research. Unique identification information was used on the extraction format and for all information taken from the chart confidentiality issue was maintained. The collected information was only used for the study purpose.

Results

Baseline socio-demographic characteristics of PLHIV

A total of 503 records of PLHIV who were enrolled from July 1, 2010 to May 2015 were reviewed. Fifty two (10.44%) of them were not included in the analysis due to incomplete information. Among the 451 patients remaining in the analysis the mean age (SD) was 32.55 ± 7.48) and almost two third 297(65.9%) of them were below the age of 35 years. Most of respondents 410 (90.9%) in the study were urban residents More than half 267(59.2%) of PLHIV were females and 275 (61%) were also Muslim in religion. (Table 1)

Characteristics		Frequency	Percentage
A	15-24	55	12.2
	25-34	242	53.7
Age	35-44	119	26.3
	45 and above	35	7.8
Sex	Male	184	40.8
Sex	Female	267	59.2
	Single	144	31.9
Manital atatus	Married	200	44.3
Marital status	Divorced /separated	orced /separated 77	17.1
	Widowed	30	6.7
Dasidana	Urban	410	90.9
Residence	Rural	41	9.1
	Muslim	275	61.0
Religion	Orthodox	165	36.6
	Others	11	2.4
	No formal education	212	47.0
educational status	Primary	177	39.2
	Secondary and above	62	13.7
	1-3	216	47.9
Family size	4-5	159	35.3
	>5	76	16.9
	Self employed	234	51.9
occupational status	Government employed	45	10.0
	No employed	172	38.1
	user	130	28.8
substance use	non-user	321	71.2

Table 1: Socio-demographic characteristics of PLHIV enrolled to chronic HIV care at Afar health facilities, northeast Ethiopia June 30, 2015.

At most half 234(51.9%) of patients were self-employed. One hundred thirty (28.8%) patients recorded as substance users either of drugs 20% or tobacco 3.1% or alcohol 5.7%. Majority, 374(93.1%) of the patients were living in family size of 1-5. Almost half 212(47%) of the patients never went to formal education. More than two third (68.1%) of the patients were currently or formerly married (**Table 1**).

$Base line clinical and HIV related follow up \, characteristics \\ of PLHIV$

Baseline clinical and HIV related follow-up characteristics as shown in table 2 below (53.4%) had a baseline WHO clinical stage III and IV. Majority 366 (81.2%) of Participants were enrolled with working functional status. Participants had baseline median CD4 cell count of 285cell/ml (IQR178-383) at enrollment. Almost half 218 (48.3%) of the participants were enrolled with BMI < 18.5. More than half 270 (59.9%) study subjects had a baseline Hgb < 12.5. During the follow up majority 413 (91.8%) of the participants provided with CPT but only 94(20.8%) of the participants received IPT (**Table 2**).

The eligibility criteria for the initiation of HAART was mainly WHO clinical stage 183 (40.6%) and both WHO clinical stage and CD4 cell count 167 (37 %.) respectively. The initial regimen frequently prescribed for the study participants were a combination of TDF,3TC and EFV 170 (37.7%) followed with AZT,3TC and EFV110 (24.4%). Ninety six (21.3%) of participants changed their initial regimen. 92 (95.8%) of change was substitution and only 4(4.2%) patients switched to second line. Majority of the drug changes was made following the development of side effect 50 (52.08%) and 29 (30.2%) changes was following development of TB.

Baseline clinical and HIV related follow up characteristics of PLHIV

From the total of 451 study participants (53.4%) had a baseline WHO clinical stage III and IV. Majority 366(81.2%) of Participants were enrolled with working functional status. The average baseline median CD4 cell counts of respondents at enrollment were 285cell/ml (IQR178-383). Almost half 218(48.3%) of the participants were enrolled with BMI <18.5. more than of 270(59.9%) study subjects had a baseline Hgb<12.5. During the follow up majority 413(91.8%) of the participants provided with CPT but only 94(20.8%) of the participants received IPT (**Table 2&3**)

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TB incidence rate

Four hundred fifty one study participants were followed for different periods in the follow up for a total of 1377.303 Person Years of observation. One hundred nineteen (26.4%) of participants develop TB while on follow up and 332 individuals censored (40 patients transferred out, 13 patients died, 21 drop out and 258 remained till end of follow up. Therefore, the overall TB incidence rate on the follow up period calculated using Person-year of follow up was 8.64 cases per 100 Person Years. Study participants stayed in the follow up for a minimum of 0.03 month and maximum of 58.83 months. The median observation period was 46.74 months [IQR=15.95-52.42 months]. The median survival time is 54.00 month. Among the TB cases occurred in the follow up period 67(56.3% were females. Majority 91(76.47%) of the cases were pulmonary TB. Forty six (38.6%) of incident TB occurred within the first months of follow up and 68(57.14%) of incident TB cases occurred within the first year of follow up. Incident of TB is more common in urban105 (88%) of cases than the rural setting and in family size of >5 households.

Incidence of TB with PLHIV and their baseline clinical and follow up characteristic

From the study participants who developed incident TB, 41(34.5%) of them had history of previous TB or treatment history and 47(39.5%) of them were either ambulatory or bedridden at enrollment. Majority 115(96.6%) of the incident cases of patients not provided with INH prophylactic therapy. Ninety five (79.9%) of participants with incident cases of TB were enrolled with Hgb level below12.5g/dl.

Test of equality for survival distribution for the different levels of the different categories was performed with Kaplan Meier using the long rank test. Association of difference was observed among

Characteristics	Number(n=451	Percent
	Past TB	
Yes	74	16.4
No	377	83.6
	OI*	
Yes	34	7.5
No	417	92.5
	Chronic illness	
Yes	35	7.8
No	416	92.8
Base I	ine functional status	
Working	366	81.2
Ambulatory and bedridden	85	18.8
	ВМІ	
<18.5	218	48.3
≥18.5	203	45.0
WH	IO clinical stage	
1	62	13.7
II	138	32.8
III	172	38.1
IV	69	15.3

Table 2: Baseline clinical and HIV related follow up characteristics of PLWHA in Afar health facilities north east Ethiopia 2015.

	Hgb level					
<10	56	12.4				
10-12.49	214	47.5				
≥12.5	181	40.1				
CD4 count						
<100						
100-200	124	27.5				
200-349	125	27.7				
≥350	158	35.0				
I	nitial regimen					
d4t-3TC-NVP	65	14.4				
AZT-3TC-EFV	89	19.7				
AZT-3TC-NVP	110	24.4				
TDF-3TC-EFV	170	37.7				
Others#	17	3.8				
EI	igibility criteria					
CD4 cell count	62	13.7				
WHO clinical stage	183	40.7				
CD4 count and WHO stage	167	37.0				
Unrecorded	39	8.6				
	CPT use					
Yes	413	91.6				
No	38	8.4				
	IPT use					
Yes	94	20.8				
No	357	79.2				
Did	regimen changed					
Yes	96	21.3				
No	355	78.7				
Type of the changed regimen						
First line	92	20.4				
Second line	4	0.9				
Reason for change						
Tuberculosis	29	6.4				
Side effect	50	11.				
Failure	4	0.9				
Others#	13	2.9				
Adherence						
Consistent	351	77.8				
Inconsistent	100	22.2				

OI*=other than TB, others#, d4t-3TC-EFV, TDF-3TC-NVP&ABC-3TC-EFV

Table 3: Baseline clinical and HIV related follow up characteristics of PLHIV in Afar health facilities, northeast Ethiopia 2015 continued

the explanatory variables like BMI and IPT. Baseline BMI had a significant difference for tuberculosis - free survival as compared for people living with HIV. BMI < 18.5 kg/m² had low TB free survival as compared to those With BMI >18.5 kg/m² with the overall comparison result long rank of p-value p< 0.002 and for the IPT was p<0.0001 which shows significant difference of TB free survival among patients provided with IPT. [Figure 1]

Predictors of tuberculosis in Cox survival analysis

In a bi-variable Cox regression analysis, variables with p<0.2 value was candidate for multivariate analysis. Eleven variables were significantly associated in the Bi variable analyses which were CD4 cell count, WHO clinical stage, substance use; marital status, OI, IPT, past TB history, BMI, Hgb, functional status and family size were included in the multivariate analysis. The Enter method was used in the multivariate analysis to see



output value of the variables showed significance in bivariate analysis. Past TB history, baseline functional status, baseline hemoglobin, baseline BMI and IPT were found statistically significant with having value of p< 0.05 in multivariate analysis. According to the Cox multivariate analysis HIV patients who had history of TB at enrollment were 2.32 times risky to develop TB at a time than those who had no past TB history (AHR=2.32, 95%CI=. 2.324(1.511-3.573). Patients enrolled to care with baseline functional status of bed redden and ambulatory were 2.42 times more prone to develop TB at any follow up time than those enrolled with working functional status (AHR=2.42,95%CI(1.05-5.59) ,(AHR=2.42 ,95%CI=(1.56-3.75) respectively. Similarly, HIV patients having baseline BMI<18.5kg/m² were1.62 times higher risky to get TB at any time than those with having BMI≥18.5kg/ m² at baseline (AHR=1.621, 95 %CI (1.09-2.40). HIV patient who did not take IPT were 6.96 times more likely to acquire TB at any time compared to those who taken IPT(AHR= 6.96,95%CI (2.53-19.08). in addition People living with HIV enrolled with baseline Hgb < 12.5g/dl were 2.54 times more to develop TB at certain time than those having Hgb above 12.5g/dl respectively (AHR=2.00 ,95%(1.08-3.71) (AHR= 2.54,95%CI(1.57-4.11).

Discussion

It is universally acknowledged that HIV infection increases the incidence of tuberculosis. TB and HIV remains as major public health problems in many parts of the world. The fact, that Ethiopia is among the TB high burden countries with an estimated annual incidence of 211case per 100,000 populations and with prevalence of 224 cases per 100,000 [4]. TB is the most common cause of morbidity and mortality among PLHIV. HIV infected individuals are 20-37 times greater risk to develop TB in life time compared to non-infected individuals [6,26]. [Table 4 & 5]

This study tried to assess the overall incidence of TB among the participants for the entire follow up period. It was found to be 8.64 cases per 100 person years. This finding was consistent with studies conducted in Ethiopia which founds (7cases /100 PY and 7.9 cases per/100 PY) [27,28]. It also in lined with findings from Tanzania 7.9 [(95% CI), 7.6-8.2] per 100 and Sub-Saharan Africa [29,30]. However, it was high as compared to studies conducted in Korea, Israel and Malaysia [17,31,32]. This could be explained by the fact that these countries might have better preventive, diagnostic and

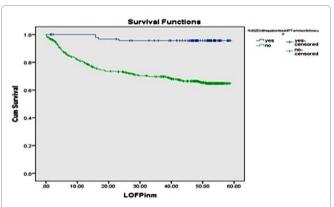


Figure 1: TB free survival probability with BMI among PLHIV in Afar health institutions northeast

Characteristics		TB status			
		Censored (n=332)	Event of B (n=119)		
	15-24	41(9.1%	14(3.1%	55(12.2%	
Age	25-34	179(39.7%	63(14.0%	242(53.7%	
	35-44	89(19.7%	30(6.7%	119(26.4%	
	≥45	23(5.1%	12(2.7%	35(7.8%	
Sex	Male	32(29.3%)	52(11.5%)	184(40.8%)	
	Female	200(44.3%)	67(14.9%	267(59.2%)	
Danidanaa	Urban	305(67.6%)	105(23.3%	410(90.9%)	
Residence	Rural	27(6.0%)	14(3.1%)	41(9.1%)	
	Never married	114(25.3%)	30(6.7%)	144(31.9%)	
Marital	Married	148(32.8%)	52(11.5%)	200(44.3%)	
status	Divorced/separated	47(10.4%)	30(6.7%)	77(17.1%)	
	Widowed	23(5.1%)	7(1.6%)	30(6.7%)	
	Edu	ıcational level			
No formal education		157 (34.8%)	55(12.2%)	212(47%)	
Primary		128 (28.4%)	49	177(39.3)	
Secondary and above		47 (10.4)	15(1.1%)	62(13.7)	
	Осси	pational statu	s		
S	elf employed*	175(38.8%	59(13.1%)	234(51.9%)	
Government employed		36(8.0%	9(2.1%)	45(10.1%)	
No employment		121(26.8%	51(11.3%)	172(38.1%)	
	ı	Family size			
1-3		165(36.6%)	51(11.3%)	216(47.9%)	
	4-5	116(25.7%)	43(9.5%)	159(35.3%)	
	>5	51(11.3%)	25(5.5%)	76(16.9%)	
	Sı	ibstance use			
User		88(19.5%)	42(9.3%)	130(28.8%)	
Non user		244(54.1%)	77(17.1%)	321(71.2%)	
		Religion			
Muslim		205(45.5%)	70(15.5%)	275(61.0%)	
Orthodox		118(26.2%)	47(10.4%)	165(36.6%)	
Others *		9(2.0%)	2(0.4%)	11(2.4%)	

Table 4: Incidence of TB and socio demographic characteristics of the study participants in Afar health facilities, northeast Ethiopia 2015.

treatment setups and strategies for controlling TB in contrast of this study was done in a high TB burden country and scarce resources might contribute for this high result. Low health care coverage and late enrollment to health care facilities might contribute for this finding. This could be also explained with progression of the latent infection to active TB after initiation of HIV chronic care with late presentation of patients to health facility. The patient might get new infection or IRIS after initiation of HAART and other HIV related services. IRIS associated TB was commonly seen within the first 6 months after initiation of HAART [33].

In different studies as indicated that multiple risk factors can predict the incidence of TB among PLHIV on HAART and Pre HAART era. Our study found that having past TB treatment history, non-use of IPT, baseline functional status of bedridden and ambulatory, low baseline Hemoglobin level and low baseline BMI were significantly associated with increased risk for acquiring TB in the study participants. This study revealed that HIV infected individuals with Past TB history had 2.3 times high risk to develop TB as compared with HIV individuals with no past TB history. Our finding was similar with findings from studies done in Israel and Malaysia and Uganda [31,32, 34]. The possible explanation could



		TB status			
Characteristics	Categories	Censored (n=322)	event of TB(119)	Total	
D4 TD	Yes	33	41	74	
Past TB	No	299	78	377	
OI*	Yes	15	19	34	
	No	317	100	417	
Chronic illness	Yes	24	11	35	
	No	308	108	416	
	Working	294	72	366	
Baseline functional status	Ambulatory	35	39	74	
	Bedridden	3	8	11	
	I	55	7	62	
WILO aliminal atoms	II	119	29	138	
WHO clinical stage	III	113	59	172	
	IV	45	24	69	
	d4t-3TC-NVP	51	14	65	
	AZT-3TC-EFV	69	20	89	
Initial regimen	AZT-3TC-NVP	82	28	110	
illiliai regillieli	TDF-3TC-EFV	118	52	170	
	Others*	12	5	17	
	<10	33	23	56	
Baseline Hgb	10-12.49	142	72	224	
	≥12.5	157	24	181	
Danalina DMI	<18.5	143	75	218	
Baseline BMI	≥18.5	161	42	203	
A	Consistent	261	90	351	
Adherence	Inconsistent	71	29	100	
	<100	22	22	44	
CD4cell count	100-200	84	40	124	
	201-349	96	29	125	
	≥350	130	28	158	
	Yes	305	108	413	
CPT use	No	27	11	38	
IDT	Yes	90	4	94	
IPT	No	242	115	357	

Table 5: Incidence of TB and clinical and follow up characteristics of the study participants in Afar health facilities, northeast Ethiopia 2015.

be due to poor compliance for their anti TB treatment at first episode and it could be due to relapse. Reactivation or re-infection might also be possible explanation for the existing dysregulated immunity. Participants not provided with IPT were 7 times higher risk to develop TB as compared to individuals who took IPT (AHR=6.96, 95%2.53-19.08). This study found that IPT were independent risk factor for the occurrence of incident TB among adult HIV patients. This is consistent with studies done in Ethiopia, South Africa and Brazil [24,35,36]. In fact, IPT is recommended to reduce and control TB among this group of people. Despite the fact, the poor uptake and the ambiguity and fear of drug resistance might contribute for these participants non- IPT user. This is an alarming to scale up the IPT on the setting.

Patients' ambulatory and bedridden functional status at baseline is 2.42 times more likely to develop TB in the entire follow up as compared to working functional status. This finding is in line with other study done in northwest Ethiopia [27]. The possible explanation was debilitated patients prone to malnutrition and less physical activity that make them prone for many diseases and TB.

Patients with BMI of <18.5 at baseline was 1.62 times higher risk of developing TB as compared to adults with BMI≥18.5 at base line. This finding was consistent with phase III randomized controlled trial study done in Tanzania(22).It was also agrees with studies done in Ethiopia and south Africa [29,37]. The possible explanations might be HIV patients are prone for malnutrition and low BMI is a sign of malnutrition. Malnutrition in HIV patients associated with increased catabolic activity, infection and loss of appetite and decreased in take. This all contributes for low BMI. Malnutrition is one of the pertinent risk factor of TB among HIV and non HIV patients.

Similarly this study found that patients with Hgb level of <10 and 10-12.5 at base line were 2.00 and 2.54 times higher risk of developing TB than those having Hgb level >12.5 at base line. Hematologic complications were risk factors for the incidence of TB among PLHIV. This finding was in line with studies conducted in Ethiopia, Uganda, Tanzania and South Africa [22,37-39]. The Possible explanation is due to malnutrition and side effect of medications, opportunistic infections and advanced stage of the disease. Undiagnosed TB could explain the low Hgb level at the early enrollment. Variables like CD4 cell count and WHO clinical stage were not independently associated in this study.

Strength of the Study

The study tried to include all possible variables that influences risk of TB among HIV patients that could accessed from the chart. The study was conducted for a five year follow up that helps to show the long term impact of HIV on TB.

Limitation of the Study

This study might have limitations that shared with limitation of most retrospective record based studies had. The retrospective and record based nature of the study design limited to include predictors that could affect the risk of TB like housing condition, house hold income and other. Due to incomplete data some study subjects were removed from the study that might undermine the finding if those study subjects had TB. The study not observed ART group and Pre ART group separately.

Conclusion

The overall incidence of TB in the study setting is high. HIV infected individuals with history of previous TB, not using IPT, base line BMI<18.5kg/ $\rm m^2$, ambulatory and bedridden functional status and having baseline Hgb <12.5g/dl were most predictors of incident TB.

Recommendation

For governmental organizations and stakeholders:

- Strengthen the TB /HIV collaborative activity
- Giving trainings on the provision of IPT that might Strengthen the strategies for prevention and control of TB among adult HIV infected people
- Close supervision for Implementation of the guidelines and standards strategies to prevent and control TB.



For health professionals:

- Strength the provision of IPT and nutritional support to all eligible HIV individuals
- Continuous follow up and early detection of malnutrition, prevention of other infection and close monitoring for HIV patients enrolled with ambulatory or bedridden functional status and low BMI <18.5and low Hgb at baseline to control TB among this groups.

For patients

 Patients would be encouraged to have improved treatment and care seeking and infection control behavior.

For researchers:

 Further prospective studies might need to include all factors that influence the risk of TB.

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Competing interests

We authors declare that they have no competing of interests.

Authors' contributions

Ausman Ahmed involved in the conception, design, data collection, analysis and report writing. Desalew Mekonnen & Melaku Kindie assisted with the design, approved the proposal with some revisions, participated in data analysis and manuscript preparation. All authors read and approved the final manuscript.

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