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Incidence and Predictors of Tuberculosis among HIV/AIDS Infected Patients: A Five-Year Retrospective Follow-Up Study

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Abstract

Background: Despite increased deliverance of antiretroviral therapy (ART), morbidity and mortality from TB are still predominant among HIV/AIDS infected patients in Ethiopia. Thus, current study aimed to determine magnitude and predictors of tuberculosis among cohort of HIV infected patients at Arba Minch General Hospital, Ethiopia, 2015. Methods: Hospital based retrospective follow-up study was conducted among study population which was HIV/AIDS infected individuals registered from September 2007 to 2013. The data were collected using structured data abstraction form and four ART trained nurses were used to abstract the data. The data were checked for completeness, cleaned and entered into Epi Info 7.0 and analyzed using SPSS version (IBM-21). Results were summarized by using table of frequency, graph, and measure of central tendency. Statistical significance was inferred at P-value ≤ 0.05. Adjusted odd ratio (AOR) with 95% confidence interval (CI) was used to determine predictors. Result: Four hundred ninety six patient's charts were abstracted. Cumulative and incidence density of tuberculosis were 21.4% (95% CI: 21.3, 21.44) and 5.36 per 100 person year respectively. Cigarette smokers (AOR: 2.82, 95% CI (1.27 - 6.27)), household with family size of 3 - 4 (AOR: 2.26, 95% CI (1.14 - 4.50)), baseline WHO clinical stage III (AOR: 20.26, 95% CI (7.09 - 57.6)) and IV (AOR: 22.9, 95% CI (6.91 - 76.4)) and heamoglobin level of <10 (AOR: 2.56, 95% CI (1.22 - 5.33)) were important predictors (risk factors) of tuberculosis among HIV infected patients. Conclusion and recommendation: Relatively high incident tuberculosis cases were established among HIV infected patients and history of cigarette smoking; family size; hemoglobin level and base line WHO clinical stage were responsible for this incidence. Therefore; early initiation of HAART as per current guideline should get stressed, and the finding that smoking was important predictors for TB in Ethiopia had obvious TB control implication which required high attention focused on fighting against cigarette smoking among HIV infected cohort.

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Keywords

Tuberculosis, HIV Infection, Incidence, Predictors, Arba Minch General Hospital, Ethiopia

1. Introduction

Tuberculosis (TB) remains one of the world's deadliest communicable diseases. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease [1]. An estimated 1.1 million (13%) of the 9 million people who developed TB in 2013 were HIV-positive. The African Region accounts for about four out of every five HIV-positive TB cases and TB deaths among people who are HIV positive and the majority of victim live in sub Saharan Africa, which accounts seventy percent (70%) [1] [2]. Some Africa countries have reported continuing rises in tuberculosis case rates despite declining HIV prevalence, while others show stable or declining tuberculosis incidence among HIV-negative individuals [3].

Tuberculosis has been recognized as a major public health problem for more than five decades in Ethiopia. Ethiopia is one of the 22 high burden countries (HBCs) and TB remains one of the leading causes of mortality. According to the 2014 WHO report, the prevalence and incidence of all forms of TB are 211 and 224 per 100,000 of the population, respectively. About 13% of all new TB cases are also HIV co-infected. Moreover, Ethiopia is one of the high TB/HIV and multidrug resistant TB (MDR TB) burden countries. Among TB patients with known HIV status, about 11% were HIV co-infected. [1] [4]

Despite increased deliverance of antiretroviral therapy (ART), morbidity and mortality from TB are still predominant among PLHIV. Among 33.2 million individuals acquiring human immune deficiency virus (HIV), one-third of them are concomitantly infected with Mycobacterium tuberculosis [5].

The TB/HIV co-infection results derangement of quality of life, poor physical health than HIV infected individuals and has a greater risk of common mental disorders [6] [7].

Moreover, the management of a TB and HIV co-infected individual is challenging because of frequent oral drug intake which can cause different problem [8], increased drug adverse effects [9], drug and drug interaction [10] and the immune reconstitution inflammatory syndrome (IRIS) [11].

The risk of tuberculosis among PLHIV is 20 times higher than HIV negative people [2] [12] [13], and baseline CD4+ lymphocyte count, history of injectable drug use, antiretroviral therapy, body mass index, anemia, and educational status were some of the contributing factors for TB in HIV patients [14] [15].

Many efforts have been made to integrate TB diagnosis and treatment with HIV care in order to prevent, diagnose and manage TB among HIV infected individuals, though TB still occur in HIV patients who are on HAART receiving individuals [1] [16]. Therefore; there should be early screening and detection of TB in PLHIV as TB can occur in any course of HIV treatment [17] [18].

Furthermore, adequate understanding of the specific situation through follow-up research should be done to provide baseline finding to program designing for respective organization. Therefore, this study aimed to determine the incidence and predictors of TB among PLHIV registered at Arba Minch General Hospital.

2. Methodology

2.1. Study Settings and Period

This study was conducted at the government owned General Hospital located in Arba Minch town, Southern Ethiopia. The town is 500 km south of Addis Ababa. In the hospital all HIV positive people from any service area were enrolled in ART clinic for comprehensive HIV care. There are multidisciplinary professional's team that includes physicians, nurses, public health professionals, laboratory technologists, pharmacists, data clerks and volunteer adherence supporters. ART is being provided for HIV infected adult patients according to CD4 count and WHO clinical stage.

2.2. Study Design and Period

Hospital based retrospective follow up study was employed from December 2014-January 2015.

2.3. Source and Study Population

All HIV infected patients attending ART clinic of Arba Minch General Hospital and HIV infected individuals registered between September 2007 and August 2013 were source and study population respectively.

Inclusion criteria: All PLHIV aged 15 years and above and were enrolled into the adult chronic HIV care at the Arba Minch general Hospital were included in the study

Exclusion criteria: An individual with incomplete chart and diagnosed clinically without sputum examination, culture and chest X-ray were excluded from the study.

2.4. Sample Size Determination

Sample size was determined for first specific objective by using StatCalc program of Epi Info, with the assumption of Z-score corresponding to 95% confidence interval, 28.9% proportion of tuberculosis among HIV positive patients, 4% degree of precision, ten percent of non-response rate and total enrolled patients (6015) in Arba Minch general hospital which resulted **502** samples.

Sample size was also calculated for second specific objective from the study conducted in Gondar University hospital and Felege-Hiwot Referral Hospital [13] [19]. Thus, Sample size calculated for the second specific objectives; CD4 count (>200) by considering 10% of lost to follow up, resulted 436, which is less than sample size calculated for first specific objective, so sample size (502) calculated for first specific objective was taken as sample size (**Table 1**).

2.5. Sampling Procedure

Simple random sampling was used through randomly generated number from patient's data of 2007-2013. Despite, charts were organized on the shelf according to the hospital card number, which is given in chronological (sequential) order. Some of charts in the hospital were not arranged in numerical order, so new numbering started from 1 up to 2000 were assigned to charts of two thousand patients registered between 2007 and 2013. After a number was assigned to each chart, investigator draw 502 sample charts and among them 496 that fulfilled the inclusion criteria was reviewed one by one and the information was transcribed to the pre-structured data abstraction form.

2.6. Data Collection Procedures

Structured data abstraction form was prepared and used for chart review. Four ART nurses abstracted the data from ART registry book of HIV infected patients who had follow up starting from 2007 up to 2013 under supervision of medical doctors who were got trained for this purpose. Principal investigator rechecked if there is incomplete and inconsistent abstraction from the chart at every day, if incomplete checklist was found, he sent back to data collectors for correction.

2.7. Operational Definitions

Incident TB case: which was defined in this study, as an event, diagnosed with Sputum smear (+) (at least two), chest X-ray (suggestive of TB finding) and culture positive during follow-up, which was ascertained retrospectively?

Cumulative Incidence of TB: It was calculated by dividing total new occurrence of Tuberculosis to all total sampled patients.

Table 1. Sample size calculated for second specific objectives, 2015.

Variables	CI	Power	OR	Ratio	Percent in unexposed	Lost to follow up	Sample size
Functional status/Working group	95%	90%	2.67	1	23.1%	10%	242
WHO stage IV/Stage I/II	95%	90%	10.3	1	10.4%	10%	57
CD4 count >200	95%	90%	2.13	1	21%	10%	396
Body mass index	95%	90%	8.2		3.8%	10%	127

Incidence rate of Tuberculosis: Incidence rate in this research was calculated by dividing all new occurrence of Tuberculosis to total follow up time of patients in year.

TB diagnosis: TB was diagnosed using microscopic examinations of sputum smears, chest radiology, fine-needle aspiration of lymph-adenopathy, cytology with very high clinical grounds and mycobacterium culture.

2.8. Data Management and Analysis

Data was coded manually, entered and cleaned using Epi-Info 7 and exported to SPSS version 21 for descriptive and inferential analyses. Frequencies and cross tabulations were used to check for missed values and variables. Data was presented by using frequency, tables, and summarized by using mean and standard deviation. Back ward Logistic regression analysis was conducted to see the effect of explanatory variables on TB incidence and Statistical significance was inferred at P-value <0.05. Adjusted odd ratios with 95% confidence interval (CI) were used to determine predictors.

2.9. Ethical Consideration

The study was approved by the institutional review board of Addis continental institute of Public health which was coordinated by Arba Minch University/CMHS. Additional written permission to conduct the study on medical records of patients was obtained from the Arba Minch General hospital. Personal identifiers were excluded during data abstraction. Since it is secondary data obtaining informed consents from the participants was not possible, but the confidentiality of information was maintained by not recording their name from the chart and keeping the data anonymous.

3. Result

3.1. Socio-Demographic and Economic Characteristics

Four hundred ninety six records of HIV Infected patients were analyzed. Their mean age was 33.8 (±8.89 SD) years and almost half, 235 (47.4%), of them were in the age group of 25 - 34 years. Over half (58.1%) of the PLHIV were females and the majority (73.4%), of them were urban dwellers.

Almost all (99.8%) patients disclosed their HIV status, to their brothers/sisters/parents. Forty three (8.7%) of them were cigarette smokers (see **Table 2**).

3.2. Base Line Clinical Characteristics

One hundred seventeen nine (36.1%) of them were at WHO clinical stage 3 during enrolment. Three hundred twenty five (65.2%) of the participants were on working status at baseline. The median CD4 count during enrollment was 221 (IQR: 125 - 340.7).

The predominant regimens initially prescribed were a combination of (TDF + 3TC + NBC) and (3TC + EFV + NVP) (38.3%), followed by Staudinger, Lamivudine and, Nevirapine (17.8%).

One hundred thirteen (22.8%) patients had changed their initial regimen during the follow up period mainly to (TDF + 3TC + NVP) + (3TC + EFV + NVP) 45 (9.6%), and ten (8.85%) patients were switched to second line HAART.

For 105 (92.9%) and 3 (2.65%) patients, regimens were changed due to drug side effect and TB occurrence respectively, while the reasons for changing the initial regimen were not recorded for 4 (3.54%) patients (see **Figure 1** and **Figure 2**, see **Table 3**).

3.3. Incidence of TB in People Living with HIV/AIDS

Cumulative incidence and incidence rate of tuberculosis among PLHIV patients was 21.4% (21.3, 21.44) and 5.36 per 100 persons year respectively (see **Figure 3**).

3.4. Bivariable Logistic Regression Analysis

Bivariable logistic regression analysis of socio-demographic and Behavioral variables on incidence of TBC revealed that age, sex, disclosure of HIV status to one of family member, history of cigarette smoking and household family size were predictors of incidence of TB, but all other variable like educational status, marital status,

Table 2. Socio-demographic characteristics of HIV Infected patients at Arba Minch General Hospital (2007 and 2013 G.C).

Variable	Frequency	(%)
Sex		
Male	208	41.9
Female	288	58.1
Age (33.2 + 8.89)		
15 - 24	66	13.3
25 - 34	235	47.4
35 - 44	137	27.6
≥45	58	11.7
Marital status		
Married	321	64.7
Single	60	12.1
Divorced	54	10.9
Separated	29	5.8
Widowed	32	6.5
Residence		
Urban	364	73.4
Rural	132	26.6
Religion		
Orthodox	334	67.3
Muslim	21	28.4
Protestant	141	4.2
Level of educational		
No education	116	23.4
Primary	169	34.1
Secondary	158	31.9
Tertiary	53	10.7
Occupation		
Farmer	24	4.8
Government employ	72	14.5
Housewife	158	31.9
Merchant	44	8.9
Private gainful work	67	26.4
Others (unspecified job)	131	13.5
Addiction		
Addicted	39	7.9
Not addicted	457	92.1
Family size		
≤2	127	25.6
3 - 4	221	44.6
≥5	148	29.8
Cigarette smoking		
Yes	43	8.7
No	453	91.3

and other analyzed were not predict Incidence of Tuberculosis among HIV infected patients (see **Table 4**).

3.5. Factors Associated with TB Incidence in People Living with HIV (Multivariable Logistic Regression Analysis)

In multivariable logistic regression analysis, Family size, History of cigarettes smoking, Baseline WHO clinical

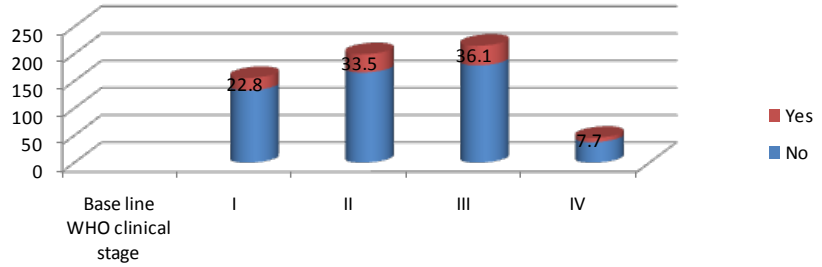

Figure 1. Baseline WHO clinical stage of HIV infected people at AGH, 2015.

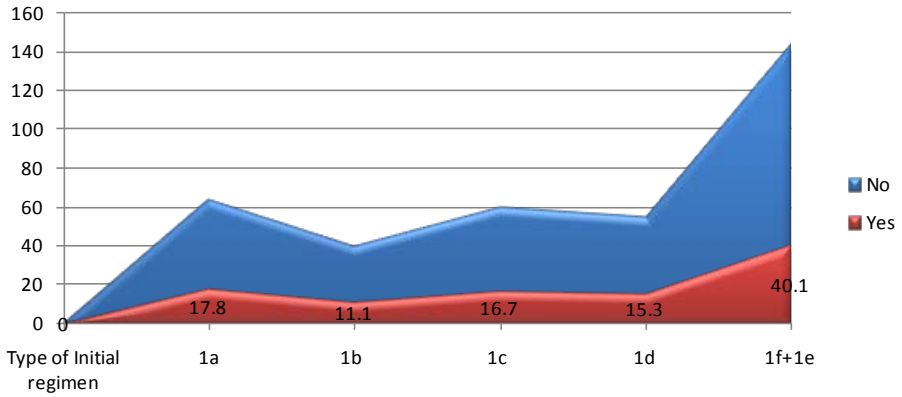

Figure 2. Anti retroviral intervention type for HIV infected patients at AGH, 2015.

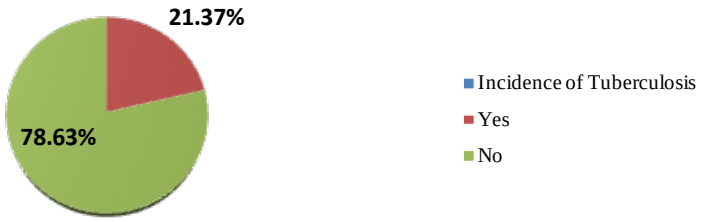

Figure 3. Cumulative incidence of tuberculosis among PLHIV patients, at AGH 2015.

Table 3. Clinical characteristics of HIV infected patients registered in Arba Minch General Hospital between 2007 and 2013.

Variables	Frequency	%
ART intervention		
Pre-ART	137	27.6
HAART	359	72.6
Regimen change during follow up		
Yes	113	22.8
No	383	77.2
New regimen		
First line	103	91.2
2nd line	10	8.85
Reason for switch first regimen		
Side effect	105	92.9
Pregnancy	1	0.88
Tuberculosis	3	2.65
Others	4	3.54
Past TB treatment history		
Yes	68	13.7
No	428	86.3

Continued

Functional status		
Working	**325**	**65.5**
Ambulatory	**134**	**27.0**
Bed redden	**37**	**7.5**
CD4 count		
<50	35	7.1
50 - 100	58	11.7
101 - 200	127	25.6
200	276	55.6
Hemoglobin		
<10	17	3.4
≥10	479	96.6
Year of follow up		
≤1	16	3.2
1 - 3	129	26.0
≥3	351	70.8

Table 4. Association between socio-demographic and behavioral characteristics with incidence of TB among HIV infected patients in Arba Minch General Hospital, 2015.

Variable	Incidence of tuberculosis		COR (95% CI)
	Yes (%)	**No (%)**	
Age			
15 - 24	8 (12.1)	58 (87.9)	1
25 - 34	46 (19.6)	189 (80.4)	1.76 (0.78, 3.95)
35 - 44	33 (24.1)	104 (75.9)	2.30 (0.99, 5.31)
≥45	19 (32.8)	39 (67.2)	3.53 (1.41, 8.87)
Sex			
Male	55 (26.4)	153 (73.6)	0.59 (0.39, 0.92)
Female	51 (17.7)	237 (82.3)	1
Marital status			
Divorced	14 (25.9)	40 (74.1)	1.25 (0.44, 3.52)
Married	69 (21.5)	252 (78.5)	0.98 (0.40, 2.36)
Single	13 (21.7)	47 (78.3)	0.41 (0.09, 1.77)
Separated	3 (10.3	26 (89.7)	0.99 (0.35, 2.79)
Widowed	7 (21.9)	25 (78.1)	1
Religion			
Muslim	6 (28.6)	15 (71.4)	1
Orthodox	69 (20.7)	265 (79.3)	0.65 (0.24, 1.74)
Protestant	31 (22.0)	110 (78.0)	0.70 (0.25, 1.97)
Level of educational			
No education	29 (25.0)	87 (75.0)	1.03 (0.48, 2.18)
Primary	30 (17.8)	139 (82.2)	0.66 (0.32, 1.39)
Secondary	34 (21.5)	124 (78.5)	0.84 (0.40, 1.75)
Tertiary	13 (24.5)	40 (75.5)	1
Occupation			
Farmer	5 (20.8)	19 (79.2)	1
Government employ	21 (29.2)	51 (70.8)	1.56 (0.52, 4.74)
Housewife	30 (19.0)	128 (81.0)	0.89 (0.31, 2.57)
Merchant	8 (18.2)	36 (81.8)	0.84 (0.24, 2.94)
Private gainful work	15 (22.4)	52 (77.6)	0.98 (0.34, 2.88)
Others (unspecified Job)	27 (20.6)	104 (79.4)	1.09 (0.35, 3.43)
Addiction			
Addicted	15 (38.5)	24 (61.5)	2.51 (1.27, 4.98)
Not addicted	91 (19.9)	366 (80.1)	1
Family size			
≤2	19 (15.0)	108 (85.0)	1
3 - 4	55 (24.9)	166 (75.1)	1.88 (1.06, 3.35)
≥5	32 (21.6)	116 (78.4)	1.57 (0.84, 2.93)
Cigarette smoking status			
Yes	20 (46.5)	23 (53.3)	3.71 (1.95, 7.06)
No	86 (19.0)	367 (81.0)	1
Disclosure status			
Disclosed	106 (21.5)	386 (78.5)	1
Not disclosed	0 (0.0)	4 (100)	2.51 (1.27 - 4.98)

stage and hemoglobin level were important risk factors for incidence of TB among HIV infected patients.

Thus, an individual who live in the family size of 3 - 4 was two times **(AOR: 2.26, 95% CI (1.14 - 4.50))** at risk of developing Tuberculosis among HIV than an individual who live in the family of less than or equal to two.

WHO clinical staging is Predictor for incidence of Tuberculosis among HIV patients; accordingly HIV patients with clinical stage III 20 times **(AOR: 20.26, 95% CI (7.09 - 57.6))** and stage IV 22 times **(AOR: 22.9, 95% CI (6.91 - 76.4))** were more likely to develop tuberculosis than an individual who were enrolled to ART clinic on the first WHO clinical stage.

Other factor that affect TB incidence among PLHIV was level of hemoglobin. According to this study an individual with hemoglobin level of less than 10 mg/dl was 2.5 times (**(AOR: 2.56, 95% CI (1.22 - 5.33)**) highly acquire TB than an individual with hemoglobin level of greater than ten (see **Table 5**)

Other socio demographic and clinical characteristics like; Age in group (≥45), addiction (Addicted), sex of respondent, CD4 count, ART intervention(HAART), type of initial regimen and history of past TB treatment

Table 5. Predictors of incidence of tuberculosis among PLHIV patients in Arba Minch General Hospital, 2015.

Variables	Incidence of TBC		COR (95% CI)	AOR (95% CI)	P-Value
	Yes	**No**			
Age					
15 - 24	8 (12.1)	58 (87.9)	1		
25 - 34	46 (19.6)	189 (80.4)	1.76 (0.78, 3.95)	-	
35 - 44	33 (24.1)	104 (75.9)	2.30 (0.99, 5.31)		
≥45	19 (32.8)	39 (67.2)	3.53 (1.41, 8.87		
Disclosure status					
Disclosed	106 (21.5)	386 (78.5)	2.51 (1.27-4.98)	-	
Not disclosed	0 (0.0)	4 (100)	1		
Family size					
≤2	19 (15.0)	108 (85.0)	1	1	
3 - 4	55 (24.9)	166 (75.1)	1.88 (1.06, 3.35)	2.26 (1.14 - 4.50)	0.02
≥5	32 (21.6)	116 (78.4)	1.57 (0.84, 2.93)	1.76 (0.83 - 3.69)	0.14
Cigarette smoking					
Yes	20 (46.5)	23 (53.6)	3.71 (1.95, 7.06)	2.82 (1.27 - 6.27)	0.011
No	86 (19.0)	367 (81.0)	1	1	
ART intervention					
Pre-ART	16 (11.7)	121 (88.3)	1	-	
HAART	90 (25.1)	269 (74.9)	2.53 (1.43, 4.49)		
Type of initial regimen					
1a	19 (11.7)	121 (88.3)	1.32 (0.68, 2.55)		
1b	19 (29.7)	45 (70.3)	2.82 (1.36, 5.85)	-	
1c	5 (8.3)	21 (52.5)	0.28 (0.11, 0.76)		
1d	13 (23.6)	55 (91.7)	0.96 (0.46, 2.00)		
1e + 1f	34 (24.3)	42 (76.4)	1		
Past TB treatment history					
Yes	22 (32.4)	46 (67.6)	1.96 (1.12, 3.43)	-	
No	84 (19.6)	344 (80.4)	1		
WHO clinical stage					
I	7 (6.1)	108 (93.9)	1	1	
II	6 (3.5)	164 (96.5)	0.56 (0.18, 1.72)	0.33 (0.06 - 1.86)	0.21
III	76 (43.9)	97 (56.1)	12.0 (5.31, 27.5)	20.26 (7.09 - 57.6)	<0.001
IV	17 (44.7)	21 (55.3)	12.5 (4.61, 33.8)	22.9 (6.91 - 76.4)	<0.001
CD4 count					
<50	20 (57.1)	15 (42.5)	13.4 (6.10, 29.4)		
50 - 100	23 (39.7)	35 (60.3)	6.59 (3.38, 12.8)		
101 - 200	38 (29.9)	89 (70.1)	4.28 (2.44, 7.50)		
200	25 (9.1)	251 (90.9)	1		
Hemoglobin					
<10			1	1	
≥10	24 (48) 82 (18.4)	26 (52) 364 (81.6)	3.46 (1.30, 9.18)	2.56 (1.22 - 5.33)	0.012

Note: significant ≤ 0.05.

(treated) were significant predictors of tuberculosis among HIV infected patients in bivariable analysis, but the association was diluted in multivariable analysis.

4. Discussion

Since the introduction of HIV infection in the world, TB is one of common opportunistic infection and Persons co-infected with TB and HIV were 21 - 34 times more likely to develop active TB disease than persons without HIV [20].

In this study, cumulative incidence and overall incidence rate of TB were 21.4% and 5.36 per 100 PY respectively.

This study used cumulative incidence of TB as outcome variable. Thus, cumulative incidence of Tuberculosis (21.4%) reported in this study was lower than study done in former capital of Tanzania, Dares Salaam (27.1%) and study done in North west Ethiopia (Debre Markos hospital) (44%) [21]. But, the finding was higher than studies done in Spain and Brazil which were 7.7% [22], and 4.62% [23] respectively. Higher incidence rate could be explained by the fact that unlike these two countries, Ethiopia is one of the high TB burden countries in the world [24] besides advanced economic development compared to Ethiopia might improve HIV chronic care and reduce occurrence of TB. Lower cumulative incidence might due to improved TB/HIV chronic care and introduction of new regimen which effectively prevent occurrence of TB among HIV. Overall cumulative density reported in this study was lower than studies done in many other Sub Sahara African countries including, Ethiopia with reported incidence rate ranging from 5.4 to 11 per 100 PY [25]-[28]. Lower incidence rate could be explained by improved TB/HIV Care and new introduction of regimen which effectively prevent occurrence of TB among HIV.

In multivariable analysis; Family size, History of Cigarettes smoking, WHO Baseline clinical stage and hemoglobin level were important predictors of incidence of Tuberculosis among HIV infected patients.

This study could establish association between TB and number of people in the household. Thus, an individual who live in the family size of 3 - 4 was two times at risk of developing Tuberculosis than an individual who live in family with <2 children. It is consistent with Studies, which have shown that risk of TB was associated with the number of people living together in the household (overcrowding) [29]-[31], but inconsistent with study done in Addis Ababa [32]. This might be related to high proportions of married persons in the study population resulted in high number of family size in the house hold which might resulted overcrowding which exposed HIV infected patients to Tuberculosis.

Others predictors associated with incidence of tuberculosis was history of cigarette smoking, thus cigarette smoker were 3 times at higher risk of developing TB than non-smokers. The finding was consistent with study done in Taiwan [33] and not consistent with study done in northwest Ethiopia and Burkina that cigarette smoking had no effect on occurrence of TB among HIV infected patients [13] [31]. This might due to person who smoke cigarette was exposed for low immunity and this would increase the risk of developing Tuberculosis among HIV infected patients. Furthermore cigarette smoking was associated with other substance abuse which can increase the risk of unprotected sexual intercourse and compromisation of immunity, resulting in occurrence of TB.

Baseline WHO clinical staging was strong predictor for Incidence of Tuberculosis; accordingly HIV patients with clinical stage III and IV were 20 and 22 times more likely develop tuberculosis than an individual who was started follow up on the first WHO clinical stage. The finding was supported by different study done in Ethiopia [12] [13] [32] [34], the similarity might be due to starting ART in advanced stage will reduce immunity and expose an individual for TB. It also suggests that HIV patients who had WHO stage III or IV might be immune-compromised and predisposed to TB.

In addition, patients having a hemoglobin level of <10 mg/dl have 2.5 times higher risk of developing TB than those patients having hemoglobin level 10.0 mg/dl, the finding was similar to other study findings in south west Ethiopia [34] and case control study done in Addis Ababa [32]. This shows that patients having higher hemoglobin level were less likely to develop TB than those with low level of hemoglobin. 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 is also consistent with the previous findings that predict the occurrence of TB which implied that advance disease condition in HIV patients may predict occurrence of Tuberculosis after ART initia-

tion.

Other factors like; Age in group, addiction, sex of respondent, CD4 count, ART intervention, type of initial regimen and past history of TB treatment were significant predictors of incidence of tuberculosis among HIV infected patients in bivariable analysis, but the effect of this socio demographic and clinical characteristics were diluted in multivariable analysis.

Analysis of the past history of TB after adjustment, that it was a TB risk factor among PLWHAs, which is in agreement with a number of previous studies [15] [29] [34], But this was not the case in the study done in Arba Minch Hospital (our study), which reported that the past history of TB was not independent predictor of incidence of TB.

Many studies have used the patients' CD4 cell counts to assess association between CD4 Count and TB incidence and found that a lower CD4 cell count was associated with a higher risk of TB infection [13] [31] [35]. These studies are not consistent with our findings where the median CD4 cell count was not significant predictors of TB among HIV infected patients, though it had significant effect on occurrence of Tuberculosis in bivariable analysis.

The main limitation of our study was the retrospective nature of the cohort. The study individuals whose charts were lost not included in the study, which could undermine the result if the charts excluded were related to incidence of TB.

6. Conclusion and Recommendation

Cumulative and overall incidence rate of tuberculosis were found to be 21.4% and 5.36 per 100 PY respectively, which one was the highest. Family size, history of cigarettes smoking, heamoglobin level and WHO baseline clinical stage were important predictors of incidence of tuberculosis among HIV infected patients.

Finding that smoking is important predictors for TB in Ethiopia has obvious TB control implication which requires high attention focused on fighting against cigarette smoking in HIV infected populations.

The health institutions particularly work on lifestyle modification specifically on halting cigarette smoking habit through counseling. Early initiation of HAART as current guideline should get emphasis and behavioral education that discourages addiction is important to reduce the risk of TB infection. Furthermore, concomitant infections and risk factors for anemia among HIV patients should get managed and prevented.

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Competing Interest

The authors declare that there is no competing interest

Authors' Contributions

[1]MD was the primary researcher, conceived the study, designed, participated in data collection and quality assurances, conducted data analysis, drafted and finalized the manuscript for publication. **[2]AT** was assisted in data collection and analysis and reviewed the initial and final drafts of the manuscript

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Abbreviations and Acronyms

AGH: Arba Minch General Hospital; AIDS: Acquired Immuno Deficiency Syndrome; ART: Active Antiretroviral Therapy; AZT: Zidovudine; EFV: Efavirenz; HAART: Highly Active Antiretroviral Therapy; IRIS: Immune Reconstitution Inflammatory Syndrome; NVP: Nevirapine; OIs: Opportunistic Infections; PY: Person Years; SPSS: Statistical Package for Social Science; TB: Tuberculosis; 3TC: Lamuvudine; WHO: World Health Organization.