

Tuberculosis-HIV Co-infection Rate among Smear Positive Pulmonary Tuberculosis Patients and Associated Risk Factors in Southern Ethiopia

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Abstract

The objective of this study was to estimate HIV infection and associated risk factors among smear positive pulmonary TB patients in Southern Ethiopia. A cross-sectional study design was used to recruit 221 consecutive smear positive pulmonary TB patients visiting three hospitals in Gamo Goffa Zone from March, 2013 to February, 2014. A structured questionnaire was used to collect data on socio demographic, behavioral and economic factors from study units. Chi-square, fisher's exact test and logistic regression were used to assess the association between the above factors and HIV infection among smear positive pulmonary TB. The rate of HIV-TB co-infection among sputum smear-positive pulmonary TB patients in southern Ethiopia was 6.8% with 95% confidence interval of 3.3 to 10.3%. Drinking alcohol was significantly associated with increased risk of HIV infection among smear positive pulmonary TB patients in univariable logistic regression but that association was not maintained after controlling for potential confounding variables. Other factors significantly associated with HIV infection among the study population were previous anti-TB treatment, being resident in urban area and participants who had monthly income of less than or equal to 1000 Ethiopian birr as compared to those who had no regular monthly income. The rate of TB-HIV infection among smear positive pulmonary TB patients in Southern Ethiopia was low. However, the government or other partner organizations should work on decreasing the burden of co-infection through designing strategy on preventing HIV transmission in the urban area; increase the monthly income of citizens while enhancing TB-HIV collaborative activity to prevent reactivation of TB.

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INTRODUCTION

Tuberculosis (TB) and HIV are the top leading causes of death among infectious diseases worldwide. TB, one of the 1st opportunistic diseases amongst person infected with HIV, is a chronic disease transmitted from an infectious person to the other susceptible individuals through air droplets. An infectious patient can infect 10-15 susceptible individuals with *Mycobacterium tuberculosis* (MTB) per annum. One-3rd of the world population was infected by MTB but only few of them progress to overt disease (Seth, 2011 and WHO, 2013). HIV infection is the most powerful risk factor for the progression of latent MTB infection to TB disease, reactivation and reinfection by MTB (Erhabor *et al.*, 2011, Getahun *et al.*, 2010 and Wondimeneh *et al.*, 2012). An HIV positive patient infected with MTB has 50-60% life time risk, equivalent to 20 to 30 times increased risk, of progressing to active TB as compared to HIV negative person who has 10% life time risk. TB significantly enhances the replication of HIV while suppressing immunity in HIV patients as compared to HIV patients without active TB (Agbaji *et al.*, 2013,

Carvalho *et al.*, 2008, Getahun *et al.*, 2010 and Seth, 2011).

TB-HIV co-infection remains the major global health problem with about 13% (1.1 million) of estimated incident TB cases were infected with HIV. Seventy five percent of 1.1 million HIV infected TB patients were living in the African region in 2012 (Gao and Fu, 2013, WHO, 2013). Unfortunately, TB was in raise in sub-Saharan Africa (SSA) because of an increased epidemic of HIV infection (WHO, 2010). The highest co-infection rate ever seen among TB patients was observed in the SSA. Moreover, there is a time in which TB and HIV were viewed as different sides of the same coin. For example, the rate of TB-HIV co-infection was 95% (270/284) among TB patients admitted to inpatient ward of Helen Joseph Referral Hospital in Johannesburg town in South Africa. In addition, HIV infection has adverse effect on quality of life in TB patients (Gao and Fu, 2013 and John *et al.*, 2007).

HIV infection lowers the quality of all domains of life in TB patients: physical, Psychological and environmental domains (Deribew *et al.*, 2009). Moreover, it makes the diagnosis and treatment of TB more difficult. For example, the rate of smear or culture negative pulmonary TB is more common among HIV infected patients. In addition, HIV infection increases (up to six folds) mortality of TB because of advanced immunosuppression as a result of their synergistic effect on immunity (Kamenju and Aboud, 2011, Macpherson *et al.*, 2011 and Mugusi *et al.*, 2009). Furthermore, case fatality rate of TB patients co-infected with HIV is 29.3% while it is 3.6% among TB patient not infected by the virus (Liberato *et al.*, 2004 and Mugusi *et al.*, 2009).

Ethiopia is a high TB, high multi-drug resistant TB (MDR-TB) and high HIV burden country. It is the 8th among 22 TB high burden countries and 15th among 27 MDR-TB high burden countries. There were an estimated 247 incident cases per 100000 population in Ethiopia with mortality rate of 18 per 100000 populations in 2012. Of 2080 estimated MDR-TB patients in the same year only 284(13.6%) were laboratory confirmed in Ethiopia (WHO, 2013). The trend of HIV infection is decreasing in Ethiopia though female populations were more affected than the male counter parts. An estimated prevalence of HIV infection in 2011 was about 1.5 and decreased to 1.3 in 2012. The prevalence of HIV infection among females is 1.8% which is two folds larger than male population in Ethiopia (<http://www.etharc.org/resources/healthstat/hiv-aids-estimates-and-projections-in-ethiopia-2011-2016>).

Ethiopia is one of 41 countries with the high prevalence of TB-HIV co-infection. In 2012, about 65% notified TB patients new their HIV status. Of 96245 TB patients tested for HIV infection, 9819(10%) were positive. Nevertheless, rate of co-infection among TB patients varies according to geographical location and people (Alemie and Gebreselassie 2014, Datiko *et al.*, 2008, Tadesse and Tadesse, 2013).

One of the five priority areas to accelerate progress towards 2015 target is accelerating response to TB-HIV co-infection. The top priority is to increase the coverage of Anti-retroviral treatment (ART) for HIV positive TB patients towards 100% target. Expanded coverage of TB preventive isoniazid therapy for 50% of new HIV patients enrolled in HIV care (WHO, 2013). A collaborative activity of TB-HIV management was started in Ethiopia but the effectiveness of the program has to be monitored periodically for better management and resource allocations such as anti-TB treatments, diagnostic equipments and ART. Therefore in the present study we have conducted a cross-sectional study involving all new smear-positive pulmonary TB patients age greater than or equal to 18 years attending three hospitals in Gamo Goffa Zone in Southern Ethiopia from March 2013 to February, 2014.

MATERIALS AND METHODS

Study Area

This study was undertaken in three hospitals found in Southern Ethiopia namely; Arba Minch, Sawula and chenchha hospitals. These hospitals are located in Gamo Goffa Zone. Gamo Goffa Zone is constituted of 15 districts and two town administrations. Projection of 2007 population size of Gamo Goffa Zone for about five years with growth rate of 2.7% indicates that a total of 1,820,105

population live in the study area in 2012. About 50.2 % of the total population was women. However, patients from surrounding Zones (second largest administrative unit next to regional state in Ethiopia) and special districts get health care service from these hospitals.

Study Design and Selection of Study Participants

A cross-sectional study design was used to recruit 221 consecutive smear-positive pulmonary TB patients visiting three hospitals from March 2013 to February 2014. Only adults aged ≥ 18 years and consented to participate, mentally fit and whose HIV status was known were involved as study units in the present research. Accordingly, 131 from Arba Minch, 47 from Sawula and 43 from chenchha hospital were used to answer the research question under investigation. One of smear-positive pulmonary TB patients whose HIV status was not recorded was excluded from analysis to assess factors associated with HIV infection.

Method of Data Collection

Sputum-smear status of participant was determined by acid fast staining (AFS) technique. A patient was defined as smear-positive pulmonary TB when sputum smear is positive in two or more of the three sputum specimens in light microscopy in HIV negative patients, one in HIV positive patients or with suggestive chest X ray (CXR). A structured questionnaire was used to collect data on socio demographic, behavioral and economic factors. The questionnaire was prepared in English and translated into local languages and then back translated to English to check accuracy. It was used to interview study units by health care providers by the appropriate colloquial language in the three hospitals. Information on the HIV status of the participant was obtained from the patient registration book. Only the health worker in TB clinic was used to interview and retrieving HIV status of the participant for confidentiality purpose.

Statistical Analysis

All collected data were checked before computerizing using EpiData version 3.1 software. After exporting the data into STATA version 11, results from frequencies and cross-tabulations were used to monitor transcription errors. Chi square and fisher's exact test were used to identify factors associated with HIV infection among smear positive pulmonary TB patients. Univariable logistic regression was used to quantify odds ratio before adjusting for potential confounding variables. Variables significantly associated in Pearson's chi square and fisher's exact test, used appropriately, were included in multivariable logistic regression to adjust potential confounding variables. Odds ratio (OR) and corresponding 95% confidence intervals (CI) were used to quantify the degrees of association between target potential risk factor and TB-HIV co-infection. Results with p-value less than 0.05 were considered as being statistically significant.

Ethical Considerations

The study protocol was approved by research ethics review committee of college of medicine and health science in Arba Minch University before commencement of the study. Permission to conduct the research was obtained from health department of Gamo Goffa zone, each hospital authorities after giving them recommendation letter written by Arba Minch University. Finally written informed consent was obtained from the

study participant before retrieving HIV status and interviewing.

RESULTS

During a one year study period 221 consecutive smear positive pulmonary TB patients were recruited from three hospitals in Gamo Goffa zone. Just more than 59% of the patients were recruited from Arba Minch hospital, located in the administrative center of the zone. About 87.8% of pulmonary TB patients were from districts of Gamo Goffa zone while others were from special districts, South Omo and Segen Hizboch Zone in South Nation's Nationalities and Peoples regional states of Ethiopia. One hundred thirteen of the study participants were male, 64.7% were residents in the rural area, 51.1% were married, 36.2% were in primary education level. Age of study participants was positively skewed as indicated in table 1 with the median age of 28 and standard deviation of 12.9 years.

The prevalence of TB-HIV co-infection among smear-positive pulmonary TB patients visiting three hospitals in Gamo Goffa zone was 6.8 % (15/220) with 95% CI of 3.3 to 10.3%. None of the socio demographic factors were significantly associated with being infected with HIV except place of residence. Smear positive pulmonary TB patients living in urban area were 4 times at increased risk to be infected by HIV as compared to smear positive pulmonary TB patients in the rural area in Southern Ethiopia. About 56% of smear positive pulmonary TB patients had no regular income per month. Nevertheless,

they were at decreased risk of being infected by HIV as compared to those who had monthly income of Ethiopian birr less than or equal to 1000.

About two third of the study participants were underweighted while only one person was over weighted. However being under weighted was not associated with TB-HIV co-infection among smear positive pulmonary TB.

Just below 10% of smear positive pulmonary TB patients had ever smoked cigarette while 57.14% of them continuo to smoke cigarette currently. Neither ever smoked cigarette nor currently smoking cigarette was associated with TB-HIV co-infection in smear positive pulmonary TB patients. One hundred forty two of the study participants enrolled in the present study had never drink alcohol. However, alcohol consumers were about 3 folds at increased risk to be co-infected with TB-HIV compared to those smear positive pulmonary TB patients who had never drank alcohol ($P=0.048$) in univariable analysis as indicated in table3. However, this association did not remain statistically significant after adjusting the effect of confounding variables in multivariable logistic regression.

As indicated in table 3, factors significantly increasing HIV infection in smear positive pulmonary TB in southern Ethiopia were being resident in urban area, monthly income of birr less than or equal to1000 Ethiopian birr as compared to those who had no regular monthly income and previous history of anti-TB treatment.

Table 1: Base line characteristics of smear-positive pulmonary TB patients in south Ethiopia, 2013-2014

Variable	Category of Variable	Number	Percentage	≠(%) HIV Positive
Sex	Male	141	60.1	2(2.3)
	Female	79	35.9	13(9.29)
Age	≤24	76	34.6	2(2.6)
	25-34	77	35.0	6(7.89)
	35-44	35	15.9	3(8.57)
	≥45	32	14.5	4(12.50)
Marital status	Single	95	43.0	7(7.45)
	Married	113	51.1	7(6.19)
	Others	13	5.9	1(7.69)
Place of residence	Rural	143	64.7	5(3.5)
	Urban	78	35.3	10(12.99)
	Civil servant	15	6.82	2(13.33)
Occupational status	Farmer	82	37.27	5(6.10)
	Merchant	18	8.18	1(5.56)
	House wife	39	17.13	2(5.13)
	Student	49	22.27	1(2.04)
	Others	17	7.73	4(25.0)
Level of education	No formal education	70	31.67	3(4.29)
	Primary (grade 1-8)	80	36.20	5(6.25)
	≥ High school	71	32.13	7(10.00)
Ever smoke cigarette	Yes	21	9.5	2(10.00)
	No	200	90.5	13(6.50)
Ever drunk alcohol	Yes	79	35.75	9(11.54)
	No	142	64.25	6(4.23)
History of anti-TB treatment	Yes	15	6.79	5(33.33)
	No	206	93.21	10(4.88)
BMI	≤18.5	145	66.21	9(6.25)
	18.5-24.5	73	33.33	6(8.22)
	≥25	1	0.46	0(00.00)

Table 2: Characteristics of smear positive pulmonary TB patients and HIV infection in southern Ethiopia, 2013-2014

Variable	Category of Variable	#PTB Patients without HIV (%)	#TB Patients with HIV (%)	Pearson χ^2	P-value
Sex*	Male	127(90.71)	13(9.27)	3.61	0.091
	Female	77(97.47)	2(2.53)		
Age*	≤24	74(97.37)	2(2.63)	4.01	0.183
	25-34	70(92.11)	6(7.89)		
	35-44	32(91.43)	3(8.57)		
	≥45	28(87.50)	4(12.50)		
Marital status*	Single	87(92.55)	7(7.45)	0.143	0.834
	Married	106(93.81)	7(6.19)		
	Others	12(92.13)	1(7.69)		
Place of residence	Rural	138(96.5)	5(3.50)	7.10	0.008
	Urban	67(87.01)	10(12.99)		
Occupational status*	Civil servant	13(86.67)	2(13.33)	11.33	0.059
	Farmer	77(93.90)	5(6.10)		
	Merchant	17(94.44)	1(5.56)		
	House wife	37(94.87)	2(5.13)		
	student	48(97.96)	1(2.04)		
	Others	12(75.00)	4(25.00)		
Monthly income*	No regular	121(97.58)	3(2.41)	9.73	0.012
	≤1000ETB	32(84.21)	6(15.79)		
	>1000 ETB	52(89.66)	6(10.34)		
Level of education	No formal education	67(95.71)	3(4.29)	1.86	0.394
	(grade 1-8)	75(93.75)	5(6.25)		
	≥ High school	63(90.00)	7(10.00)		
Ever smoke cigarette*	Yes	18(90.00)	2(10.00)	0.35	0.633
	No	187(93.50)	13(6.50)		
Ever drunk alcohol	Yes	69(88.46)	9(11.54)	4.24	0.04
	No	136(95.77)	6(4.23)		
History of anti-TB treatment	Yes	10(66.67)	5(33.33)	17.81	0.000
	No	195(95.12)	10(4.88)		
BMI	≤18.5	135(93.75)	9(6.25)	0.26	0.608
	>18.5	68(91.89)	6(8.11)		

*P value calculated from fisher exact test

Table 3: multivariable logistic regressions of smear positive PTB patients characteristics and HIV infection in southern Ethiopia, 2013-2014

Variable	#PTB Patients without HIV (%)	#TB Patients with HIV (%)	COR(95%CI)	P-value	AOR(95% CI)	P-value
Residence place						
Rural	138(96.50)	5(3.50)	1	0.013	1	0.05
Urban	67(87.01)	10(12.99)	4.12(1.35-12.53)		3.7(1.04-14.19)	
Monthly income						
No regular	121(97.58)	3(2.41)	1	0.016	1	0.048
≤1000 ETB	32(84.21)	6(15.79)	5.4(1.37-21.00)		4.2(1.01-17.76)	
>1000 ETB	52(89.66)	6(10.34)	6.7 (1.41-31.98)		2.1(0.35-12.42)	
Ever drink alcohol						
Yes	69(88.46)	9(11.54)	2.96(1.01-8.64)	0.048	1.51(0.45-5.10)	0.50
No	136(95.55)	6(4.23)	1			
Previously anti-TB treated						
Yes	10(66.67)	5(33.33)	9.75(2.80-33.95)	0.000	7.03(1.79-27.60)	0.004
No	195(95.12)	10(4.88)	1			

DISCUSSION

The rate of TB-HIV co-infection among smear-positive pulmonary TB in southern Ethiopia was low as indicated in this study. However, HIV infection among this

subpopulation was significantly increased among previous anti-TB treated patients, patients living in urban area and TB patients who had monthly income of less than or equal to 1000 Ethiopian birr as compared to those who

had no regular monthly income. Even though the association was not statistically significant after taking care of confounding variables, drinking alcohol was increasing the chance of acquiring HIV.

Prevalence of HIV infection among smear-positive pulmonary TB was 6.8 % (15/220). It was in agreement with the rate estimated by Datiko and co investigators in rural area of Gamo Goffa zone and the national estimate of TB-HIV co-infection in Ethiopia, Angola (Datiko *et al.*, 2008 and WHO, 2013) and also in south central China (Xu *et al.*, 2014), Gambia (Hill *et al.*, 2006), and in some districts of India (Seth, 2011). However, it was in contrast to most studies carried out in Ethiopia (Alemie and Gebreselassie, 2014 and Tadesse and Tadesse, 2013), South Africa [Louwajie and Ayo-Yosuf, 2013 and John *et al.*, 2007], Tanzania (Macpherson *et al.*, 2011), Brazil (Carvalho *et al.*, 2008) Nigeria (Erhabor *et al.*, 2010, Olugbue and Onuoha, 2012 and Pennap *et al.*, 2010), in eastern and western European countries and European economic areas (Pinpin *et al.*, 2011) and Kenya (Nymagoba *et al.*, 2012). The possible reason for estimated lower rate of TB-HIV co-infection might be associated with involving only smear-positive TB patients in the present study. Studies have indicated that the rate of HIV infection was higher among smear negative pulmonary TB patients than among smear positive counterparts. The second important explanation for the difference will be difference in the prevalence of HIV infection in the background population from where study subjects were recruited (Gao and Fu, 2013 and Datiko *et al.*, 2008). Even though the rate of co-infection was lower in the study area, some factors potentially influencing HIV infection among smear-positive pulmonary patients were identified by this study.

One of the factors favoring increased risk of HIV infection was sex. In the present study just above 90% of HIV infected smear positive pulmonary TB patients were male. Being male gender is about 4-folds increased risk to acquire HIV infection but it is not statistically significant. However, in some of the studies reviewed, the co-infection rate was more common among male TB patients (Liberato and Campelo, 2004) while in others it was higher among female category of the same population (Erhabor *et al.*, 2010, Olugbue and Onuoha, 2012 and Pennap *et al.*, 2010). This calls for further research to explore factors increasing the rate of HIV transmission between each gender group.

The second important factor increasing the rate of TB-HIV co-infection was being resident in urban area in the southern Ethiopia. The finding of the present study was in agreement with previous study in south Ethiopia (Datiko *et al.*, 2008); in private clinics in Amhara regional state in Ethiopia (Tadesse and Tadesse, 2013). This corroborates the claim that prevalence of HIV infection was higher among the urban population than in the rural counter parts in Ethiopia.

The other important factors associated with increased risk of TB-HIV co-infection among TB patients were drinking alcohol and previous history of anti-TB treatment. In the present study HIV infection among smear positive pulmonary TB was higher among those drinking alcohol as compared to those who had not ever drunk alcohol only in univariable logistic regression. Drunken persons will not think about HIV transmission and would have a

sex without condom. This might be the main reason for higher HIV infection among alcohol drinking patients. It was in agreement with one study carried out in south central china (Xu *et al.*, 2014). TB patients previously diseased by the same health problem were more likely to be infected with HIV in the present study. This corroborates that HIV infection significantly increases the chance of reactivation in previously diseased people.

Finally, this study was done with certain limitations. One of the limitations of the current study emanates from the study design being case control as this has poor ability to establish causal link between HIV infection among the study population and factors which are significantly associated with co-infection. Another limitation of this study was the risk of recall bias. The response of study participants about risk factors might not be always correct, (i.e. there is possibility of over or under reporting). Thus, the findings of the current study should be interpreted in light of the above limitations.

CONCLUSIONS

In conclusion, the result of this study reveals that the rate of TB-HIV co-infection among smear positive pulmonary TB patients was low. Nevertheless, people living in the urban area were at increased risk to acquire HIV infection. Previously TB diseased individuals were more likely to be infected with HIV calling for more effective TB-HIV collaborative activity to enhance the progress towards the 2015 millennium development goal. TB patients who earn monthly income of less than or equal to 1000 Ethiopian birr were significantly at increase risk to be infected with HIV.

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