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Predictors of Smear-Positive Pulmonary Tuberculosis in Southern Ethiopia: Unmatched Case Control Study

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Abstract

Background and objectives: Ethiopia is among TB high burden countries and people in economically productive age group are more affected. Therefore, the purpose of the present study was to identify factors associated with Smear-positive pulmonary tuberculosis in Southern Ethiopia.

Methods: unmatched case control study design was used to enroll 221 smear-positive pulmonary TB patients and 442 hospital based controls from three governmental hospitals in the Gamo Goffa Zone from February, 2013 to May, 2014. A structured questionnaire was used to collect information on risk factors. Chi-square or Fishers exact test and Logistic regression were used to assess the association between predictor variables and smear-positive pulmonary TB. P-value and 95% confidence interval were used to test level of significance.

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Results: Smear-positive pulmonary TB in Southern Ethiopia was associated with HIV infection, previous episode of TB, low body-mass index, drinking unpasteurized milk and sharing a bed room with more than three individuals. Even though not significant after controlling the effect of confounders; being male gender, illiteracy, low monthly income, being farmer and bad housing condition were associated with active pulmonary TB in univariate analysis.

Interpretation and Conclusions: increased prevalence of infectious pulmonary TB was multi factorial in southern Ethiopia. Health education on pasteurizing milk before consumption and increasing awareness of TB transmission at house hold level and ceasing smoking should be given to halt transmission of TB or progression of latent TB. An integrated approach of TB-HIV management should be strengthened to prevent TB among HIV patients and factors associated with recurrent TB should be studied.

Keywords: Predictors; pulmonary Tuberculosis; Southern Ethiopia.

1. Introduction

Tuberculosis (TB) is chronic disease of all age groups caused by bacteria of the genus Mycobacterium which primarily affects the lungs [1-3]. One-third of the world population is infected by *Mycobacterium tuberculosis* [4]. Its primary infection may actively develop in to clinical TB or remain latent in the individual for months or years depending on the host factors, environmental factors and on the doze of the infecting bacterium [5-7]. Globally there are about 12 million cases of TB in 2010 [8]. TB disproportionately affects people in the resource poor countries. Ninety five percent of TB cases and 98% deaths due to TB occur in developing countries [1,9].

According to the world health organization report 2011, the global epidemic of TB is on the threshold of decline except sub-Saharan Africa (SSA) [8, 9]. This part of Africa is off track to achieve the millennium development goal (MDG) which is proposed to save the life of 14 million individuals from 2006-2015. The major identified factor threatening the control of TB in SSA is increased prevalence of HIV infection [10].

Ethiopia is the 8th among the world 22 TB high burden countries with an incidence of 220 cases per 100,000 population among HIV negative individuals and mortality rate of 35.0 per 100,000 populations [11]. TB is the leading cause of morbidity, 2nd cause of death next to malaria and the 3rd cause of hospital admission [12]. Most deaths associated with TB in Ethiopia occur in adult's most productive age group (15-34) which leads to premature death and has effect on the country's economic development [13, 14].

TB is completely curable disease though it requires adherence to a minimum of six months with multiple drugs. Identification of factors increasing transmission and/or activation of latent TB is important to prevent TB. The most important factor for TB is HIV infection while other factors increasing TB differ according to population and geographical location. Therefore the present study is aimed to identify factors associated with smear-positive pulmonary TB in southern Ethiopia. Unmatched case control study design was commenced to enroll 221 smear-positive pulmonary TB patients and its two-folds of controls from outpatient departments of the three hospitals in Gamo Goffa Zone from February, 2013 to May, 2014.

2. Material and methods

2.1. Study design and procedure of data collection

Unmatched case control study design was used to recruit 221 smear-positive pulmonary TB patients age greater than or equal to 18 years and its two fold controls from outpatient department of three government hospitals in Gamo Goffa Zone. Three sputum specimens (spot-morning-spot) were collected from outpatients suspected for pulmonary TB. The collected specimen was subjected to acid fast staining following the national guide line of TB diagnosis. Smear positivity status of pulmonary TB of these patients was determined according to the world health organization (WHO) definition of smear-positive pulmonary TB [11]. Smear-positive pulmonary TB patients whose HIV status was known were included as cases in the present study. Based on the provider initiated testing and counseling, all patients visiting health facilities in Ethiopia are tested for HIV infection. The 1st two patients who were not suspected for any form of TB and tested for HIV infection on the day when a TB suspect is confirmed to be smear-positive were included as controls from each hospital.

Structured questionnaire was used to collect data on socio demographic factors, economic factors, behavioral and morbidity related factors. HIV status of the TB patient was transcribed from their treatment registration book and for controls it was obtained from voluntary counseling and testing unit.

2.2. Statistical methods and ethical considerations

The data collected by questionnaire were scrutinized before computerizing. It was computerized using EpiDta version 3.1 and analyzed using STATA version 11 statistical software. Pearson's Chi square and Fishers exact test were used to assess the association between smear-positive pulmonary TB and independent factors. Univariate logistic regression was used to quantify odds ratio before adjusting for potential confounding variables. Those factors significantly associated with smear-positive pulmonary TB by using chi square or fisher's exact test were used in multivariate logistic regression to adjust the effect of potential confounding variables. Odds ratio (OR) and corresponding 95% confidence interval were used to quantify the association between smear-positive pulmonary TB and potential risk factors in univariate and multivariate logistic regression. In all cases p_values less than 0.05 were considered as statistically significant.

An informed written consent was obtained from all study participants before interviewing and document review. The study protocol is approved by research ethics review committee of college of medicine and health science, Arba Minch University, before commencement (Reference number of the approval letter: IRC/003/05).

3. Results

3.1. Socio demographic factors

A case control study was employed in three hospitals in Southern Ethiopia by recruiting 221 cases and its two-fold controls from February, 2013 to May, 2014 to assess predictors of smear-positive pulmonary TB. About 59.2% of the cases were from Arba Minch general hospital while the number of cases from Chencha and Sawula hospitals was 43 and 47 respectively. The major causes of hospitalization for controls were acute febrile illness followed by gastrointestinal problems, pneumonia and urinary tract infections and others.

About 376 study participants were male; half of the patients were from urban area. Just above two-third of the study participants were age below 34 years and about half were married and in the educational level of high school or above. The household size of the study participants was not normally distributed with the median of 4 individuals per household. The detail background characteristic of cases and controls in the study area was presented in Table1.

Table 1: Socio demographic characteristics of smear positive pulmonary TB and other non TB patients in Southern Ethiopia

Characteristics	Categories of characteristics	Number (%)	≠ (%) of cases
Place of residence	Rural	329 (49.70)	143 (43.47)
	Urban	333 (50.30)	78 (23.42)
Sex	Male	376 (56.88)	141 (37.5)
	Female	285 (43.12)	79(27.72)
Age in years	≤ 24	208 (31.52)	76 (36.54)
	25-34	237 (35.91)	77(32.49)
	35-44	120(18.18)	35 (29.17)
	≥45	95 (14.39)	32(33.68)
Marital status	Single	301(45.4)	95 (31.56)
	Married	316 (47.66)	113 (35.76)
	Others	46 (6.94)	13(28.26)
Level of education	No formal education	158 (23.83)	70(44.30)
	Primary (grade 1-8)	202(30.47)	80(39.60)
	≥high school	303(45.7)	71(23.43)
Occupational status	Civil servant	103 (15.56)	15 (14.58)
	Farmer	162 (24.47)	82 (50.62)
	Merchant	77 (11.63)	18 (23.38)
	Housewife	112 (19.92)	39 (34.82)
	Student	174 (26.28)	49 (28.16)
	Others	34 (5.14)	17 (50.00)
House hold size	≤ 5	472 (71.30)	156 (33.05)
	>5	190 (28.70)	65 (34.21)
Number of individuals sharing bed room	≤3	377 (56.95)	97 (25.73)
	>3	285 (43.05)	124 (43.51)

Among socio demographic factors, being resident in rural area (COR= 2.51; 95% CI=1.80-3.51), male gender (COR=1.56 ; 95% CI= 1.12-2.18), sharing a bed room with >3 individuals (COR= 2.22; 95%CI= 1.60-3.09) and being farmer or other occupations (except merchant) as compared to civil servants (COR=6.01 ; 95% CI=3.21-11.27 or COR=2.87 ; 95% CI=1.58-5.20 respectively) were significantly associated with smear positive PTB in univariate analysis. However, only sharing a bed room with more than 3 individuals remains to be statistically significant (AOR=1.59; 95%CI=1.06-2.41) after controlling the effect of confounding variables in multivariate logistic regression (Table 2 and 5).

Table 2: Association between socio demographic characteristics and smear positive pulmonary TB in Southern Ethiopia

Characteristics	Categories of characteristics	Number (%) control	≠ (%) of cases	Pearson χ^2	P-value
Place of residence	Rural	186 (56.53)	143 (43.47)	29.89	0.000
	Urban	255 (76.58)	78 (23.42)		
Sex	Male	235 (62.50)	141 (37.5)	6.98	0.008
	Female	206(72.28)	79(27.72)		
Age in years	≤ 24	132 (63.46)	76 (36.54)	1.98	0.577
	25-34	160 (67.51)	77(32.49)		
	35-44	85 (70.83)	35 (29.17)		
	≥45	63 (66.32)	32(33.68)		
Marital status	Single	206 (68.44)	95 (31.56)	1.79	0.408
	Married	203(64.24)	113 (35.76)		
	Others	33 (71.74)	13(28.26)		
Level of education	Illiterate	88 (55.70)	70(44.30)	25.50	0.000
	grade 1-8)	122 (60.40)	80(39.60)		
	≥high school	232 (76.57)	71(23.43)		
Occupational status	Civil servant	88 (85.44)	15 (14.58)	48.01	0.000
	Farmer	80 (49.38)	82 (50.62)		
	Merchant	59 (76.62)	18 (23.38)		
	Housewife	73 (65.18)	39 (34.82)		
	Student	125 (71.84)	49 (28.16)		
	Others	17 (50.00)	17 (50.00)		
House hold size	≤ 5	316 (66.95)	156 (33.05)	0.08	0.775
	>5	125 (65.79)	65 (34.21)		
Number of individuals sharing bed room	≤3	280 (74.27)	97 (25.73)	23.07	0.000
	>3	161 (56.49)	124 (43.51)		

3.2. Other factors

In addition to socio demographic factors other factors considered in the current study were economic, behavioral and other concurrent morbidities or previous episode of TB. Economic status indicators used were educational status, house ownership, housing condition and monthly income of the participant (Table 4).

Good housing condition expressed by ceiled roof (COR=0.47; 95%CI=0.37-0.66) and cemented floor (COR=0.45; 95%CI= 0.31-0.65) significantly reduced the risk of TB in univariate analysis but that association was not significant in multivariate analysis (table 4 and 5). Concerning, monthly income of the patients, it was skewed to the right with median of 200 Ethiopian birr. Individuals whose monthly income of greater than 200 Ethiopian birr per a month were less likely suffered from active PTB than those who earn less (COR=0.61; 95%CI=0.44-0.85)

Table 3: Behavioral, economic and morbidity related characteristics of smear positive pulmonary TB and other non TB patients in Southern Ethiopia

Characteristics	Categories of characteristics	Number (%)	≠ (%) of cases
Type of home where the patient is living	Owned	506 (76.44)	183 (36.17)
	Rented	156 (23.56)	38 (24.36)
Roof of the house	Not ceiled	344 (51.96)	142 (41.28)
	Ceiled	318 (48.04)	79 (24.84)
Floor of the house	Soil	423 (64.20)	170 (40.00)
	Cemented	222 (33.53)	51 (22.97)
	Others	15 (2.27)	0(0.00)
History of imprisonment	Imprisoned	25 (3.78)	8 (32.00)
	Not imprisoned	637 (96.22)	213 (33.44)
Ever smoke cigarette	Yes	41 (6.19)	21 (51.22)
	No	621 (93.81)	200 (32.21)
Current smoking cigarette	Yes	21 (51.22)	12 (57.14)
	No	20 (48.78)	9(45.00)
Ever drink alcohol	Yes	197 (29.76)	79 (40.10)
	No	465 (70.24)	142 (30.54)
Ever drink unpasteurized milk	Yes	336 (50.76)	135 (40.18)
	No	326 (49.24)	86 (26.38)
Diabetes mellitus status	Diabetic	4 (0.60)	0 (0.00)
	Not diabetic	658 (94.00)	221 (33.59)
Asthmatic	Yes	11 (1.66)	2 (18.18)
	No	651 (98.34)	219 (33.64)
HIV infected	Yes	17 (2.57)	15 (88.24)
	Not	644 (97.43)	205(31.83)
Previous anti-TB	Treated	19 (2.87)	15 (78.95)
	Not treated	643 (97.13)	206 (32.04)
Had contact with TB patient at home	Yes	20 (3.02)	5 (25.00)
	No	642 (96.98)	216 (33.64)
BMI	Undernourished	281 (42.58)	145 (51.60)
	Well nourished	379 (57.42)	74 (19.53)

Table 4: Association between smear positive pulmonary TB and behavioral, economic and co morbidity factors in Southern Ethiopia.

Characteristics	Categories of characteristics	≠ (%) controls	≠ (%) of cases	Pearson χ^2	P-value
Type of participant's home	Owned	323 (63.83)	183 (36.17)	7.47	0.006
	Rented	118 (75.64)	38 (24.36)		
Roof of the house	Not ceiled	202(58.72)	142 (41.28)	20.07	0.000
	Ceiled	239(75.16)	79 (24.84)		
Floor of the house	Soil	255 (60.00)	170 (40.00)	26.70	0.000
	Cemented	171(77.03)	51 (22.97)		
	Others	15 (100)	0(0.00)		
History of imprisonment	Imprisoned	17 (68.00)	8 (32.00)	0.022	0.881
	Not imprisoned	424 (66.56)	213 (33.44)		
Ever smoke cigarette	Yes	20 (48.78)	21 (51.22)	6.25	0.012
	No	421 (67.79)	200 (32.21)		
Current smoking cigarette	Yes	9 (42.86)	12 (57.14)	0.60	0.437
	No	11 (55.00)	9(45.00)		
Ever drink alcohol	Yes	118 (59.90)	79 (40.10)	5.69	0.017
	No	323 (69.46)	142 (30.54)		
Ever drink unpasteurized milk	Yes	201 (59.82)	135 (40.18)	14.16	0.000
	No	240 (73.62)	86 (26.38)		
HIV infected	Yes	2 (11.76)	15 (88.24)	23.73	0.000
	Not	439 (68.17)	205(31.83)		
Previous anti-TB	Treated	4 (21.05)	15 (78.95)	18.26	0.000
	Not treated	437 (67.96)	206 (32.04)		
Had contact with TB patient at home	Yes	15 (75.00)	5 (25.00)	0.65	0.419
	No	426 (66.36)	216 (33.64)		
BMI(kg/m^2)	<18.5	136 (48.40)	145 (51.60)	74.88	0.000
	≥18.5	305 (80.47	74 (19.53)		

The three behavioral factors assessed in the present study: smoking (COR= 2.21; 95%CI=1.17-4.17), drinking alcohol (COR= 1.52; 95%CI= 1.08-2.15) and drinking unpasteurized milk (COR=1.87; 95%CI= 1.35-2.60) were significantly increased the risk of smear-positive pulmonary TB than those did not exhibit such behavior in univariate analysis but alcohol addiction (AOR=1.58; 95%CI=0.95-2.61) in multivariate logistic regression (table 5).

With respect to co morbidities considered in this study, 17 (2.57%), 11(1.66%) and 19 (2.87%) of the patients were HIV infected, asthmatic and had previous episode of TB respectively. All these morbidities are significantly associated with smear-positive pulmonary TB except asthma both in the Univariate and multivariate logistic regressions. Body mass index (BMI) of the study participants was normally distributed with the mean (SD) of cases and controls were 20.38 kg/m^2 (3.29) and 17.61 kg/m^2 (2.55) respectively.

Table 5: Univariate and multivariate logistic regression of predictors of sputum smear-positive pulmonary TB in Southern Ethiopia

Characteristics	Categories of character	Crude OR	95%CI	Adjusted OR	95%CI
Place of residence	Rural	2.51	1.80-3.51	1.82	0.92-3.63
	Urban	1		1	
Sex	Male	1.56	1.12-2.18	1.42	0.90-2.24
	Female	1		1	
Level of education	Illiterate	1			
	grade 1-8)	0.82	0.54-1.23	1.19	0.67-2.12
	≥high school	0.38	0.25-0.58	0.83	0.39-1.76
Monthly income	≤ 200 birr	1		1	
	>200 birr	0.61	0.44-0.84	0.66	0.41-1.06
Occupational status	Civil servant	1		1	
	Farmer	6.01	3.21-11.27	1.84	0.73-4.65
	Merchant	1.79	0.83-3.83	0.77	0.29-2.07
	Others	2.87	1.58-5.20	1.13	0.56-2.51
Number of individuals sharing bed room	≤3	1		1	
	>3	2.22	1.60-3.09	1.59	1.06-2.41
Type of home where the patient is living	Owned	1.76	1.17-2.65	1.24	0.69-2.23
	rented	1		1	
Roof of the house	Not ceiled	1		1	
	Ceiled	0.47	0.34-0.66	0.60	0.30-1.19
Floor of the house	Soil	1		1	
	Cemented	0.45	0.31-0.65	0.86	0.45-1.63
	Others	Empty	Empty	Empty	
Ever smoke cigarette	Yes	2.21	1.17-4.17	2.46	1.01-6.02
	No	1		1	
Ever drink alcohol	Yes	1.52	1.08-2.15	1.58	0.95-2.61
	No	1		1	
Ever drink unpasteurized milk	Yes	1.87	1.35-2.60	2.05	1.34-3.14
	No	1		1	
HIV infected	Yes	16.06	3.64-70.88	38.09	4.07-356.49
	No	1		1	
Previous anti-TB	Treated	7.96	2.6-24.27	14.43	3.05-68.16
	Not treated	1		1	
BMI(kg/m^2)	<18.5	4.39	3.11-6.21	4.97	3.23-7.64
	≥18.5	1		1	

This difference in the mean BMI among these two categories of patients was statistically significant and it was also true after dichotomizing BMI in to undernourished and normal or over weighted (AOR= 4.97; 95CI= 3.23-7.64) (table 4 and 5).

4. Discussion

Our study has indicated factors significantly increasing the most infectious form of pulmonary TB in Southern Ethiopia by taking smear positive pulmonary TB patients and other non TB patients from outpatient departments. The most important factors favoring active PTB in Southern Ethiopia were HIV infection, smoking cigarette, sharing bed room with greater than two other individuals, drinking unpasteurized milk, previous history of anti-TB treatment and decreased body mass index. Though the association was not maintained after controlling the effect of confounding variables, place of residence, being male sex and drinking alcohol and housing condition were factors associated with +PTB in southern Ethiopia.

Drinking unpasteurized milk in the present study is significantly associated with smear positive pulmonary TB. This is an indication for the transmission of the bacteria causing tuberculosis from cows to human beings in the study area. This finding calls for a study which focuses on strain similarity of the isolates of *Mycobacterium* from human and animal origins in the study area. A case control study conducted in Russia corroborated as drinking unpasteurized milk was associated with pulmonary TB [15]. Unlike this, similar inquiry made in northwestern Ethiopia, Gonder hospital, there was no difference in the prevalence of extra –pulmonary TB between those drinking raw milk and those did not [16]. This difference might be due to difference in background prevalence of animal TB in the study area.

The most important factor fueling TB in SSA in general and in the present study area was HIV infection. It is increases the progression of latent TB infection in to active TB by its effect on the immune system [10, 17]. For example, in a case control study conducted in three West African countries, HIV infection was significantly associated with pulmonary TB [18]. In a retrospective study conducted in Tanzania [19] and a cross-sectional study in south eastern Ethiopia [20], HIV infection was significantly associated with TB. In contrast to the present and the above studies, another similar study carried out in India and a clinic based case control study in Gambia, HIV is not associated with TB [17, 21]. The main reason for this disagreement between the present study and studies in India and Gambia might be because of low prevalence of latent TB among in India and Gambia. The other two important co morbidities considered in this study were previous history of ant-TB medication and contact with TB patient at home.

According to the present study patients who had contact with TB patients at home were as equally risky to +PTB to those who had no contact. Unlike this, a cross-sectional study conducted in Matehara sugar cane hospital in eastern Ethiopia [22], Croatia and south east Ethiopia [20, 23], hospital based cross-sectional study conducted in northwest Ethiopia [16], in three west African countries [18] patients who had contact with TB patients at home were at increased risk of acquiring the disease from the patient at home. The main reason for the variability between these studies and the present study might be due to difference in delay of TB patients before diagnosis and treatment.

The time before diagnosis and treatment of pulmonary tuberculosis, time when actual transmission of the disease from an infectious patient occurs, might be lower in the present study area.

The other important risk factor associated with increased risk of active TB in southern Ethiopia was previous episode of TB. Patients who had previous anti-TB treatment were at high risk of active TB. This indicates that the previous medication was failed to eradicate the bacteria from such patients or it might be due to primary or acquired drug resistance. In agreement with the current study, a community based case control study conducted in three West African countries [18] and a hospital based cross-sectional study conducted in northwest Ethiopia [16] previously treated patients were at increased risk of TB. Unlike these, a cohort study conducted in rural community in China [24] and India [25] found that there was no difference in the prevalence of TB between patients who were treated before or not.

Most reviewed articles indicate that smoking was the major risk factor of TB which is also true in the present study. Smoking makes people more vulnerable to TB and the conversion of latent form of TB to active TB. In similar, two studies conducted in south east and eastern Ethiopia [20, 22], a case control study conducted in Russia [15], south and central India and three western countries in Africa [18, 26, 27], smoking significantly increases the prevalence of TB. In contrast to the present study, a community based cohort study conducted in china and in tea garden community in India had found no association between smoking and active TB [24, 25].

At last the current study is done with some limitations. One of the limitations of the current study emanates from the study design being case control. This study design was not strong enough to indicate our causal link between PTB and factors significantly associated with smear-positive pulmonary TB. The second limitation of the study was due to recall bias of the study participants. The response of participants on the risk factors assessed might not be always correct. Thus, the above findings of the present study should be interpreted in light with these limitations.

5. Conclusions and recommendations

Factors increasing the prevalence of TB either through increased transmission or progression of latent TB to active TB in southern Ethiopia were identified. Factors significantly increasing the prevalence of smear-positive pulmonary TB in southern Ethiopia were overcrowding in a bed room, habit of drinking unpasteurized milk or smoking cigarette, HIV infection, previous episode of TB and decreased body-mass index. Health education on pasteurizing milk before consumption and about the symptoms and the route of transmission from an infectious patient should be given to the general patient. Moreover, the TB-HIV management among HIV patients should be strengthened to prevent the progression of latent form of TB to active one.

An association of drinking unpasteurized milk indicates the possibility of transmission from cows to humans which needs further study to determine the transmission of bacterium from cows to humans and vice versa. The association between previous episodes of TB also indicates that relapse of TB play great contribution to the burden of the diseases or increased risk of drug resistance.

Therefore, prevalence of MDR-TB and relapse of pulmonary TB and their determinants in the study area should be better understood to enhance the prevention and control of TB.

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