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Associated risk factor of tuberculosis infection among adult patients in Gedeo Zone, Southern Ethiopia

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Abstract

Background: Tuberculosis remains a major global health problem causing death among millions of people each year. Even though many of the World Health Organization recommended tuberculosis control strategies were implemented, there is still a major gap in tuberculosis case detection and treatment which resulted in rapid transmission of the cases in high burden countries. This study aimed to provide updated information on the contributing factors for the development of tuberculosis.

Methods: A case–control study was carried out in Gedeo Zone from February to July 2021 to assess the risk factors of tuberculosis. Cases were confirmed pulmonary tuberculosis patients with age ⩾18 years, while controls were participants who were confirmed to be pulmonary tuberculosis negative with the same age. Multivariate logistic regression models were used to assess the associated risk factor.

Results: A total of 368 individuals (173 cases and 173 controls) were included in this study. Based on the multivariable logistic regression analysis, we identified six variables as independent risk factors for the development of tuberculosis after controlling possible confounders. Those were patients with income <1500 Ethiopian birr per month (adjusted odds ratio = 2.35; 95% confidence interval: 1.22–3.97), patients with no educational background (illiterate) (adjusted odds ratio = 2.10; 95% confidence interval: 1.17–2.51), patients smoking cigarette (adjusted odds ratio = 2.89; 95% confidence interval: 2.10–3.82), patients chewing khat (adjusted odds ratio = 2.86; 95% confidence interval: 1.28–3.79), patients in close contact with known tuberculosis cases (adjusted odds ratio = 3.63; 95% confidence interval: 2.24–4.46), and patients being positive for HIV (adjusted odds ratio = 3.01; 95% confidence interval: 1.07–3.52) who were found to be significantly associated with tuberculosis development, while Bacille Calmette-Guérin vaccination had a protective effect against the development of tuberculosis (adjusted odds ratio = 0.52; 95% confidence interval: 0.21–0.88).

Conclusion: The priority should be given to the identified contributing factors through application of coordinated efforts on screening of patients suspected for pulmonary tuberculosis and all contacts of pulmonary tuberculosis patients and treatment of known tuberculosis cases, and appropriate control methods to reduce *Mycobacterium tuberculosis* cases.

Keywords

Tuberculosis, pulmonary tuberculosis, risk factor, case–control

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Introduction

The World Health Organization (WHO) recently announced that tuberculosis (TB) remains a major global health problem causing deaths among millions of people each year. TB is the ninth leading cause of death worldwide by killing almost three people every minute and the leading cause from a single infectious agent.[1] Despite the tremendous efforts and encouraging progresses obtained toward the control of TB epidemic, it remains to be the single infectious agent that takes more lives and affect all age groups each year.[2] Despite several efforts to improve case identification and treatment compliance and falling TB mortality by 3% and incidence rate by 2%, in 2019, the WHO estimated 9.6 million people developed TB and 1.2 million died from the disease.[1,3,4]

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About 5%–10% of infected persons who do not receive treatment for latent TB infection will develop TB disease at some time in their lives.[5] According to the WHO report, more than 95% of TB deaths happen in low- and middle-income countries that made up two-thirds of the world. Poverty may result in poor nutrition, which may be associated with alterations in immune function. On the other hand, poverty resulting in overcrowded living conditions, poor ventilation, and poor hygiene habits is likely to increase the risk of transmission of TB.[6,7] The WHO has been targeting an end TB strategy based on an assessment of the TB epidemic and progress in TB diagnosis, treatment, and prevention efforts. This shift in the approach to TB control, which includes among its 2030 targets (90% TB case detection and treatment) including in high-risk populations, and a cure rate of 90% of detected TB cases.[8]

TB is exclusively transmitted based on environmental and personal associated risk factors. The risk factors contributing to acquiring TB infection are social and behavioral risk factors that include smoking, alcohol, khat chewing, and indoor air pollution.[9] People with comorbidities (people with certain chronic diseases) like diabetes, cancer, and HIV that affect the immune defense system; people in close contact with active pulmonary tuberculosis (PTB) patients; intravenous drug abuse; patients receiving immunosuppressive therapies; and health care workers are those peoples at high risk of acquiring the TB infection.[10–12]

The early diagnosis and treatment of TB patients is mandatory to reduce transmission of the disease. Millions of people are diagnosed and successfully treated for TB each year, averting millions of deaths, but there are still large gaps in detection and treatment. For the application of control policy, there is a need to re-examine the characteristics of the patients and identification of the contributing factors. Efforts for the identification of TB cases and treatment are not sufficient. Updated information is also needed on the associated risk factors to decide health priorities, to allocate resources to monitor the emergency of resistance for planning effective use of anti-TB drugs.

Therefore, this study provides updated information on the contributing factors for the development of TB and provides information for health programmers to give special attention and design a package in the national TB control program that addresses such areas where thousands of people are living in overcrowded areas.

Methods

Study design and study area

An institutional-based case–control study design was conducted between February and July 2021 in Gedeo Zone. Gedeo Zone is located in the Southern direction of Ethiopia with a total estimated population of 1,694,868 according to the 2007 population census conducted by the Central Statistical Agency of Ethiopia (data are from zonal health office). Gedeo Zone is found at a distance of 85 km from Hawasa and 365 km far from Addis Ababa, the capital city of Ethiopia. It is located in Kola Agro ecological zone with an altitude of 1400 km above the sea level and annual temperatures range from 22°C to 29°C.[13] In this zone, coffee cultivation is the predominant means of livelihood for residents. Gedeo Zone has 35 health centers, 3 district hospitals, and 1 referral hospital. It serves for patients' lives in Gedeo Zone and for patients coming from the neighboring Sidama and Oromia regions. All health institutions have TB clinic where patients with TB are registered and treated based on DOTS strategy, according to the national TB cases treatment recommendation. Ethiopia ranks 10th among the high TB pandemic countries, 15th among the 27 high multidrug-resistant tuberculosis (MDR-TB) countries in the world, and 3rd in Africa following South Africa and Nigeria, and TB is also highly prevalent in Gedeo Zone.[14,15]

Study population

The study populations were all PTB suspected patients of age $\geqslant$18 years who visited the selected health institution during the study period. The cases were all patients $\geqslant$18 years of age who were confirmed to be positive for PTB during the study period. TB diagnoses were made based on the national comprehensive Tuberculosis, Leprosy, TB/HIV diagnosis and treatment manual. The controls were all patients $\geqslant$18 years of age who have a sign and symptoms of TB but were confirmed to be negative for PTB during the study period. The inclusion criteria for the cases were *Mycobacterium tuberculosis* (MTB) confirmed patients of age $\geqslant$18 years, while the inclusion criteria for the controls were TB suspected cases with confirmed *M. tuberculosis* negative. The exclusion criteria for the cases and controls were as follows: patients with age $<$18 years, study subjects who were unable to give informed consent, and subjects with suspected but unconfirmed TB.

Sample size determination

A formula from Kelsey' statistical method for rate and proportions was used to calculate the sample size with Epi-Info version 7 assuming a double population proportion formula based on the following parameters: an estimated exposure of known TB contact for controls was assumed to be 20%, a marginal error of 5%, an estimated odds ratio (OR) of 2.0, 80% power ($1-\beta$), 95% confidence interval (CI), and a 1:1 ratio of cases to controls. Accordingly, the calculated sample size was 346 (173 for cases and 173 for controls) using the two-proportion formula. The sample size was calculated for the exposure status of different variables. We took the largest sample among these exposure variables.

Sampling technique

Among four hospitals that deliver TB laboratory examination service in Gedeo Zone, two hospitals (Dilla University

referral hospital and Gede primary hospital) that have Gene Xpert and used it for TB testing were selected purposefully for this study. Selection of cases: The cases were newly detected bacteriologically confirmed PTB patients of age ⩾18 years, enrolled for treatment in the selected hospitals in Gedeo Zone. The data collection has taken place by including all newly confirmed TB patients until the required sample size was met. Selection of controls: all patients ⩾18 years of age who were confirmed to be negative for PTB during the study period. The data collection for the control has taken place by including the next newly confirmed TB-negative study participants following the confirmed TB patients until the required control sample size was met.

Data collection

Before data collection, the diagnosis of the patients was done by experienced physician and suspected cases for PTB with clinical manifestation of cough for two or more weeks, chest pain, or pain with breathing or coughing, night sweats, weight loss, fatigue, fever, chills, and known or possible TB exposure were sent to laboratory for confirmation. Data were collected by trained laboratory technologists and nurses using pretested (5% of total sample size selected individual from the study population) (pilot-tested) structured questionnaires that were prepared in English, translated into local language (Gedeofa), and back-translated into English to check its consistency.[16] Socio-demographic characteristics of study participants (age, sex, monthly income, educational, religion, occupation, resident, and marital status) and clinical feature-related variable (cigarette smoking, khat chewing, alcohol consumption, vaccination for Bacille Calmette-Guérin (BCG), imprisonment, previous treatment for TB, contact with known TB patients, HIV status using antibody test, diabetes mellitus, and blood pressure) data were collected by the trained data collector. Data collection procedures were supervised by the principal investigators. The Xpert MTB/RIF automated cartridge-based nucleic acid amplification assay was used for the confirmation of all positive and negative sputum results collected from TB suspected patients.

Close contacts. If persons shared air space with an individual with PTB in the household or other indoor setting for >15 h per week or >180 h total during an infectious period, defined as the interval from 3 months before collection of the first culture-positive sputum specimen or the date of onset of cough through 2 weeks after the initiation of appropriate anti-TB treatment.[17]

Statistical analysis

After the whole demographic data and patients' history were collected from the study participants, data were entered into Epi-Data 3.1 and data analyses were performed with SPSS version 23.0 software. Frequency count and percentage were used to present the findings. Prevalence figures were calculated for the total study population and separately by clinical features of the disease. Odds ratio (95% CI) and p values were used to measure the strength of association and identify statistically significant results. Multivariate logistic regression models were applied to assess the relationship between determinants and TB. The Hosmer–Lemeshow test was applied and the fit of the model was checked.[18–20] In this study, the model adequately fitted the data and the p value was 0.25; p values less than 0.05 were considered statistically significant.

Ethics approval and consent to participate

The protocol for patient recruitment and participation in the study followed the principles of the Declaration of Helsinki and was approved by the Dilla University Health Research Ethics Review Committee under the protocol unique number 005/21-01. In this study, personal life condition and comorbidity data of TB suspected patients were collected from study participants after getting permission to conduct the study from Dilla University referral hospital medical director and respective departments. Written informed consent was taken from each study participant. Strict confidentiality was maintained by removing all patient identifiers and only code numbers were used throughout the study.

Operational definition. Regarding the Ethiopian per capital income or minimum wage, the minimum wage in Ethiopia is around 924–1500 birr (around US$22).

Results

Socio-demographic and clinical features of study participants

A total of 346 study participants suspected with PTB (173 cases and 173 controls) aged ⩾18 years were included in this study. The age of the study participants ranged from 18 to 88 years with the median age of 31 (interquartile range: 24.7–49.3 years). Most of the cases and controls (41.6% and 39.9%, respectively) were found within the age range of 30–44 years. The majority of the cases and control (71.7% and 63.6%, respectively) were male. More than half (60.1%) of the cases and 72.8% of controls were from high school or below as seen in Table 1.

Personal life style and comorbidities

In this study, 20.8% of the cases and 9.8% of controls smoke cigarettes and more than half of both cases and controls smoke 5–11 cigarettes per day. About one-third of cases (31.2%) and 17.3% of controls reported as they were khat chewers. In this study, one-third of cases (32.4%) and 2.9% of

Table 1. Socio-demographic characteristics of patients with TB (cases = 173) and without TB (controls = 173), Gedeo Zone, July 2021.

Variables	Categories	Cases (n = 173)		Controls (n = 173)	
		n	%	n	%
Gender	Male	124	71.7	110	63.6
	Female	49	28.3	63	36.4
Age categories	18–29	36	20.8	40	23.1
	30–44	72	41.6	69	39.9
	45–59	40	23.1	43	24.9
	>60	25	14.5	21	12.1
Income	<1500ETB	55	28.3	30	17.3
	1500–3000ETB	72	41.6	87	50.3
	>3000ETB	46	30.1	56	32.4
Residence	Rural	80	46.2	85	49.1
	Urban	93	53.8	88	50.9
Marital status	Single	93	53.8	93	53.8
	Married	74	42.8	74	42.8
	Divorced	6	3.5	6	3.5
Educational level	Illiterate	53	30.7	30	17.3
	High school or lower	104	60.1	126	72.8
	Collage and above	16	9.2	17	9.8
Occupation	Employed	78	45.1	81	46.8
	Unemployed	95	54.9	92	53.2

TB: tuberculosis; ETB: Ethiopian birr.

Table 2. Personal life condition and comorbidity data of patients with TB (cases = 173) and without TB (controls = 173), Gedeo Zone, July 2021.

Variables	Categories	Cases (n = 173)		Controls (n = 173)	
		n	%	n	%
Smoke	Yes	36	20.8	17	9.8
	No	137	79.2	156	90.2
Khat chewing	Yes	54	31.2	30	17.3
	No	119	68.8	143	82.7
Vaccination for BCG	Yes	28	16.2	12	6.9
	No	145	83.8	161	93.1
Close contact with known TB	Yes	56	32.4	5	2.9
	No	117	67.6	168	97.1
History of imprisonment	Yes	17	9.8	9	5.2
	No	156	90.2	164	94.8
Frequent alcohol	Yes	19	11	23	13.3
	No	154	89	150	86.7
Status of HIV antibody test	Yes	13	7.5	4	2.3
	No	160	92.5	169	97.7
Diabetes status	Yes	12	6.9	4	2.3
	No	161	93.1	169	97.7
Blood pressure	Yes	7	4.1	3	1.7
	No	166	95.9	170	98.3

TB: tuberculosis; BCG: Bacille Calmette-Guérin.

controls reported a history of close contact with known TB, while only 16.2% of cases and 6.9% of controls reported as they were vaccinated for TB. In this study, only 5.5% of cases and 2.3% of controls reported to be positive for HIV, while 4%–7% of cases and 1.7%–3% of controls were living with diabetes mellitus and abnormal blood pressure (Table 2).

Table 3. Bivariate analysis of contributing factors among patients with TB (cases = 173) and without TB (controls = 173), Gedeo Zone, July 2021.

Variables	Categories	Cases, n (%)	Controls, n (%)	COR (95% CI)	p value
Gender	Male	124 (71.7)	110 (63.6)	1	1
	Female	49 (28.3)	63 (36.4)	0.70 (0.43–1.13)	0.145
Age categories	18–29	36 (20.8)	40 (23.1)	1	1
	30–44	72 (41.6)	69 (39.9)	1.16 (0.55–2.46)	0.411
	45–59	40 (23.1)	43 (24.9)	1.0 (0.51–1.99)	0.553
	>60	25 (14.5)	21 (12.1)	1.05 (0.51–2.18)	0.573
Income	<1500ETB	55 (28.3)	30 (17.3)	2.44 (1.42–4.21)	0.007*
	1500–3000ETB	72 (41.6)	87 (50.3)	1.14 (0.68–1.90)	0.420
	>3000ETB	46 (30.1)	56 (32.4)	1	1
Residence	Rural	80 (46.2)	85 (49.1)	0.95 (0.63–1.46)	0.621
	Urban	93 (53.8)	88 (50.9)	1	1
Marital status	Single	93 (53.8)	93 (53.8)	1.43 (0.44–4.63)	0.550
	Married	74 (42.8)	74 (42.8)	0.73 (0.23–2.34)	0.591
	Divorced	6 (3.5)	6 (3.5)	1	1
Educational level	Illiterate	53 (30.7)	30 (17.3)	2.14 (1.28–3.59)	0.016*
	High school or lower	104 (60.1)	126 (72.8)	1.88 (0.83–4.24)	0.131
	College and above	16 (9.2)	17 (9.8)	1	1
Occupation	Employed	78 (45.1)	81 (46.8)	1.09 (0.72–1.68)	0.565
	Unemployed	95 (54.9)	92 (53.2)	1	1
Smoke	Yes	36 (20.8)	17 (9.8)	2.52 (2.12–3.77)	0.005*
	No	137 (79.2)	156 (90.2)	1	1
Khat chewing	Yes	54 (31.2)	30 (17.3)	2.86 (1.28–3.79)	0.003*
	No	119 (68.8)	143 (82.7)	1	1
Vaccination for BCG	Yes	28 (16.2)	12 (6.9)	0.35 (0.19–0.71)	0.009*
	No	145 (83.8)	161 (93.1)	1	1
Close contact with known TB	Yes	56 (32.4)	5 (2.9)	3.63 (2.24–4.46)	<0.0001*
	No	117 (67.6)	168 (97.1)	1	1
History of imprisonment	Yes	17 (9.8)	9 (5.2)	1.05 (0.22–1.16)	0.108
	No	156 (90.2)	164 (94.8)	1	1
Frequent alcohol	Yes	19 (11)	23 (13.3)	1.24 (0.65–2.38)	0.311
	No	154 (89)	150 (86.7)	1	1
Status of HIV antibody test	Yes	13 (7.5)	4 (2.3)	2.91 (1.06–3.51)	0.002*
	No	160 (92.5)	169 (97.7)	1	1
Diabetes status	Yes	12 (6.9)	4 (2.3)	0.44 (0.15–1.29)	0.134
	No	161 (93.1)	169 (97.7)	1	1
Blood pressure	Yes	7 (4.1)	3 (1.7)	0.42 (0.11–1.65)	0.212
	No	166 (95.9)	170 (98.3)	1	1

TB: tuberculosis; COR: crude odds ratio; CI: confidence interval; ETB: Ethiopian birr; BCG: Bacille Calmette-Guérin.
*$p < 0.05$.

Bivariate analysis of contributing factors

In this study, sex, different age groups, residence, marital status, and occupation had not shown an association with developing TB. Study participants with income <1500 Ethiopian birr (ETB) (crude odds ratio (COR): 2.44; 95% CI: 1.42–4.21)) were more likely to develop TB than patients with higher income. Study participants who had no educational background (2.14; 1.28–3.59) were more likely to develop TB than the educated one. Cigarette smokers (2.52; 2.12–3.77), khat chewers (2.86; 1.28–3.79), vaccination (0.35; 0.19–0.71), close contact (3.63; 2.246–4.46), and study participants who were positive for HIV (2.91; 1.06–3.51) were more likely to develop TB.

In this study, however, the study participants who had a history of imprisonment, frequent alcohol consumers, diabetes status, and blood pressure status were not a contributing factor for TB (Table 3).

Multivariate analysis of contributing factors

For the identification of independent risk factors for TB, all candidates in bivariate logistic regression were entered into multivariable logistic regression. After controlling for possible confounders, the following variables had shown association in the multivariable model: patients with income <1500ETB were found to be more than twice more likely to develop TB compared to those with higher income (adjusted

Table 4. Multivariate analysis of contributing factors among patients with TB (cases = 173) and without TB (controls = 173), Gedeo Zone, July 2021.

Variables	Categories	Case, n (%)	Control, n (%)	COR (95% CI)	AOR (95% CI)	p value
Income	<1500ETB	55 (28.3)	30 (17.3)	2.44 (1.42–4.21)[a]	2.35 (1.22–3.97)	0.007[a]
	1500–3000ETB	72 (41.6)	87 (50.3)	1.14 (0.68–1.90)	0.83 (0.42–1.66)	0.241
	>3000ETB	46 (30.1)	56 (32.4)	1	1	1
Educational level	Illiterate	53 (30.7)	30 (17.3)	2.14 (1.28–3.59)[a]	2.10 (1.17–2.51)	0.014[a]
	High school or lower	104 (60.1)	126 (72.8)	1.88 (0.83–4.24)	1.36 (0.71–4.11)	0.130
	College and above	16 (9.2)	17 (9.8)	1	1	1
Smoke	Yes	36 (20.8)	17 (9.8)	2.52 (2.12–3.77)[a]	2.89 (2.10–3.82)	0.002[a]
	No	137 (79.2)	156 (90.2)	1	1	1
Khat chewing	Yes	54 (31.2)	30 (17.3)	2.86 (1.28–3.79)[a]	2.86 (1.28–3.79)	0.003[a]
	No	119 (68.8)	143 (82.7)	1	1	1
Vaccination for BCG	Yes	28 (16.2)	12 (6.9)	0.35 (0.19–0.71)[a]	0.52 (0.21–0.88)	0.009[a]
	No	145 (83.8)	161 (93.1)	1	1	1
Close contact with known TB	Yes	56 (32.4)	5 (2.9)	3.63 (2.24–4.46)[a]	3.63 (2.24–4.46)	<0.0001[a]
	No	117 (67.6)	168 (97.1)	1	1	1
History of imprisonment	Yes	17 (9.8)	9 (5.2)	1.05 (0.22–1.16)	0.74 (0.26–2.08)	0.108
	No	156 (90.2)	164 (94.8)	1	1	1
Status of HIV antibody test	Yes	13 (7.5)	4 (2.3)	2.91 (1.06–3.51)[a]	3.01 (1.07–3.52)	0.001[a]
	No	160 (92.5)	169 (97.7)	1	1	1
Diabetes status	Yes	12 (6.9)	4 (2.3)	0.44 (0.15–1.29)	0.89 (0.24–3.32)	0.134
	No	161 (93.1)	169 (97.7)	1	1	1
Blood pressure	Yes	7 (4.1)	3 (1.7)	0.42 (0.11–1.65)	0.29 (0.06–1.55)	0.149
	No	166 (95.9)	170 (98.3)	1	1	1

TB: tuberculosis; COR: crude odds ratio; CI: confidence interval; AOR: adjusted odds ratio; ETB: Ethiopian birr; BCG: Bacille Calmette-Guérin; 1: reference.
[a]Statistically significant.

odds ratio (AOR) = 2.35; 95% CI: 1.22–3.97). The likelihood of TB occurrence in illiterate subjects was 2.1 times higher than patients who have an educational background (AOR = 2.10; 95% CI: 1.17–2.51). Smoking and chewing khat were found to be an important risk factors for developing TB by more than 2 times (AOR = 2.89; 95% CI: 2.10–3.82) and (AOR = 2.86; 95% CI: 1.28–3.79) than non- smokers and non-khat chewers, respectively. The likelihood of TB occurrence in study subjects in close contact with known TB was 3.63 times higher than patients who had no story of close contact with known TB (AOR = 3.63; 95% CI: 2.24–4.46). BCG was found to be protective against TB, reducing the risk by half (AOR = 0.52; 95% CI: 0.21–0.88). Being positive for HIV was found to be an important risk factor for developing TB by 3 times (AOR = 3.01; 95% CI: 1.07–3.52), as seen in Table 4.

Discussion

A total of 346 study participants suspected with PTB (173 newly confirmed TB patients taken as cases and 173 newly confirmed TB negatives taken as controls) aged ⩾18 years were included in this study. Patients with income <1500ETB per month, illiterate patients, cigarette smoker, khat chewer, close contact with known TB, and being positive for HIV were significantly associated with TB development, while BCG vaccination had a protective effect against the development of TB. The early diagnosis and treatment of TB patients is mandatory to reduce transmission of the disease. Millions of people are diagnosed and successfully treated for TB each year, averting millions of deaths, but there are still large gaps in detection and treatment. For the application of control policy, there is a need to re-examine the characteristics of the patients and identification of the contributing factors. Efforts for the identification of TB cases and treatment are not sufficient. Updated information is also needed on the associated risk factors to decide health priorities, to allocate resources to monitor the emergency of resistance for planning effective use of anti-TB drugs.[21]

In this study, the sex of the study participants had no association with TB development. However, different studies reported that being male had an increased risk for the development of TB.[22,23] In both cases (41.6%) and controls (39.9%), most of the study participants were within the age range of 30–44 years. This is in line with different studies conducted in Ethiopia where most of the cases were found within this age range.[24,25]

When these young and productive age groups were affected by TB, the development of the country will be directly affected. As they can also move from place to place

and contact with other parts of the community, they will be resulting in easy and rapid transmission of the diseases in the community, which can be caused in the death of many of the risk groups.[26,27]

In this study, low income was one of the contributing factors to develop TB. This is in agreement with studies conducted in different areas that reported low income was directly associated with the development of TB.[28–32] In addition, our report is consistent with the WHO report, which indicates more than 95% of TB deaths happen in low- and middle-income countries that made up two-thirds of the world. Poverty may result in poor nutrition which may be associated with alterations in immune function which may result in overcrowded living conditions, poor ventilation, and poor hygiene habits that are likely to increase the risk of transmission of TB.[6,7,33]

In our study, TB patients who had no educational background (illiterate) were found to be more likely to develop TB compared to patients who had an educational background. Similar to our study, different studies reported that being illiterate was one of the contributing factors to develop TB.[30,32,34,35] Most of the communities living in developing countries were illiterate and have a low level of knowledge on TB. Low level of knowledge on TB can lead to complications and worse health outcomes, increasing the transmission and delaying health-seeking behavior, lack of adherence, resulting in MDR, treatment failure, and disease complications and death.[36,37]

In this study, smoking and khat chewing were found to be contributing factors for developing TB. This is in agreement with studies conducted in different areas which reported being smokers and khat chewers were risk factors for developing TB.[30,38–40] Smoking damages the lungs and impacts the body's immune system, making smokers more susceptible to TB infection. The occurrence of TB has been directly associated with impairment of the immune response and multiple defects in immune cells.[41] Smoking also results in histological changes in the lower respiratory tract, including peri-bronchial inflammation, fibrosis, vascular intimal thickening, and destruction of alveoli. This can be resulted in abnormal function of epithelial and damaged ciliary clearance of inhaled substances. Mechanical disruption of cilia function and hormonal effects could also appear secondarily to smoking.[42–45] Khat chewing is also associated with immune modulations that facilitate TB development.[46]

In our study, the occurrence of TB was lower in those study participants who were vaccinated for BCG than those who were not vaccinated. This is in line with other studies conducted in different areas where lack of vaccination for BCG is a significant contributing factor for developing TB.[34,35,47,48] The BCG vaccine is one of the most widely used of all current vaccines for neonates and infants in countries where it is part of the national childhood immunization program. BCG vaccination may be considered for health care workers who are employed in settings in which the likelihood of transmission and subsequent infection with *M. tuberculosis* strains resistant to isoniazid and rifampin is high. The protective efficacy of BCG for PTB in adults is uncertain.[49,50]

Our study demonstrates that close contact with known TB is one of the risk factors for the transmission and development of TB. Close contacts of patients with infectious TB are at increased risk of developing *M. tuberculosis* infection and disease.[51,52] The prevalence of PTB in close contact was reported to be the highest among many risk groups where there is an overcrowded population like homeless people, injection drug users, and prisoner live.[53,54] Close contact is also one of the common risk factors for progression from latent TB infection to active disease.[55] Therefore, early diagnosis, isolation of known PTB, and treatment are important to reduce and control the transmission of the disease.

In this study, HIV-positive patients were found to be contributing factors for the development of TB. HIV kills our immune system cells that help the body to fight infections and diseases and facilitate for the development of TB. HIV and TB are considered as the double burden diseases of the world. According to the WHO reports, there were 1.5 million deaths attributed to TB, out of which 26% were due to HIV-associated TB.[56,57] In under-developed countries, the prevalence of HIV is high and this resulted in an increased number of TB infections.[58] Of the 1.2 million TB-HIV cases worldwide, Africa accounts about 74% of the cases.[58] In Ethiopia, 4 in 100 people died due to TB-HIV co-infection and the incidence of MDR-TB was estimated to be 5.8 per 1000 people.[59] In this study, being in prison, consumption of alcohol, diabetes mellitus, and blood pressure had no association with the development of TB.

Limitations of this study

Even though we tried to control it, there is a possibility for residual confounders in this study. In our study, we included only small sample sizes. This can be resulted in under-representation of the total population to identify the effect of each factor on the development of TB.

Conclusion

In general, socio-demographic characteristics such as patients with income $<$1500ETB per month and patients without educational background (illiterate); personal life conditions such as cigarette smoking and khat chewing, and others clinical features such as close contact with known TB and being positive for HIV were found to be significantly associated with TB development, while BCG vaccination had a protective effect against the development of TB. Health care provider should be given priority to the identified contributing factors. Patients with sign and symptom of PTB should be screened and tested. All contacts of PTB patients should be screened as early as possible to reduce the number of active TB cases, and appropriate

prompt treatment should be given to minimize the transmission. Special attention should also be given to address broader socio-economic issues such as poverty, overcrowding, and smoking as elements of the national response to control TB. Health education on contributing factor at the health care facility level is an important means of prevention and control of TB.

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Author contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave the final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Informed consent

Written informed consent was obtained from all subjects before the study.

Trial registration

Not applicable.

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Data availability statement

All data relevant to the study are included in the article and other raw data set used for analysis during this study are available from the corresponding author on reasonable request.

Supplemental material

Supplemental material for this article is available online.

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