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Research Article

Determinants of Pulmonary Tuberculosis among Patients Attending at Public Health Facilities of Omonada District, South West Ethiopia: A Matched Case Control Study

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Abstract

Background: Tuberculosis (TB) is an infectious disease and has remained a major global health problem. It is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS. Ethiopia is among the 30 high TB and MDR-TB burden countries.

Objective: To assess the determinants of Pulmonary Tuberculosis (PTB) among patients attending at public health facilities of Omonada District.

Methods: Institution based matched case-control study was conducted among 116 cases who were on TB care and matched for age 232 controls at health facilities in Omonada District from March 1-20, 2019. A simple random sampling method was used and for each case, two age matched controls were recruited. Determinants of PTB were identified using logistic regression method and odds ratio were calculated with 95% confidence intervals to assess the strength of association.

Results: In the multivariate analysis of determinant factors of TB, patients who were from rural area were 2.33 times more likely to develop active PTB than with those who were from urban areas (AOR: 2.33; 95% CI: 1.26-4.3), patients who had history of close contact with TB patient were 3.6 times more likely to develop active PTB than those who had no history (AOR: 3.6; 95% CI: 2.3-10.5), patients who lived in the house without ceiling were 2.66 times more likely to develop Pulmonary TB than those who lived in the house with ceiling (AOR: 2.66; 95% CI: 1.3-5.5), and Patients who lived in the house with mud type of floor were 1.5 times more likely to develop Pulmonary TB than those who lived in the house with cement floor type (AOR: 1.5; 95% CI: 1.04-2.3).

Conclusion: In this study, the place of residence, history of severe acute malnutrition, history of close contact with TB patient, absence of separated kitchen from the living house, being live in the house without ceiling and being live in the house with mud floor were the major determinants of Pulmonary TB. Therefore, measures taken to reduce the burden of active PTB should consider these contributing factors.

Abbreviations and Acronyms

AIDS: Acquired Immunodeficiency Syndrome; ART: Anti-Retroviral Therapy; BMI: Body Mass Index; CBE: Community Based Education; CDC: Centers for Disease Control; CI: Confidence Interval; DM: Diabetes Mellitus; EPTB: Extra-pulmonary Tuberculosis; FMOH: Federal ministry of health; HH: Household; HIV: Human Immune-deficiency Virus; IPT: Isoniazid Preventive Therapy; Kg: Kilogram; KM: Kilometer; MDG: Millennium Development Goal; MDR-TB: Multidrug-resistant Tuberculosis; MRN: Medical Record Number; MUAC: Mid upper arm circumference ; OPD: Out Patient Department; COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio; PLWHIV: People Living With HIV; RR: Relative Risk; RR-TB: Resistant to rifampicin Tuberculosis; SAM: Sever Acute Malnutrition; SES: Socioeconomic Status; TB: Tuberculosis; WHO: World Health Organization.

Operational Definitions and Definition of Terms

Pulmonary Tuberculosis: Bacteriologically Confirmed (Smear-positive pulmonary TB) and clinically diagnosed (Smear-negative pulmonary TB).

Overcrowding: a house was deemed to be overcrowded when the area of the room per person was less than 4 m^2.

Body mass index (BMI): is defined as the weight in kilogram of the individual divided by the square of the height in meter and used to determine the nutritional status of TB patients and classified as follows: Severe malnutrition (BMI < 16.0 Kg/m^2), moderate malnutrition (BMI = 16.0-16.99 Kg/m^2), mild malnutrition (BMI = 17.0-18.49 Kg/m^2), normal weight (BMI = 18.5-24.99 Kg/m^2).

Multidrug-resistance TB (MDR-TB): The Tuberculosis that resistance to at least isoniazid and rifampicin from the first line anti TB drugs.

Public Health facility: Government owned facility that provides standardized treatment regimens for TB patients.

Introduction

Background

Tuberculosis (TB) is an infectious disease caused by Mycobacterium Tuberculosis and has remained a major global health problem [1]. Globally in 2016 there were an estimated 10.4 million incident cases of TB and it threatens the global TB care and prevention and about 82% of TB deaths among HIV-negative people occurred in the African Region and South-East Asia Region [2].

The links between TB and poverty, social protection, the prevalence of under nutrition, diabetes, HIV, alcohol use, smoking, indoor air pollution and income per capita also have been reviewed and summarized as varied in low income countries to developed ones [3]. The risk of being infected from a single contact with an infectious case is determined by the extent of the close contact, the length of exposure and the amount of TB bacilli in the sputum of infectious TB cases. A single untreated infectious case can infect approximately 5-10 individuals every year, and can generate about 20 patients for an average two-year period [4].

Statement of the Problem

Tuberculosis (TB) remains a major global health problem and it causes ill-health for approximately 10 million people each year. It is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS [2].

TB affects all countries and all age groups, but overall the best estimates for 2017 were that 90% of cases were adults (aged ≥15 years), 64% were male, 9% were people living with HIV (72% of them in Africa) [3]. Africa bears 30% of HIV prevalence among TB patients and 75% of about 1.03 million of TB/HIV co-infection cases that occur each year globally [5].

Ethiopia is among the 30 high TB and MDR-TB burden countries that account for annual estimated TB incidence of 164 per 100,000 populations and death rate of 25 per 100,000 populations by 2017 [3].

A comprehensive strategy focusing on major risk factors of TB is essential to achieve the 'End TB' partnership targets. Risk factors of TB can be categorized as distal or proximate. Distal risk factors such as socio-economic status contribute to the development of TB indirectly whereas proximate determinants include those that increase exposure to the infectious agent such as crowding and that impair the host immune system [8].

Study conducted in Metema district, north-west Ethiopia recommended that further study should be conducted for better information by including other factors which not included under that study such as TB co-infection with HIV and malnutrition is important for TB control and prevention [9].

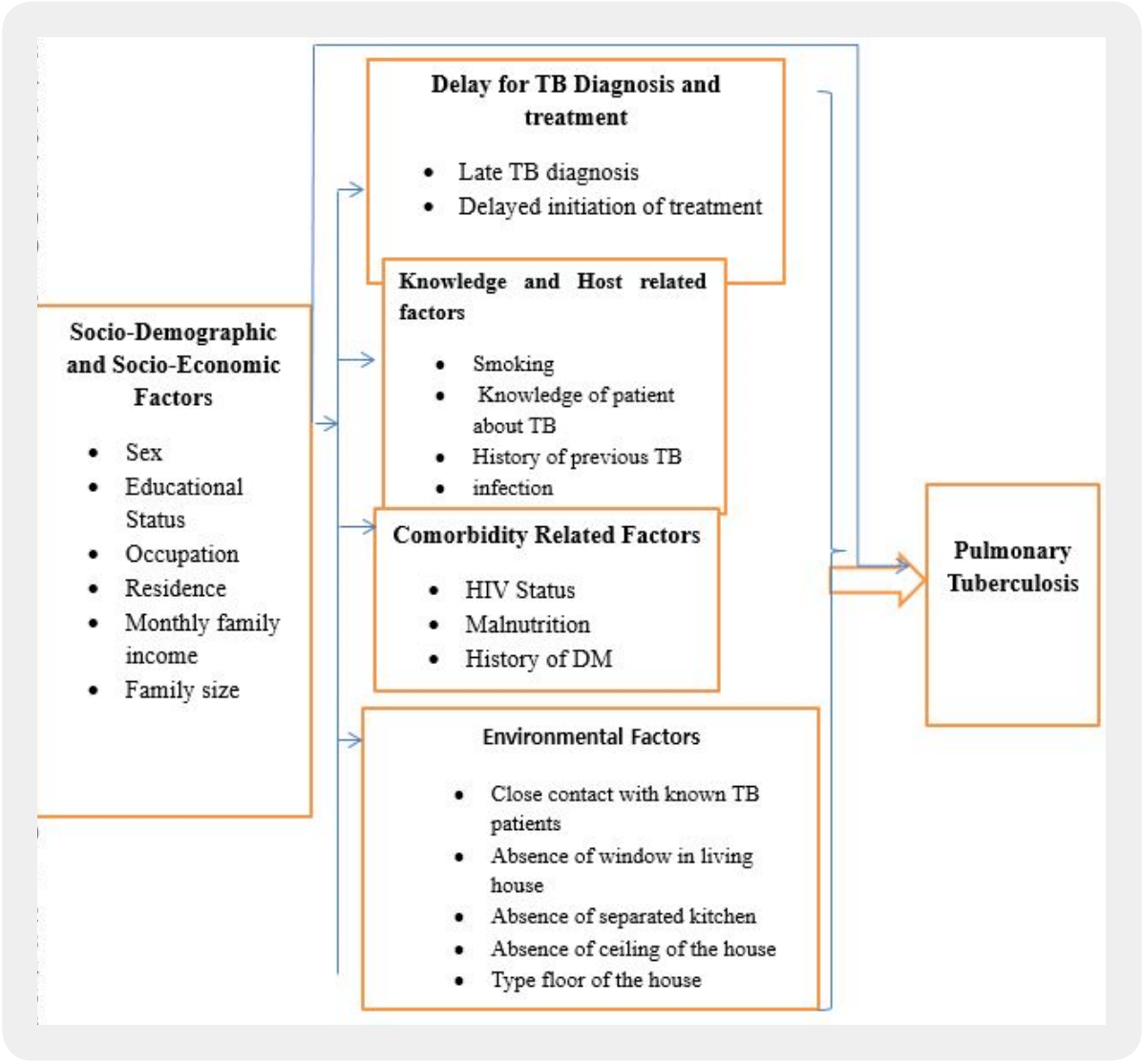
Understanding the role of various determinants of tuberculosis (TB) is particularly important in countries like Ethiopia where TB is endemic and the resources available to public health intervention are limited. Assessment of proximate determinants of TB which are amenable for interventions helps to target strategies to effectively and efficiently control TB and reduce the burden of TB. Several studies on risk factors of TB were done in the different countries including Ethiopia, but rare studies on a matched case control have been conducted in this country and Southwest Ethiopia in particular. Therefore this study tries to fill the gap.

Significance of the Study

Achieving the Tuberculosis (TB) targets and milestones of the End TB Strategy set in the Sustainable Development Goals requires provision of TB care and prevention within the broader context of health care and multidimensional action to address the determinants and consequences of TB. This may have a crucial role in the improving the community health and even in the development of the country.

This study identified the gaps on the specific determinant factors related to developing active TB; which encourage the District program managers, non-government organizations and respective health workers to work on the essential strategy to decrease the burden of the disease through effective TB control program and academic wise, it add additional research finding to the academics world and shows possible areas of research to other interested scholars on TB.

Conceptual Framework



Objective

To assess the determinants of pulmonary TB in patients who are attending at public health facilities of Omonada District, Southwest Ethiopia, 2019.

Methods and Materials

Study Area and Period

The study was conducted from March 1-20, 2019 in Omonada District which located at Latitude: 7°37'36.48"N Longitude: 37°15'14.68"E and 289 KM from capital city Addis Ababa. Omonada is one of

the highly populated Districts in Jimma Zone, with about 212,466 populations. It has 7 health centers and one Primary Hospital.

Study Design

Institution based matched case control study design was conducted.

Population

Source Population

All aged 15 years and above Pulmonary TB patients were the source population for cases and all the patients of 15 years and above who were attending OPD were the source population for controls.

Cases

Pulmonary TB patients aged 15 years and above who were selected randomly from each health facility TB clinic and on TB care during the study period.

Controls

Two patients matched for age to each case, who had no productive cough for at least 2 weeks previously and randomly selected from the OPD attending patients during the study period. According to the WHO standards, individuals who were free of these constitutional symptoms were declared free of active TB although they may be infected with the TB bacterium.

Sample Size Determination

The sample size was calculated using Stats Direct version 4.7.2 statistical software for a matched case-control study design. The percent of contact history of Pulmonary TB among controls (39 %) was considered from previous study as the main exposure. A case to control ratio of 1:2, an odds ratio of contact history of TB from previous studies 2.05, a 95% confidence interval (CI), a study power of 80%, and a 5% nonresponse rate was assumed [9].

Then the probability of exposure in controls = 0.39, odds ratio = 2.05 and controls per case subject = 2. (Alpha = 0.05, power = 0.8). Therefore the estimated minimum sample size (cases required) = 111. Reduction in sample size, relative to paired design, when using 2 controls per case was = 0.705. Based on the above assumptions, the sample size was 111 cases and matched for age 222 controls. With addition of 5% non-respondent rate the sample size was 116 cases and matched for age 232 controls. Therefore, a total of 348 study participants were included.

Sampling Methods

Simple random sampling method was used to recruit the Pulmonary TB patients who enrolled on the TB care from the health facilities TB register. For each case, two controls matched with case according to age (within ± 2 years difference) were taken randomly from the patients attending at OPD during study period. The cases were taken randomly from the re-arranged and coded list of the total 192 Pulmonary TB patients in the District by merging the patients from 8 health facilities.

Eligibility Criteria

Inclusion criterion

All aged 15 years and above Pulmonary TB patients who were selected by simple random sampling and on TB treatment during the study period were included in the study.

Exclusion Criterion

All TB patients who were completed TB treatment before the study period and the respondents who were not willing to give consent were excluded for cases and all the patients who had constitutional sign and symptoms of TB from OPD attendees were excluded for controls.

Variables

Dependent Variable

Pulmonary Tuberculosis

Independent Variables

The explanatory variables that were included in the study: sex, occupation, educational status, place of residence, monthly income of the family, patient history of TB, family history of TB, human immunodeficiency virus (HIV) status, smoking, knowledge of patient about TB, body mass index (BMI), diabetes status, duration of the 1st consultation for TB diagnosis and treatment, history of close contact with TB patients, and housing condition.

Data Collection Tool and Procedures

A pre-tested structured questionnaire for interview was used to collect all data on the study variables. Height and weight was used to calculate body mass index to assess the nutritional status of the respondents. Information was collected on a wide range of potential risk factors such as socio-demographic, socio-economic, delay for diagnosis and treatment, co-morbidity, host related and environmental factors.

Four diploma nurses were trained and assigned for data collection as well as one Bachelor degree holder nurse for supervision prior to data collection. All included participants were interviewed by trained data

collectors and answer a structured questionnaire that was conducted in regional language, Afan Oromo and then translated to English language.

Data Quality Control

A properly designed and pre-tested questionnaire was used to address the study variables. The questionnaire was first prepared in English and translated into the regional language (Afan Oromo) for data collection and translated back to English for consistency. The instrument was pre tested on 5% of the sample in two public health facilities of Omo Beyem district which is similar to Omonada district. To ensure the completeness and consistency of information close supervision during data collection and double data entry was implemented as quality control measures.

Data Processing and Analysis

Data was checked, cleaned, and entered in to Epi Data and exported to SPSS version 23 software for analysis. After the data exported to SPSS each case was coded by unique identification and then matched dataset was built with match tolerance or fuzzy factor by case control matching. The matched groups (controls) were checked for similarities with cases on matching variable (age) before analyzing outcome.

All variables of the study were initially tested for association with Pulmonary TB by using logistic regression model. Those variables which have a p-value less than 0.25 by bivariate analysis were put in the multivariate analysis to control the possible effect of confounders. Finally, the variables which had association with PTB were identified on the basis of odd ratio with 95 % confidence interval and P value less than 0.05 to assess the strength of association. The likelihood ratio test was used to test the fitting model and variables candidate for the multivariate model were selected using the backward conditional method.

Ethical Consideration

Ethical clearance was obtained from Ethical Review Committee of Institute of Health, Jimma University. Permission letter was obtained from District Health Office to conduct the study in the study area.

Results

Socio-Demographic and Economic Characteristics

A total of 348 study participants, 116 active Pulmonary TB patients (cases) and age matched 232 OPD attendant patients (controls) were recruited for this study. As expected based on matching criteria, cases and controls were of similar age at enrollment.

Table 1: *Bivariate analysis of socio-demographic and economic factors associated with Pulmonary Tuberculosis in Omonada District health facilities, Southwest Ethiopia, 2019*

Variables	Cases (%)	Controls (%)	Cr OR (95% CI)	P-Value
Sex- Male	68 (58.6)	128 (55.2)	1.3 (0.79-2.17)	0.28
Female	48 (41.4)	104 (44.8)		
Marital status-Single	18 (15.5)	42 (18.1)		
Married	76 (65.5)	176 (75.9)	0.64 (0.11-3.8)	0.625
Widowed	22 (18.9)	14 (6)	0.85 (0.15-4.6)	0.85
Educational status				
Illiterate	37 (31.9)	94 (40.5)	1.37 (1.11-1.7)	0.03
Read and write	20 (17.2)	36 (15.5)	0.65 (0.27-1.5)	0.3
Primary education	38 (32.2)	54 (23.3)	0.97 (0.38-2.5)	0.9
Secondary education and above	21 (18.1)	48 (20.6)		
Occupation-Farmer	53 (45.7)	114 (49.1)		
Merchant	22 (19)	60 (25.9)	0.27 (0.09-0.8)	0.02
Gov. employee	18 (15.5)	28 (12)	0.7 (0.2-2.15)	0.61
Daily laborer	15 (12.9)	14 (6.0)	1.07 (0.34-3.3)	0.9
House wife	8 (6.9)	16 (6.9)	2.1 (0.6-7.1)	0.26
Residence- rural	78 (67.2)	132 (56.9)	1.7 (1.2-2.8)	0.001
Urban	38 (32.8)	100 (43.1)		
Monthly income				
<1000ETB	46 (39.7)	62 (26.7)	0.64 (0.38-1.05)	0.7
≥1000ETB	70 (60.3)	170 (73.2)		

Among socio demographic factors the educational status, occupation and place of residence were candidate variables identified by bivariate analysis. Being resident in rural area (COR= 1.7; 95% CI=1.2 -2.8) and being illiterate (COR=1.37, 95% CI=1.11- 1.7) were associated with Pulmonary TB in bivariate analysis (Table: 2). However, only being resident in rural area (OR= 2.33; 95% CI=1.26-4.3) remains to be statistically significant after controlling the effect of confounding variables in multivariate analysis.

Table 6: *The multivariate analysis of determinants of Pulmonary TB in Omonada District health facilities, Southwest Ethiopia, 2019*

Variables	Cases (%)	Controls (%)	COR (95% CI)	AOR (95% CI)	P– value
Place of residence –rural	78 (67.2)	132 (56.9)	1.7 (1.2-2.8)	2.33 (1.26, 4.3)	0.007
urban	38 (32.8)	100 (43.1)			
Educational status					
Illiterate	37 (31.9)	94 (40.5)	1.37 (1.11-1.7)	0.87 (0.7, 1.09)	0.244
Read and write	20 (17.2)	36 (15.5)	0.65 (0.27-1.5)	0.48 (0.13-1.7)	0.26
Primary education	38 (32.8)	54 (23.3)	0.97 (0.38-2.5)	0.4 (0.1-1.4)	0.15
Secondary education	11 (9.5)	24 (10.3)	1.4 (0.6-3.3)	0.7 (0.16-2.9)	0.62
Diploma and above	10 (8.6)	24 (10.3)			
HIV status – yes	6 (5.2)	2 (0.9)	2.8 (2.4, 33.7)	0.3 (0.29, 3.6)	0.36
no	110 (94.8)	230 (99.1)			
History of DM- yes	5 (4.3)	2 (0.9)	2.9 (0.4, 20.5)	0.25 (0.04, 1.6)	0.13
no	111 (95.7)	230 (99.1)			
History of close contact with TB patient -yes	63 (54.3)	28 (12.1)	10.8 (6-19.5)	3.6 (2.3, 10.5)	0.000
no	53 (45.7)	204 (87.9)			
History of SAM - yes	19 (16.4)	6 (2.6)	3.6 (1.2, 10.5)	2.4 (2.1, 6.7)	0.013
no	97 (83.6)	227 (97.8)			
History of smoking- yes	10 (8.6)	4 (1.7)	3.5 (1.2, 9.9)	0.54 (0.15, 1.8)	0.33
no	106 (91.4)	228 (98.3)			

Family history of TB yes no	 37 (31.9) 79 (68.1)	 18 (7.8) 214 (92.2)	5.2 (2.7, 10.05)	0.72 (0.3, 1.67)	0.44
Presence of kitchen - yes no	72 (62.1) 44 (37.9)	152 (65.5) 80 (34.5)	2.5 (1.3-4.9)	1.43 (1.02, 2.9)	0.01
Presence of ceiling -yes no	35 (30.2) 81 (69.8)	102 (44.0) 130 (56.0)	3.7 (2.0- 6.9)	2.66 (1.3, 5.5)	0.007
Floor type- cement mud	6 (5.2) 110 (94.8)	32 (13.8) 200 (86.2)	2.6 (0.86-8.1)	1.5 (1.04, 2.3)	0.03

Multivariate analysis identified that place of residence (p=0.007), history of severe acute malnutrition (p=0.013), history of close contact with TB patient (p=0.000), absence of a separate kitchen (p=0.01), house without a ceiling (p=0.007) and the mud type floor of house (p=0.03) had a significant association with the Pulmonary Tuberculosis (Table: 2).

In the multivariate analysis of determinant factors of TB, patients who were from rural area were 2.33 times more likely to develop active PTB than with those who were from urban areas (AOR: 2.33; 95% CI: 1.26–4.3), (p= 0.007). Patients who had history of close contact with TB patient were 3.6 times more likely to develop active PTB than those who had no history (AOR: 3.6; 95% CI: 2.3–10.5), (p= 0.000). Patients who lived in the house without ceiling were also 2.66 times more likely to develop Pulmonary TB than those who lived in the house with ceiling (AOR: 2.66; 95% CI: 1.3–5.5), (p= 0.007) and Patients who lived in the house with mud type of floor were 1.5 times more likely to develop Pulmonary TB than those who lived in the house with cement floor type (adjusted OR: 1.5; 95% CI: 1.04-2.3), (p= 0.03) (Table: 2).

Discussion

This Institution based matched case-control study inves¬tigated determinants of Pulmonary TB among TB patients (cases) and patients attending OPD (controls) at public health facilities in Omonada District, southwest Ethiopia. As expected based on matching criteria, cases and controls were of similar age at enrollment. Among the socio demographic variables, place of residence showed a significant association with Pulmonary TB in multivariate analysis.

Being resident in rural area was another socio demographic factor significantly associated with Pulmonary TB. This finding identified that patients who were from rural area were two times more likely to develop Pulmonary TB than those who were from urban areas. This is similar finding with the study conducted in southern Ethiopia that shows, being resident in rural area significantly associated with Pulmonary TB [10]. Other study conducted at Ambo Hospital, west Ethiopia showed that patients who were from rural areas

were 3.3 times more likely to develop active PTB than those who were from urban areas [11]. This may be due to the differences in lifestyle or differences in standard of living or socio-economic status.

This study also revealed that having history of severe acute malnutrition was significantly associated with Pulmonary TB in bivariate analysis and from the co-morbidity determinants of Pulmonary TB, it remains to be statistically significant after controlling the effect of confounding variables in multivariate analysis. In the multivariate analysis, patients who had history of severe acute malnutrition were 2.4 times more likely to develop Pulmonary TB than those who had no history severe acute malnutrition.

Similarly, the study showed that Tuberculosis and under-nutrition are inter-linked in a complex relationship and under-nutrition is a predictor of increased risk of death and TB relapse among TB infected patients [12]. Another study also shown that malnutrition (both micro- and macro-deficiency) increases the risk of TB because of an impaired immune response [13].

History of close contact with TB patient was the major determinant of PTB among the environmental factors. Patients who had history of close contact with TB patient were four times more likely to develop active Pulmonary TB than those who had no history (AOR: 3.6; 95% CI: 2.3-10.5), (p= 0.000). Similarly, the study conducted in Dessie and Debre Berhan shows that close contact with known TB patients and close contact with chronically cougher patients are the significant environmental factors associated with TB [14]. Close contacts of infectious TB cases including household contacts and care givers/health care workers are at a higher risk of becoming infected with Mycobacterium tuberculosis and development of primary active tuberculosis. The overall yield for all tuberculosis (bacteriologically confirmed and clinically diagnosed) was 4.5% (CI = 4.3-4.8) of contacts investigated; for cases with bacteriological confirmation the yield was 2.3% (CI = 2.1-2.5) [15].

Another environmental determinant that showed a sig¬nificant association with TB was whether there was a ceiling in the house. Study conducted in Metema district, north -west Ethiopia show that people living in a house without a ceiling were 1.46 times more likely to develop TB than those living in a house with a ceiling (AOR 1.46, 95% CI 1.07-2.21) [9]. In this study the patients who lived in the house without ceiling were 2.66 times more likely to develop Pulmonary TB than those who lived in the house with ceiling (AOR: 2.66; 95% CI: 1.3-5.5). This might be because a room with a ceiling might have result high refraction power of radia¬tion than room without ceiling. So the radiation will kill the causative agent of TB which might be found suspended in the room.

The present study also revealed that the type of floor of the house has a significant association independently with Pulmonary TB. People who lived in the house with mud floor were 1.5 times more likely to develop PTB than those who lived in the house with cement. This factor has not been previously addressed by other studies and may be due to the increases exposure to dust and particles that increase the prevalence of TB and further study is needed to explore this association.

Limitations of the Study

The recall bias is inherent to case-control studies. In this study, recall bias might have led to the

underestimation of the effect; short recall duration for the patients who are currently on TB care (during study period) were used to limit the effect and the other was the effect of the matching factor (age) on the Pulmonary TB could not evaluated as it was one drawback of matched case control study.

Another concern in this study was its failure to identify the temporal relationships between exposure factors and the outcome variable. This could be the situation with smoking, to minimize the effect data was collected the information on the duration of smoking to differentiate past from current smoking, so that reverse causality was unlikely to explain the finding. Since interview was conducted inside health facilities there may possibility of social desirability bias. In order to minimize this effect interview was conducted after the purpose of the study was addressed and it was conducted in separate room [16-33].

Strength of the Study

Different literatures were reviewed to maximize sample, during sample size estimation. Data were collected by those who trained and have an experience on comprehensive TB service in health facilities. Identifying the most important risk factors for TB from the multiple factors may allow more effective allocation of our limited resources.

Conclusion

This study identified the determinant factors that contribute to the development of active Pulmonary TB. Environmental factors like; history of close contact with known TB patient, absence of separated kitchen from the living house, being live in the house without ceiling and being live in the house with mud floor were the major determinants of Pulmonary TB.

The most powerful predictor of Pulmonary TB was having history of close contact with TB patient. Patients who had history of close contact with TB patients were four times more likely to develop active Pulmonary TB than those who had no history of close contact. This shows that close contacts of infectious TB cases including household contacts and health care workers who give care for patients are more likely becoming infected with Pulmonary Tuberculosis.

Furthermore, the place of residence and history of severe acute malnutrition were the most important contributing factors to developing active Pulmonary TB. Therefore, measures taken to reduce the burden of active PTB should consider these contributing factors.

Recommendations

Special focus should be given to reduce the risk of exposure and transmission of PTB by minimizing close contact with known TB patient through contact tracing for early diagnosis and treatment as well as educating the patients on how to protect their family and community. Health extension workers should also provide health education regarding the care of any family members who have developed active PTB to reduce the risk of exposure in other family members.

Government should strengthen the measures to tackle the prevalence of severe acute malnutrition in the community through different approaches and the kitchen should be separate from the main living room and the living houses should have a ceiling.

Other study should be conducted by including other factors not included under this study such as accessibility of health service, attitudes of health care provider and the community to the disease in more broader setting and further cohort studies should be conducted to clearly identify other determinant factors, as the current study could not identify the temporal relationships between predictor variables and outcome variable.

Bibliography

1. FMOH (2013). Guidelines for Clinical and Programmatic Management of TB, TB/HIV and Leprosy in Ethiopia. Fifth Edition, March, 2013.

2. WHO (2017). World Health Organization: Global Tuberculosis Report 2017.

3. WHO (2018). World Health Organization: Global Tuberculosis Report 2018.

4. Daba, S., *et al*. (2017). Tuberculosis Control in Arsi, Ethiopia: Program Performance and Disease Burden, 2017.

5. Mohammed, *et al*. (2018). Prevalence of extra-pulmonary tuberculosis among people living with HIV/AIDS in sub-Saharan Africa. HIV/AIDS - Research and Palliative Care

6. FMOH (2016). Guidelines for Clinical and Programmatic Management of TB, TB/HIV and Leprosy in Ethiopia, 2016.

7. Amare, D., *et al*. (2016). Tuberculosis Burden in Ethiopia from 1990 to 2016: Evidence from the Global Burden of Diseases 2016 Study. *Ethiop J Health Sci., 28*(5), 2018.

8. Mohammed, T., *et al*. (2011). Risk Factors of Active Tuberculosis in People Living with HIV/AIDS in Southwest Ethiopia. *Ethiop J Health Sci., 21*(2).

9. Tesema, *et al*. (2015). Environmental and host-related determinants of tuberculosis in Metema district, north-west Ethiopia. *Drug, Healthcare and Patient Safety*.

10. Zeleke, Z., *et al*. (2015). Predictors of Smear-Positive Pulmonary Tuberculosis in Southern Ethiopia: International Journal of Sciences: Basic and Applied Research: Unmatched Case Control Study.

11. Ephrem, T., *et al.* (2015). Determinants of active pulmonary tuberculosis in Ambo Hospital, west Ethiopia. *Afr J Prm Health Care Fam Med*.

12. World Health Organization (2013). Guideline: Nutritional care and support for patients with tuberculosis.

13. Devan, J., *et al*. (2012). Childhood Tuberculosis and Malnutrition • JID 2012.

14. Semunigus, *et al*. (2016). Smear positive pulmonary tuberculosis and associated factors among homeless individuals in Dessie and Debre Birhan towns, Northeast Ethiopia. *Ann Clin Microbiol Antimicrob*, 2016

15. Padmanesan, N., *et al*. (2013). Risk Factors for Tuberculosis. *Pulmonary Medicine*, 2013.

16. Meseret, S., *et al*. (2016). Socioeconomic Factors Associated with Knowledge on Tuberculosis among Adults in Ethiopia. *Tuberculosis Research and Treatment, 201*6.

17. Shetty, N., *et al*. (2013). An epidemiological evaluation of risk factors for tuberculosis in South India. *Int J Tuberc Lung Dis.,* 2013.

18. Mekonnen, Y. A., *et al*. (2014). Delay for First Consultation and Associated Factors among Tuberculosis Patients in Bahir Dar Town Administration, North West Ethiopia. *American Journal of Health Research, 2014*.

19. Bogale, *et al*. (2017). Factors associated with the length of delay with tuberculosis diagnosis and treatment among adult tuberculosis patients attending at public health facilities in Gondar town, Northwest, Ethiopia. *BMC Infectious Diseases*, 2017.

20. WHO (2016). Global Tuberculosis Report 2016, World Health Organization, Geneva, Switzerland, 2016.

21. Melkamu, H., *et al*. (2013). Determinants of tuberculosis infection among adult HIV positives attending clinical care in western Ethiopia: a case-control study. *AIDS Research and Treatment,* 2013.

22. Mitku, A., *et al.* (2016). Prevalence and associated factors of TB/HIV co-infection among HIV Infected patients in Amhara region, Ethiopia. *Afri Health Sci., 16*(2).

23. World Health Organization (2016). Equity, Social Determinants and Public Health Programs. *Geneva: World Health Organization,* 2010.

24. WHO (2016). World Health Organization; Tuberculosis and diabetes. Geneva: 2016.

25. Pizzol, D., Di Gennaro, F., *et al*. (2016). Tuberculosis and diabetes: current state and future perspectives. *Trop Med Int Health.,* 2016.

26. Denise Rossato, S. (2018). Risk factors for tuberculosis: diabetes, smoking, alcohol use, and the use of other drugs. *J Bras Pneumol.*

27. Edson, W., Mollel, *et al.* (2017). Predictors for Mortality among Multidrug-Resistant Tuberculosis Patients in Tanzania. *J Trop Med.,* 2017.

28. Wen, C. P., Chan, T. C., *et al*. (2010) The reduction of tuberculosis risks by smoking cessation. *BMC Infect Dis.,* 2010.

29. Abebe, D. S., *et a*l. (2011). Assessment of knowledge and practice about tuberculosis among eastern Ethiopian prisoners. *Int J Tuberc Lung Dis., 15*(2), 2011.

30. Fikru, M., *et al*. (2018). Assessment of community knowledge about Tuberculosis and its treatment in rural areas of Shashemane, Southern Ethiopia. *J. Public Health Epidemiol,* 2018.

31. Sarker, M., *et al*. (2017). A Matched Case-Control Study to Identify Risk Determinants of Tuberculosis in Bangladesh.

32. Ndishimye, P., *et al.* (2016). A case control study of risk factors associated with pulmonary tuberculosis in Romania: Experience at a clinical hospital of pneumology. *Clujul Medical*.

33. Abera, A., *et al*. (2018). Pulmonary Tuberculosis and Associated Factors among Diabetic Patients Attending Hawassa Adare Hospital, Southern Ethiopia. *The Open Microbiology Journal,* 2018.