Pulmonary Tuberculosis and Associated Factors among Diabetic Patients Attending at Public Hospital in East Shewa Zone, Ethiopia

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Abstract

Background: Pulmonary tuberculosis as a diabetes co-morbidity is the most challenging issue of tuberculosis control programs across the world. However, there is limited evidence on Tuberculosis's burden and risk factors in people with diabetes. This study aimed to determine the prevalence and associated factors of pulmonary tuberculosis among people with diabetes in East Shewa, Ethiopia.

Methods: A cross-sectional study was conducted among 210 tuberculosis presumptive diabetic patients who were selected using a simple random sample technique from six public Hospitals in East Shewa Zone. Data were collected using a structured questionnaire, record review, and measurements of weight and, height. Sputum specimens were collected and *mycobacterium tuberculosis* was identified using Lowenstein-Jensen culture media. Data were analyzed using SPSS version 22.

Results: The prevalence of pulmonary tuberculosis was 8.6% (95% CI: 5.2% - 12.8%). Being urban dwellers (AOR=5.13; 95% CI: 1.07, 24.47), history of alcohol consumption (AOR = 13.06; 95% CI = 2.23, 76.55), Human immune deficiency virus positive (AOR=7.44; 95% CI: 2.23, 24.87) and duration of diabetes morbidity >5 years (AOR=15.36; 95% CI: 1.85, 127.57) were found to be associated with pulmonary tuberculosis.

Conclusions: This study revealed that the prevalence of pulmonary tuberculosis among people with diabetes was high. Therefore, regular screening for pulmonary tuberculosis is required to improve diabetes care by emphasizing the identified factors.

***Keywords*:** *Pulmonary Tuberculosis*, Diabetes, Risk Factors, East Shewa, Ethiopia

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Introduction

Tuberculosis (TB) is caused by *Mycobacteria tuberculosis* which affects the lungs (pulmonary TB) and spread to other parts of the body (extrapulmonary TB) (Hawn et al., 2014). It affects a quarter of the world's population (Haddad *et al.*, 2018). It is also one of the top ten causes of death worldwide. Every day, over 4000 people die from TB and nearly 30 000 people fall ill with this disease (WHO, 2019). According to the 2018 Global TB Report, Ethiopia is one of the 30th high TB burden countries, with an estimated incidence of 172,000 in 2017(WHO, 2018).

Diabetes mellitus (DM) increases susceptibility and worsens outcomes of TB (Abbas *et al.*, 2022). The biological basis for the association between both diseases is not fully understood but studies suggest that diabetes depresses the immune response, which in turn facilitates infection and/or progression to symptomatic TB (Ayelign et al., 2019; Ferlita *et al*; 2019; Nathella and Babu S. 2017).

The magnitude of pulmonary tuberculosis (PTB) in diabetics has been reported differently over the world. It was reported to be 0.03% in Australian and 0.6% in Korean (Dobler et al., 2012; Yoo et al., 2021). It was slightly higher in African countries, with 3.0% in South Africa and 1.8% in Tanzania (Berkowitz *et al.*, 2018; Makuka *et al.*, 2022).In Ethiopia, the prevalence reported ranged from 5.8%- 6.2% (Feleke *et al*., 1999; Amare *et al*., 2013).

Different factors were found associated with PTB among DM patients. Previous history of TB infection, contact with TB patients in the family, long duration of DM, cigarette smoking, and HIV serostatus were some of the identified factors(Jabbar *et al*., 2006; Wagnew *et*

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al., 2018; Amare *et al*., 2013; Kermansaravier *et al*., 2014; Stevenson *et al*., 2007).

Early detection, intervention, and avoidance of risk factors PTB have an enormous benefit for DM Patients. However there is limited evidence on PTB burden and risk factors in people with diabetes. Therefore, this study aimed to assess the prevalence and associated factors of pulmonary tuberculosis in people with diabetes in East Shewa, Ethiopia.

Materials and Methods

Study Setting, Design, and Period

A cross-sectional study was conducted among adult diabetes patients attending six government Hospitals (Adama Hospital, Bishoftu Hospital, Batu Hospital, Wonji Hospital, Wolenchit Hospital, and Metehara Hospital) in East Shewa Zone from February 13 to May 30, 2017. East Shewa zone is found in the central part of the Oromia Region State. Based on the Central Statistical Agency of Ethiopia (CSA), the zone has a total population of 1, 751, 116, of whom males account for 882,774 (50.4%) and females account for 868,342 (49.6%) (CSA, 2014). The zone had 6 hospitals 6 health centers and 312 health posts. This study was conducted in sex hospitals in the zone which provide care and treatment services to 4569 DM patients.

Population, Inclusion/ Exclusion Criteria

Presumptive TB adult diabetes patients who were being treated at six government hospitals in the East Shewa Zone was the study population.People with diabetes who had a cough for at least two weeks, weight loss, night sweating, and loss of appetite were included in the study. While those patients <18 years of age and those on anti-TB treatment were excluded from the study.

Sample Size and Sampling Technique

The sample size was determined by a single population proportion formula considering the estimated proportion of tuberculosis among adult people with diabetes from the previous study which was 6.2% (Amare et al., 2013) with a 95% confidence interval, and a margin of error of 3.5%. The final sample size was 210 including a non-response rate of 15%. This sample size was allocated proportionally for the six hospitals based on the average number of people with diabetes attending each hospital. Then, participants from each institution who meet the inclusion requirements were selected using a simple random sample technique (Figure 1).

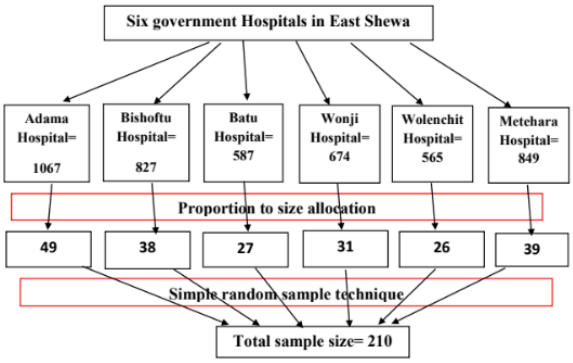

Figure-1; Schematic representation of sampling procedure.

Data Collection Techniques

Data were collected by the following method;

Face-to-face interview: was conducted using structured questionnaire which was used to collect data on socio-demographic characteristics (age, sex, residence, marital status, monthly income, educational status, occupation); clinical factors such as diabetics medication, contact with known TB patients, duration of diabetes mellitus; behavioral factors including history of cigarette smoking and alcohol consumption. The questionnaire was developed by reviewing the literature (Amare *et al*., 2013; Animaw and Seyoum, 2017; Berkowitz *et al*., 2018; Feleke *et al*., 1999; Kermansaravi *et al*., 2014; Masood *et al*., 2016).

Patients' medical records review: Clinical data such as HIV status, type of DM, blood glucose level, and blood pressure of participants were collected from the patient's medical records. Hypertension was defined as blood pressure (SBP≥140 or DBP ≥90mmHg) or receiving an anti-hypertensive agent. Adequate glycemic control was defined as average fasting blood glucose measurement between 70 and 130 mg/dL. Poor glycemic control was defined as patients whose average blood glucose measurements of the three consecutive visits were above 130 or below 70 mg/dL (American Diabetes Association, 2018).

Anthropometric measurements: Height was measured to the nearest 0.5 cm by using a stadiometer while the participants were standing erect against the wall with heels together and touching the wall, and head

held in an upright position. Weight was measured using a digital weighing scale. The scale was calibrated to the zero level before each measurement. Weight was measured with minimum clothes and no footwear on a standardized weighing machine marked from 0 to 130 kg and was recorded to the nearest 0.5 kg. Body mass index (BMI) was calculated using the formula weight in kilograms divided by the square of the height in meters' (weight (kg)/ height (m2)). Then, it was categorized as underweight (BMI <18.5 kg/m^2), normal (BMI=18.5–24.9 kg/m^2), overweight (BMI=25.0–29.9 kg/m^2), and obese (BMI ≥30 kg/m^2) (WHO, 2010).

Sputum collection and examination: Approximately 5ml of one-morning mucoid or mucopurulent sputum sample was collected from each participant following standard sputum collection procedures. Samples were labeled, packed by a triple packaging system, and transported immediately to Oromia Public Health Research Capacity Building Quality Assurance Laboratory. If not, the specimens were refrigerated (2-8^{O}C) to inhibit the growth of unwanted microorganisms. In the laboratory, about 2-5ml of sputum was processed by the standard N-acetylL-cysteine NaOH method and centrifuged at 3000 revolutions per minute for 20 minutes. The sediment was then reconstituted to 3ml with phosphate-buffered saline (PH 6.8) and the suspension was inoculated on egg-based Lowenstein-Jensen culture media. The media was incubated at 37^{O}C for 3-8 weeks by observing weekly for growth. A culture was considered negative when no growth was seen after 8 weeks of incubation.

Data Quality Control

Three days of training were given for data collectors (six Bachelor of Science (BSC) nurses and 6 BSC laboratory professionals) and supervisors (2 BSC public health officers) on how to collect data and sample and supervise the entire activities. The questionnaire was first prepared in English then translated to the local languages (Amharic, and Afaan Oromo), and back-translated to English to maintain the consistency of the questionnaire. Data collection instruments were pretested on 5% of the study participants at Adama Referral Hospital and appropriate modifications were made accordingly. The supervisors carried out daily supervision, spot checks, and reviews of completed questionnaires to ensure the accuracy and consistency of the data. After Lowenstein-Jensen media was prepared 5% of the media was picked up randomly and continued for incubation for 14 days to check for sterility. Standard Operating Procedure (SOP) was sternly followed during sample collection and laboratory testing. The weighting scale was checked for correctness against known weight each day before patients' measurements were started.

Data Processing and Analysis

The completeness and consistency of data were checked manually before entry. The data were double-entered into EPI data version 3.1 and exported to SPSS version 22 for further analysis. The magnitude of PTB was determined as a proportion of study participants with *Mycobacteria tuberculosis* growth in Lowenstein-Jensen media. Multivariable logistic regression analyses were used to identify factors associated with PTB among DM patients. Those variables with p-value < 0.20 in the bivariable analysis were included in the multivariable logistic regression analysis. Those variables with P-value ≤ 0.05 at a 95% confidence interval were considered statistically significant factors associated with PTB.

Ethical Consideration

Ethical clearance was obtained from the Institutional Health Research Ethical Review Committee of Colleges of Health and Medical Sciences, Haramaya University (IHRERC/069/2017). Respondents were fully informed about the purpose of the study and signed their consent. Information obtained during the study was kept confidential. Participants found PTB positive were linked to nearby health facilities to start anti-tuberculosis treatment.

Results

Socio-Demographic Characteristics of Participants

A total of 210 study participants were included in this study. One hundred nine (51.9%) were males. The mean and standard deviation age of the participant was 46.1 (± 13.5) years and ranged from 18 - 86 years. Seventy-eight (37.1%) of them belonged to the age categories between 36 and 50 years. The majority of study participants were rural dwellers (57.6%) and married 159 (75.7%). In terms of their educational status, 65(31%) were diploma and above holders. Regarding their occupational status, 91(43.3%) were government employees. Fifty-two (24.8%) of the study participants had an income of less than 960 ETB (Table 1).

Table 1: Socio-demographic and economic characteristics of people with diabetes in East Shewa, Ethiopia, 2017(n=210)

Characteristics		Number	Percentage
Sex	Male	109	51.9
	Female	101	48.1
Age in a year	18 – 35	52	24.8
	36-50	78	37.1
	51-65	65	31.0
	≥ 66	15	7.3
Residence	Rural	121	57.6
	Urban	89	42.4
Marital status	Single	37	17.6
	Married	159	75.7
	Divorced	3	1.4
	Widowed	11	5.2
Monthly income	≤ 960	52	24.8
in Ethiopian Birr	961- 1500	32	15.2
	1501 – 3500	69	32.9
	>3500	57	27.1
Education of paricipant	Unable to read and write	16	7.6
	Able to read and write	39	18.6
	Primary	40	19
	Secondary	50	23.8
	Diploma and above	65	31
Ocupational status	Un employed	9	4.3
	Student	11	5.2
	Daily laborer	15	7.5
	Farmer	23	11.0
	Housewife	56	26.7
	Employed	96	45.7

Behavioral and Clinical Characteristics

Thirty-five (16.7%) participants had a history of smoking cigarettes and 62(29.5%) had a history of drinking alcohol. More than half (64.8%) had normal BMI (18.5- 24.99 kg/m2) and only 6(2.9%) were obese (> 30 kg / m2). One hundred and twenty-three (58.6%) people with diabetes were type II diabetes mellitus patients,112(53.3%) were using insulin and 93(44.3%) patients had hypertension. Only 13(6.2%) patients had contact with TB patients in the last two years. Twenty-six (12.4%) participants were HIV positive and 102 (48.6%) were live with diabetes mellitus for more than 5 years (Table 2).

Table 2: Behavioral and Clinical characteristics of people with diabetes in East Shewa, Ethiopia, 2017(n=210).

Characteristics		Frequency	Percent
Cigarette Smoking			
	Yes	35	16.7
	No	175	83.3
Alcohol consumption			
	Yes	62	29.5
	No	148	70.5
Body Mass Index (in Kg /M^2)			
	< 18.5	23	11.0
	18.5 - 24.99	136	64.8
	25 - 29.9	45	21.4
	≥ 30	6	2.9
Types of diabetics			
	Type I	87	41.4
	Type II	123	58.6
Diabetics Medication			
	Insulin	112	53.3
	Oral glycemic agents	93	44.3
	Combination of insulin & OGAs	5	2.4
Contact with known TB patients			
	Yes	13	6.2
	No	197	938
Past History of TB Treatment			
	Yes	13	6.2
	No	197	93.8
Hypertension			
	Yes	93	44.3
	No	117	55.7
HIV Status			
	Positive	26	12.4
	Negative	97	46.2
	Unknown	87	41.4
Duration of diabetes mellitus(year)			
	≤ 5	108	51.4
	6 - 10	50	23.8
	> 10	52	24.8
Blood gucose level (n=191)(mg/dl)			
	< 70	2	1
	70 – 130	47	24.6
	>130	142	74.4

HIV; Human immunodeficiency virus, TB; Tuberculosis, OGAs; oral hypoglycemic agents

Prevalence and Factors Associated with PTB

The overall prevalence of pulmonary tuberculosis was 8.6% (95% CI: 5.2%, 12.8%). Variables such as residence, monthly income, occupation status, cigarette smoking, alcohol consumption, types of diabetes, hypertension, HIV infection, and duration of diabetes in the bivariable analysis were included in multivariable logistic regression analysis. Place of residence, alcohol consumption, HIV Status, and duration of diabetes remained independent predictors of PTB. Urban dwellers were 5 times (AOR=5.13; 95% CI: 1.07, 24.47) more likely to develop PTB than rural residents. Those participants who consumed alcohol were 13 times (AOR=13.06; 95%CI: 2.23, 76.55) more likely to develop PTB than those who did not consume

alcohol. Those participants who had diabetes for >5 years were 15 times (AOR=15.36; 95% CI: 1.85, 127.57) more likely to develop PTB than those who have lived with DM for ≤ 5 years. Those HIV-positive participants were 7 times (AOR= 7.44; 95%CI: 2.23, 24.87) more likely to develop PTB than those who were HIV-negative (Table 3).

Table 3: Factors associated with pulmonary tuberculosis among people with diabetes in East Shewa, Ethiopia, 2017(n=210)

Variables	TB-Diabetes Comorbidity		COR (95% CI)	AOR(95%CI)
	No	Yes		
	No. (%)	No. (%)		
Residence				
Rural	116(95.9)	5(4.1)	1	1.00
Urban	76(85.4)	13(14.6)	3.97(1.36 - 11.58)	5.13(1.07 – 24.47)
Occupation				
Unemployed	108(94.7)	6(5.3)	1	1
Employed	84(87.5)	12(12.5)	2.77(0.93 – 7.13)	1.06(0.17 – 6.49)
Monthly income in ETB				
≤ 1500	81(96.4)	3(3.6)	0.32(0.08 – 1.31)	0.55(0.05 – 5.59)
1501 – 3500	60(87)	9(13)	1.28(0.43 – 3.82)	8.85(0.97 – 81.12)
>3500	51(89.5)	6(10.5)	1	1.00
Cigarette smoking				
No	167(95.4)	8(4.6)	1	1.00
Yes	25(71.4)	10(28.6)	8.35(3.01 - 23.16)	2.29(0.45 – 11.81)
Alcohol consumption				
No	144(97.3)	4(2.7)	1	1:00
Yes	48(77.4)	14(22.6)	10.50(3.30 - 33.44)	13.06(2.23 – 76.55)
Hypertension				
No	112(95.7)	5(4.3)	1	1.00
Yes	80(86)	13(14)	3.64(1.25 –10.62)	2.74(0.46 – 16.26)
HIV Status				
Negative	91(47.4)	15(7.8)	1	1:00
Positive	6(13.3)	11(61.1)	11.12(3.57-34.5)	7.44(2.23-24.87)
Unknown	86(44.8)	1(5.6)	0.17(0.02-1.49)	0.18(0.02-1.58)
Duration DM				
≤ 5 years	100(96.2)	4(3.8)	1	1.00
≥ 6 years	92(86.8)	14(13.2)	3.80(1.21 – 11.98)	15.36(1.85 – 127.57)
Diabetics Types				
Type I	83(95.4)	4(4.6)	1	1.00
Type II	109(88.6)	14(11.4)	2.67(0.85 – 8.39)	2.49(0.45 – 13.88)

HIV; Human immunodeficiency virus, CI; Confidence interval; COR; Crude odd ratio; DM; Diabetics mellitus, EB; Ethiopian birr, AOR; Adjusted odd ratio

Discussion

The magnitude of PTB among diabetes patients in selected hospitals in the East Shewa Zone was 8.6%. Being urban dwellers, alcohol consumption, a bit longer duration of diabetes (> 5 years), and being infected with HIV were found independent predictors of PTB among people with DM.The magnitude of TB among people with diabetes was 8.6%. This is in line with reports from India (10.6%) (Nair *et al.*, 2016) and Ethiopia (5.8% and 6.2%) (Amare *et al.*, 2013; Feleke *et al.*, 1999). But the current study finding was higher than the reported from another study reported from Pakistan which was 4.1% (Masood *et al.*, 2016*)*. This difference might be due to laboratory diagnosis, region/study area, and characteristics of study partici-

pants. For instance, the diagnostic method in the Pakistan study was smear microscopy which has a low detection rate (Masood *et al.*, 2016).

Urban dwellers were a predictor of PTB in this study. It was in agreement with previous studies conducted in Ethiopia (Amare *et al.*, 2013), India (Stevenson *et al.*, 2007), and Indonesia (Alisjahbana *et al*., 2006). The possible reasons for this similarity could be because of crowded living conditions in urban areas. Urban dwellers might also have lower levels of physical activity and mostly consume a calorie-rich diet, which increases fat accumulation in the body which might increases insulin resistance, resulting in impairment of the immune cells against TB infection (Lopez *et al*., 2008).

This study identified that a history of alcohol consumption is associated with PTB. Alcohol may assert direct toxic effects on the immune system rendering the host more susceptible to TB disease. Studies suggest that cell-mediated immunity and macrophage functions, which are essential for the host response to *M. tuberculosis* infection, are directly impaired by chronic and acute alcohol consumption (Kany *et al.*, 2019; Lönnroth *et al*., 2008; Malherbe and Messaoudi, 2022). People who abuse alcohol are less likely to eat regularly and healthy meals lead to malnutrition which is an additional risk of contracting TB (Lönnroth *et al*., 2008).

This study also indicated that DM/HIV co-infection patients were more likely to be infected with TB. This finding was consistent with a study conducted in South Africa (Oni *et al*., 2017). This might be due to both DM and HIV suppressing the immune system which in turn increases the risk of contracting new TB infection or reactivation of latent infection. These findings point to the importance of screening for diabetes patients for TB and diabetes/HIV-1 patients, to achieve TB elimination goals. The coexistence of a high prevalence of HIV, TB, and diabetes has significant implications for optimal control of each condition, highlighting the importance of targeting TB control interventions.

The longer duration with DM (> 5 years) had found to be associated with PTB. This finding was in line with studies done in Pakistan (Jabbar *et al*., 2006) and in Dessie, Northeast Ethiopia (Amare *et al*., 2013). This may be because persistently high blood glucose levels weaken immunity, increasing the risk of exposure to opportunistic illnesses like tuberculosis.

This study used the gold standard method of TB diagnosis among people with diabetes was the strength of this study (Gholoobi *et al*., 2014), whereas a cross-sectional nature of the design used could not establish causal relations. In addition, institutional-based studies could not address unidentified diabetes cases in the community.

Conclusion

The prevalence of PTB among people with diabetes was high in the East Shewa Zone, which may have a negative impact on TB prevention and control efforts in countries with high TB-HIV burdens like Ethiopia. Place of residence, alcohol consumption; HIV Status, and duration of diabetes remained independent predictors of PTB. Therefore, pulmonary tuberculosis screening in people with diabetes is required to improve patient care and prevent TB-related morbidity and mortality, specifically, among urban dwellers, alcohol users, HIV positive, diabetes duration of more than five years should be highlighted.

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Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

BB contributed towards conceiving and designing the study, acquisition of the data, analysis, interpretation, drafting and critical revision, and final approval of the manuscript. BS and HM contributed towards conceiving and designing the study, analysis and interpretation and final approval of the manuscript. AB contributed towards acquisition of the data, analysis and interpretation of the data and final approval of the manuscript.

List of Abbreviations

AOR; Adjusted Odds Ratio, BMI: Body Mass Index, CSA; Central Statistical Agency of Ethiopia, CI: Confidence Interval, COR; Crude Odds Ratio, DM: Diabetics Mellitus, EB; Ethiopian Birr, HIV: Human immunodeficiency virus, OGAs; Oral Hypoglycemic Agents, PTB; Pulmonary Tuberculosis, SOP; Standard Operating Procedure, TB; Tuberculosis.

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