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ORIGINAL RESEARCH

Diabetes Mellitus and Tuberculosis Comorbidity and Associated Factors Among Bale Zone Health Institutions, Southeast Ethiopia

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Background: Globally, tuberculosis and diabetes mellitus co-morbidity is higher than tuberculosis and human immunodeficiency virus comorbidity. Considering this, the World Health Organization and the International Union against tuberculosis and lung disease recommend bi-directional screening of the two diseases. However, in Ethiopia, bi-directional screening has not been started yet.

Objective: The objective of this study was to assess the prevalence of diabetes mellitus and tuberculosis comorbidity and its predictors among adult tuberculosis patients in Bale Zone Health Institutions, Southeastern Ethiopia.

Materials and Methods: Institutional-based cross-sectional study carried out using interviewer administered questionnaire, registration review, anthropometric and blood glucose level measurement from March, 30, 2019 to April, 30, 2019. Three hundred twenty-one tuberculosis patients were selected from tuberculosis registration log book using lottery methods. The collected data were checked for completeness, coded and entered in to EpiData3.0.2 and exported to SPSS version 20. Independent variables that had p value less 0.25 were used as candidates for multiple logistic regressions to control confounders. Variables that had significant association were identified by calculating odds ratio, with 95% confidence interval, and p value less than 0.05 used to declare statistical significance.

Results: Diabetes mellitus and tuberculosis comorbidity among adult tuberculosis patients was 5.1% (95% CI: 2.7%, 7.5%). Age with ≥50 years (AOR=3.98, 95% CI: 1.13, 14.36), having extra pulmonary tuberculosis (AOR=3.31, 95% CI: 1.16, 9.44) and being females (AOR=3.8, 95% CI: 1.17, 12.33) were significantly associated with the comorbidity of the two diseases.

Conclusion and Recommendation: The prevalence of diabetes mellitus and tuberculosis comorbidity was high. Female tuberculosis patients, tuberculosis patients with age ≥50 years and those having extra pulmonary tuberculosis patients should be screened for diabetes mellitus.

Keywords: diabetes mellitus, tuberculosis, pre-diabetes mellitus

Background

Globally, a number of people who live with diabetes mellitus (DM) are about 451 million and this number is estimated to be 693 million by 2045.[1] In Africa, about 16 million people have diabetes mellitus and there are about 69.2% undiagnosed diabetes mellitus. In the region, it is projected to be 41 million by 2045.[2]

Diabetes mellitus alters specific cytokines, which have roles in tuberculosis (TB) protection and it is a risk factor for the development of active tuberculosis . The impairment of immune response in patients with diabetes mellitus results in either primary infection with tuberculosis or reactivation of latent tuberculosis.[3]

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In Sub-Saharan Africa, infectious diseases, including tuberculosis are likely to increase in the region due to diabetes mellitus.[4] Diabetes mellitus increases the risk of tuberculosisdevelopment three-fold.[5] Bi-directional screenings of tuberculosis and diabetes mellitus ranges 1.7–36% and 1.9–35% respectively.[6] Another systematic review indicated that the prevalence of DM in TB patients ranged from 1.9% to 45%.[7] Several studies show that diabetes mellitus increases the risk of tuberculosis.[8–12]

A systematic review of Asian countries showed that diabetes mellitus prevalence among tuberculosis patients was between 5% to 50%, whereas tuberculosis prevalence among diabetes mellitus patients was 1.8–9.5 times higher than the general population in developing Asian countries.[13]

A systematic review conducted on diabetes mellitus and tuberculosis comorbidity in most low and middle income countries (LMICs) varies from 1.8% to 45%, with the majority found between 10% and 30%.[14] Factors associated with comorbidity of diabetes mellitus and tuberculosis were age, sex, being pulmonary tuberculosis, being hypertensive, family history of diabetes mellitus, alcohol consumption and residence.

Globally, the number of patients with diabetes mellitus comorbidity is higher than the number of patients with tuberculosis and human immunodeficiency virus coinfection.[15] Considering this, the World Health Organization and the International Union Against Tuberculosis and Lung Disease recommend bi-directional screening of the two diseases.[16]

Several studies indicated that diabetes mellitus and tuberculosis comorbidity results in treatment failure, prolongs sputum positivity, relapse and risk of developing multi-drug resistant tuberculosis and high risk of death.[17–21] Therefore, the present study carried out to assess the prevalence and factors associated with diabetes mellitus and tuberculosis comorbidity in the study area.

Methods

Study Design, Area and Period

An institutional-based cross-sectional study was conducted from March 30, 2019 to April 30, 2019 in Bale Zone Health Institutions, Southeast Ethiopia. Bale Zone is located in Southeastern Ethiopia. The capital city of the Zone (Robe) is 430 Km far from Addis Ababa, capital city of Ethiopia.

Source Population, Sample Size and Sampling Technique

The source population was adult tuberculosis patients in the selected Health Institutions. The sample size was calculated using single population proportion formula. The sample size was calculated using single proportion formula with the assumption of 95% CI and a 5% margin of error and 15.8% prevalence of diabetes mellitus among tuberculosis patients at a St. Peter hospital in Addis Ababa.[34] Then, the calculated sample size became 204 and using a design effect of 1.5 and with addition of five percent non-response rate and the final sample size became 321.

$N=\frac{z^2}{d^2}p\ (1\text{-}P)\ =\frac{1.96^2}{0.05^2}*0.158(1–0.158)\ =204*1.5=306$ with the addition of five percent non-response rate it became 321.

The sampling technique was using a lottery method. Among Bale zone health institutions fifteen health centers and two hospitals were selected using the lottery method. Then for each selected health institutions sample size was allocated proportionally. The simple random sampling technique was used to select the study participants using tuberculosis registration book as the sampling frame.

Data Collection Tools and Procedure

The data were collected using a structured questionnaire adapted from WHO STEPwise instrument and registration review. WHO STEPwise instrument has three sequential steps. First information regarding socio-demographic and behavioral factors was collected using a questionnaire adapted from the WHO STEPwise instrument. Then, after anthropometric measurement and finally, blood glucose level measurement was done. The patients, height were measured with their removal of foot wear and head gear and recorded in centimeter. Weight of the patient was also measured with removal of foot wear and recorded in kilograms. Finally, all patients diagnosed as having active TB was screened for DM through measurement of fasting blood glucose (FBG) level using glucometer. Diabetes mellitus was diagnosed if the fasting blood glucose level (FBG) level was ≥ 126 mg/dl at 2 different time points.

Data Quality Issues

The questionnaire was first translated from English to Afan Oromo (local language) and then retranslated to English language. Data collectors were fluent speakers of Afan Oromo (local language) and Amharic. Training was

given for data collectors and supervisor for two days on the objective, relevance of the study and confidentiality of information. Data collection tools were pretested on 5% of the study subject out of the selected Health facility.

Data Processing and Analysis

The questionnaire was checked, cleaned, coded and entered to Epidata 3.0.2 and analyzed by using SPSS version 20. A binary logistic regression model was primarily used to see the association of independent variables with diabetes mellitus and tuberculosis comorbidity. Variables that had an association with diabetes mellitus and tuberculosis comorbidity (at p value of less than 0.25) in bi-variable logistic regression were entered in to the multivariable logistic regression model to control the effects of confounders.

Finally, the variables that had significant association were identified by calculating odds ratio, with 95% confidence interval, and p- value less than 0.05 was used to declare statistical significance.

Results

Socio-Demographic Characteristics of Tuberculosis Patients on Follow-Up at Bale Zone Health Institutions, Southeast Ethiopia, 2019 (N=316)

In this study, tuberculosis patients who were on directly observed treatment among health institutions of Bale zone participated. The response rate of the study was 316 (98.4%). Among the study participants, 172 (52.5%) were males. The mean age of the study participants was 32.7±14.69 years. The majority of the study participants were urban dwellers 199 (63%) and most of study participants 188 (59.5%) were in the age group of 25–44 years (Table 1).

Table 1 Socio-Demographic Characteristics of Tuberculosis Patients on Follow-Up at Bale Zone Health Institutions, Southeast Ethiopia, 2019 (N=316)

Characteristics	Number	Percent
Age		
≤24	78	24.7%
25–44	188	59.5%
45–64	41	13%
≥65	9	28%
Sex		
Male	172	54.4%
Female	144	45.6%
Residence		
Rural	117	37%
Urban	199	63%
Education		
No formal education	79	25%
Primary	144	45.6%
Secondary	37	11.7%
Diploma graduate	6	1.9%
Degree and above	50	15.8%
Marital status		
Single	82	25.9%
Married	220	69.6%
Widowed	9	2.8%
Divorced	5	1.6%
Occupation		
Farmer	98	31%
House wife	99	31.3%
Government employee	37	11.7%
Non-government employee	35	11.1%
Daily laborer	47	14.9%

Prevalence of Diabetes Mellitus and Tuberculosis Comorbidity Among Tuberculosis Patients at Bale Zone Health Institutions, Southeast Ethiopia, 2019 (N=316)

In this study, the prevalence of diabetes mellitus and tuberculosis comorbidity was 5.1% (2.7–7.5%). Diabetes mellitus and tuberculosis comorbidity distribution among sex, age category and type of tuberculosis (Figure 1).

Health and Behavioral Factors Among Tuberculosis Patients at Bale Zone Health Institutions, Southeast Ethiopia, 2019 (N=316)

In this study, about 21 (6.6%) of study participants consumed alcohol within the past 12 months. Regarding tuberculosis among the study participants pulmonary tuberculosis and extra tuberculosis patients were 233 (73.7) and 83 (26.3%) respectively (Table 2).

Factors Associated with Diabetes Mellitus and Tuberculosis CoMorbidity

Both bi-variable and multiple logistic regressions were carried out. Variables with p value of ≤ 0.25 were used

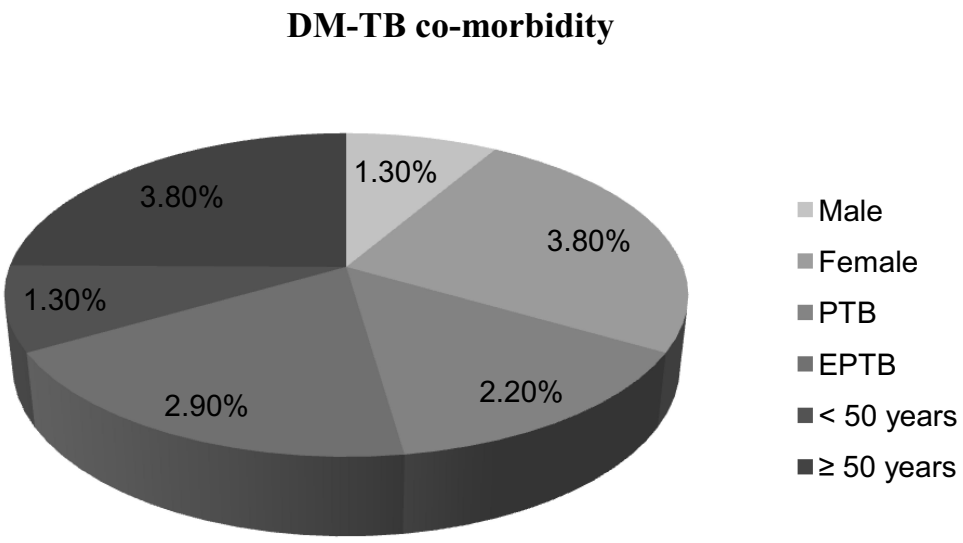

Figure 1 Diabetes mellitus and tuberculosis comorbidity among sex, age category and type of tuberculosis among study participants of Bale zone health institutions, Southeast Ethiopia (n=316).

as candidates for multiple logistic regressions. According, variables that were used in bi-variable logistic regressions were age, sex, residence, type of tuberculosis and education status. However, in multiple logistic regressions having extra pulmonary tuberculosis, being females and age equal to or older than fifty years were factors associated with diabetes mellitus and tuberculosis comorbidity (Table 3).

Discussion

The present study was carried out among 316 adult tuberculosis patients who were on follow-up at selected Health Institutions of Bale Zone. The response rate was 97.8%. Diabetes mellitus and tuberculosis has bi-directional association. Diabetes mellitus can cause tuberculosis due hyperglycemia damage cytokines that have roles in tuberculosis prevention.

In the present study, the prevalence of diabetes mellitus and tuberculosis comorbidity was 16 (5.1%). This finding was consistent with study conducted in Pakistan (5.69%),[22,23] Gujarat in India (6.5%),[23] Nigeria (5.5%)[24] and Lusaka in Zambia (5%).[25] The finding of this study was higher compared to studies conducted in Sri Lanka (2%),[26] Mozambique (1%)[27] and Egypt (2.09%).[28] The possible reason might be due study area and also might be due methods used to screen for diabetes mellitus. Screening of diabetes mellitus using different methods can affect the prevalence. In the present study diabetes mellitus were screened using capillary blood. This might increase the prevalence as it might be affected with stress.

However, the finding of this study was lower compared to study conducted in Nepal (9.1%),[29] Vietnam (13.7%),[30] in Madhya Pradesh in India (15.4%),[31] tribal South India (15%),[32] in Bhopal in India,[33] Kerala in India (24%),[34] Beijing in China (16.2%),[35] Uganda (8.5%),[36] Sri Lanka (22.5%)[37] and Lagos in Nigeria (12.3%).[38] This difference of prevalence compared to these countries might be due to socio-demographic difference and might be also due to socio-economic difference.

The prevalence of this study was also lower compared to studies conducted in St. Peter hospital, Addis Ababa (15.8%),[25] in Gondar, Gondar teaching and referral hospital (8.5%),[24] and in Amhara Region (8.3%).[23] The possible reason might be due time of screening tuberculosis patients for diabetes mellitus. Screening of tuberculosis patients for diabetes mellitus during their presentation might be hyperglycemic due to severity of illness. Another possible reason might be also due to study areas. Since the prevalence of diabetes mellitus has difference between urban and rural. Sample size might be also a possible reason for the discrepancy of the prevalence.

Factors associated with diabetes mellitus and tuberculosis co-morbidity in the present study both in binary logistic regressions and multiple regressions were being female, age equal to or older than 50 years, and having extra pulmonary tuberculosis. Accordingly, the odds of being diabetes mellitus and tuberculosis co-morbidity

Table 2 Health and Behavioral Characteristics Among Tuberculosis Patients at Bale Zone Health Institutions, Southeast Ethiopia, 2019 (N=316)

Characteristics	Number	Percentage
Family history of Diabetes mellitus		
Yes	1	0.3%
No	315	99.7%
Previously known hypertension		
Yes	2	0.6%
No	314	99.4%
TB treatment duration		
≤ 2 months	117	37%
>2 months	199	63%
Type of TB		
Pulmonary TB	233	73.7%
Extra pulmonary TB	83	26.3%
TB-HIV co-infection		
Yes	12	3.8%
No	304	96.2%
Physical activity		
Yes	38	12%
No	278	88%
Alcohol consumption		
Yes	21	6.6%
No	295	93.4%

were about four times more likely among tuberculosis patients with age of equal to or older than 50 years patients compared to those with age of less than 50 years old tuberculosis patients (AOR=3.98, CI: 1.11–14.3). The possible reason might be due lack of physical activity during the age of old age.

This finding was in line with study conducted in Pondicherry in India and in Nepal.[37,39] On the other hand, being female was also significantly associated with diabetes mellitus and tuberculosis comorbidity.

The odds of diabetes mellitus and tuberculosis comorbidity among tuberculosis were about four times more likely compared to male tuberculosis patients (AOR=3.7, CI: 1.14–12.16). The possible reason might be due gestational diabetes mellitus during her previous pregnancy and this might be a risk factor for developing diabetes mellitus.

This finding was comparable with study conducted in Egypt[28] and Amhara Region.[23] However, the present study was inconsistent with study conducted in Bhopal India and Italy. In Bhopal and Italy being males were significantly associated with diabetes mellitus among tuberculosis patients. This inconsistency might be due to the difference of behavioral factors across different regions. In some regions male and female behavioral factors are different. This difference might result different association regarding diabetes mellitus and sex.

Table 3 Factors Associated with Diabetes Mellitus and Tuberculosis Comorbidity Using Both Bi-Variable and Multiple Logistic Regressions Analysis Among Tuberculosis Patients at Bale Zone Health Institutions, Southeast Ethiopia, 2019 (N=316)

Variables	Diabetes Mellitus		95% COR	95% AOR	P value
	Yes	No			
Sex					
Male	4	168	1		
Female	12	132	3.8 (1.2,12.3)	3.73 (1.14,12.16)	0.029*
Age (years)					
<50	4	277	1		
≥ 50	12	23	4.03 (1.13,8.58)	3.98 (1.11,14.3)	0.034*
Education status					
No formal education	7	73	1		
Formal education	9	227	0.41 (0.15,1.15)	0.64 (0.21,1.97)	0.44
Residence					
Urban	7	192	1		
Rural	9	108	2.29 (0.83,6.31)	2.03 (0.68,6.01)	0.44
Type of TB					
PTB	7	226	1		
EPTB	9	74		3.31 (1.16, 9.44)	0.025*

Note: *p value <0.05.

Having extra pulmonary tuberculosis was also associated with diabetes mellitus and tuberculosis comorbidity. In the present study the odds of being diabetes mellitus and tuberculosis co-morbidity among extra pulmonary tuberculosis were about three times more likely compared to pulmonary tuberculosis patients (AOR=3.31, CI: 1.16–9.44). This finding was consistent with a study conducted in United Kingdom.[39] However, the present study was inconsistent with study conducted in Bhopal in India and in South East of Amhara Region.[33,40] The possible reason for this might be due extra tuberculosis can affect pancreas and this can result in developing diabetes mellitus.

Conclusion

The prevalence of diabetes mellitus and tuberculosis comorbidity among adult tuberculosis patients in the present study was high. In the present study age with equal to or older than fifty years, having extra pulmonary tuberculosis and being females were significantly associated with diabetes mellitus and tuberculosis comorbidity.

Strength and Limitation of the Study

The strength of the study was that patients from both health centers and hospitals were included and its limitation was using capillary blood to screen for diabetes mellitus. Therefore, it was better if hemoglobin A1c used to screen for diabetes mellitus.

Abbreviations

AOR, adjusted odds ratio; COR, crude odds ratio; DM, diabetes mellitus; LMIC, low and middle income countries; TB, tuberculosis; WHO, World Health Organization.

Data Sharing Statement

The data sets of the current study were available from the corresponding author on reasonable request and these data sets will be deidentified.

Ethical Approval and Consent to Participate

This study was conducted in accordance with Declaration of Helsinki. Ethical clearance was obtained from Jimma University, Institutional Review Board. Written consent was obtained from the study participants after explaining the purpose of the study and the benefits. Respondents were interviewed voluntarily and confidentiality was assured.

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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 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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Disclosure

The authors have no conflicts of interest.

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