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Prevalence of Diabetes Mellitus among Active Pulmonary Tuberculosis Patients at St. Peter Specialized Hospital, Addis Ababa, Ethiopia

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Abstract: Background the merging epidemics of pulmonary tuberculosis (PTB) and diabetes mellitus (DM) have been raised concerns by many experts but no large scale screening and intervention have been launched yet, especially in low-income countries like Ethiopia. The thought that tuberculosis could cause diabetes seems farfetched, but is not. The peculiar relationship and frequent association of diabetes mellitus and tuberculosis has been observed for more than 2000 years, yet the reason for this correlation is, to this day, not known. Objective the aim of this study was to determine the prevalence of diabetes mellitus among active PTB patients at St. Peter hospital. Methods/design a cross-sectional Hospital based study was carried out and the study included all active pulmonary tuberculosis patients visiting St. Peter specialized hospital until the required sample size was obtained. We included 120 active PTB patients: 67 of these were male and 84 of them were urban dwellers. Analysis of fasting blood glucose was carried out using venous blood samples by enzymatic colorimetric test for glucose (GOD-PAP Method). For testing significance, the categorical data were compared using a chi-square test and expressed as proportion with a 95% confidence interval. Result the prevalence of DM was found to be 15.8% (95% CI:9.20-22.45), which was higher (25.4%) among male than female TB patients(3.8%).Likewise 70% of the patients were from urban and 30% of them were from rural areas. The prevalence of newly diagnosed diabetic cases was 84.2% of all patients tested positive for DM. And all of the patients diagnosed as diabetic were in the age group greater than 25 years of age. The prevalence of IFG was (26.7%) and that of HIV co-infection in the study population was (52.5%). The occurrence of DM in HIV co-infection was a little bit higher (15.9%) than HIV negative TB patients (15.8%). Of all patients with active tuberculosis, 60 (50%) were sputum smear negative. The proportion of DM was (25%) among smear positive and (6.7%) among smear negative patients. Conclusion the prevalence of diabetes mellitus and pre-diabetes (IFG) among active pulmonary tuberculosis cases was higher compared to the published prevalence of DM in Ethiopia. Therefore, it is important to implement a screening program of each TB patient for diabetes and Vis versa.

Key words: TB/DM · IFG · HIV Co-Infection

INTRODUCTION

It has been projected that the prevalence of diabetes mellitus among adults worldwide will more than double, from 135 million to 300 million by the year 2025. The major part of this tremendous increase will occur in developing countries, where an increase from 84 million to 228 million was projected [1]. The prevalence of diabetes in Ethiopia is estimated to be 2% nationally, evidence suggests that its prevalence could be >5% in those older than 40 years of age in some settings [2].

Tuberculosis remained to be a major cause of morbidity and mortality throughout the world [3]. It still ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus [4]. WHO Global TB Report

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showed Ethiopia had an estimated incidence rate of 261 cases per 100,000 population and 29 thousands deaths, with an estimated prevalence rate of 394 cases per 100,000 populations [5]. Ethiopia is a country with about 90 million people and ranks third in Africa and eighth in the list of 22 high burden countries severely affected by tuberculosis [6].

The connection between DM and TB has even been reported to be more significant than the well recognized connection between HIV/AIDS and TB [7]. The growing prevalence of diabetes poses a challenge for TB control as uncontrolled diabetes leads to a greater risk of developing TB [8]. Several studies have looked at the association between diabetes and tuberculosis in developed countries and found that people with diabetes are around 2.5 times more likely to develop tuberculosis [9,10].These findings were also true of developing regions including Africa where the prevalence of diabetes was twice as high in people with tuberculosis than in people without tuberculosis [11]. Eight of the ten countries with the highest incidence of DM worldwide are also classified as high burden countries for TB by WHO; as a result, a growing number of patients with TB will present with DM [12].Despite the evidences which support DM as a risk factor for TB, no large scale research has been done in Ethiopia. Therefore, this study aimed to assess the prevalence of DM and associated risk factors of TB like HIV, smoking and alcoholism on patients with active pulmonary TB.

MATERIALS AND METHODS

Study Design and Area: A cross-sectional study was conducted at St. Peter specialized hospital which serves as a referral TB hospital in Addis Ababa Ethiopia. The hospital has DOTS (Directly Observed Treatment, Short course) follow up clinic and wards. The hospital provides various services especially in tuberculosis diagnosis and treatment and has a vision to become Center of Excellence for diagnosis and treatment of TB in East Africa.

Study Period: A cross-sectional study was employed to determine the prevalence of DM among active PTB patients from February 2014 to May 2014.

Study Subjects: This cross-sectional hospital-based study was conducted among patients with active pulmonary TB admitted in the wards and from DOTS follow up clinic of age 15 years and above. All eligible subjects with active TB cases during the study period were included.

Sampling: The samples size for the study was determined by assuming the prevalence of DM in patients with TB to be 8.5% [13] and a 5% level of significance. Accordingly the calculated final sample size was found to be 120.

All consecutive subjects with active pulmonary TB who volunteered to participate and signed a written consent were enrolled. The diagnosis of pulmonary TB was made according to the national guideline using sputum smear microscopy for acid fast bacilli (AFB), clinical presentation and imaging features.

Screening for DM and HIV: All patients diagnosed as having active pulmonary TB were screened for DM through history, previous medical records and measurement of fasting blood glucose (FBG) concentrations.

DM was diagnosed if the FBG concentration was ≥ 126 mg/dL at 2 different time points; FBG concentrations of 110–125 mg/dl were considered to indicate impaired fasting glucose (IFG), in accordance with the International Diabetes Federation (IDF) criteria [3, 4]. Blood was collected from each subject for fasting blood glucose testing. HIV testing was carried out for all patients with TB according to the hospital routine for provider initiated HIV testing and counseling practice. Prevalence estimations of diabetes were made for all study subjects and similar prevalence was determined based on HIV status, residence (For urban and rural) and age, past history of diabetes, smear status and sex among TB-DM cases directly from our study data.

Measurement and Data Collection

Data Collection Tools: Participant's Socio demographic variables and risk factors of DM was carefully collected using pre-tested standard questionnaire to obtain relevant information. No personal identifier was included; each individual given a unique code numbers on the questionnaire and laboratory specimens. The data for the study was derived from laboratory results and questionnaires.

Specimen Collection and Laboratory Investigation: After obtaining informed consent, 5 ml of fasting venous blood was drawn under aseptic conditions from peripheral vein by experienced nurses. Samples from confirmed TB

patients at two different points were collected, allowed to clot, centrifuged at 3000 RPM for 5 minutes at room temperature; the serum was separated and tested immediately to look for the blood glucose level. Results with abnormal blood glucose (≥126mg/dl) and those between 110 & 125 were communicated with the hospital clinicians for further evaluation and treatment.

Statistical Analysis: Data was entered into Microsoft Excel sheets and exported to software STATA Version 11 for analysis. The data was summarized and organized using graphs, tables and texts. The chi square was used to see the association. Odds ratios (OR) and their 95% confidence intervals (CI) were estimated using bivariate and multivariate logistic regression analysis to identify possible explanatory variables on occurrence of DM. The result at p-value <0.05 was considered as statistically significant.

Ethical Considerations: Before starting the study, ethical clearance was obtained from the ethical review committee of Addis Ababa University College of health Sciences, Department of Medical Laboratory Sciences and St. Peter specialized hospital. Information about the study was given to all TB. Patients and assured about the confidentiality, protection and anonymity of data and are only for research purposes. Written informed consent was obtained from voluntary study participants.

Information obtained at any course of the study was kept confidential. Those participants with blood glucose level ≥126 mg/dl were referred to physicians for proper management, further investigations and follow-up.

RESULTS

Socio-Demographic Characteristics of TB Patients Screened for DM: Of the total 120 active pulmonary TB cases, 67 (55.8%) were male and 53(44.2) were female. In terms of residence place, 84 (70.0%) of them were urban dwellers and the rest 36 (30.0%) were from rural settings. The mean age (±SD) of the study group was 37.3 (±13.3) ranging from 15 to 86 years. The majority of the participants 74(61.7%) were between the age of 25 to 44 followed by 45 to 64 25(20%), ≥24 14(11.7%), =65 7(5.8%). More than half of the respondents 71 (59.2%) were married, whereas 3 (2.5%) were divorced and 2 (1.7%) of them were widowed. In terms of literacy, 65 (54.2%) of the respondents had no formal education and just completed primary school; and the rest (45.8%) either completed high

Table 1: Socio-demographic characteristics of study participants at St. Peter hospital, 2014 (N=120)

Characteristics	No (%)
Age	
≤ 24	14 (11.7)
25-44	74 (61.7)
45-64	25 (20.8)
≥65	7 (5.8)
Sex	
Male	67 (55.8)
Female	53(44.2)
Residence	
Urban	84 (70.0)
Rural	36 (30.0)
Education	
No formal education	37 (30.8)
Grade 1-6	28 (23.3)
Grade 7-12	43 (35.8)
Diploma & above	12 (10)
Total	
Marital status	
Single	44 (36.7)
Married	71 (59.2)
Widowed	2 (1.7)
Divorced	3 (2.5)
Occupation	
Self employed	86 (71.7)
Gov. / pvt. Employed	24 (20)
Student	7 (5.8)
Unemployed	3 (2.5)

Table 2: Distribution of Health related characteristics of study subjects by sex at St. Peter hospital, 2014 (N=120)

Characteristics	Total no (%)	Male n (%)	Female n (%)
HIV/AIDS status			
HIV positive	63 (52.5)	31(49.2)	32(50.8)
HIV negative	57 (47.5)	36 (63.2)	21 (36.8)
FBG level			
70-109	67 (55.83)	35 (50.7)	34 (49.3)
110-125	32 (26.7)	14 (43.7)	18 (56.3)
≥126	19 (15.8)	17 (89.5)	2 (10.5)
Smoking			
Yes	18 (15)	16 (88.9)	2 (11.1)
No	102 (85)	51 (50)	51 (50)
Drinking alcohol			
Yes	58 (48.3)	45 (77.6)	13 (22.4)
No	62 (51.7)	22 (35.5)	40 (64.5)
Sputum smear test for AFB			
Positive	60 (50.0)	39(65.0)	21 (35.0)
Negative	60 (50.0)	28 (46.7)	32 (53.3)
History of diabetes			
Yes	3 (2.5)	3 (1.0)	0 (0)
No	117 (97.5)	64 (54.7)	53 (45.3)
Former diabetes status			
Diabetic	3 (2.5)	3 (1.0)	0 (0)
Not diabetic	117 (97.5)	64 (54.7)	53 (45.3)
Habit of physical exercise			
Yes	65 (54.2)	39 (61.5)	26 (38.5)
No	55 (45.8)	28 (50.9)	28 (49.1)

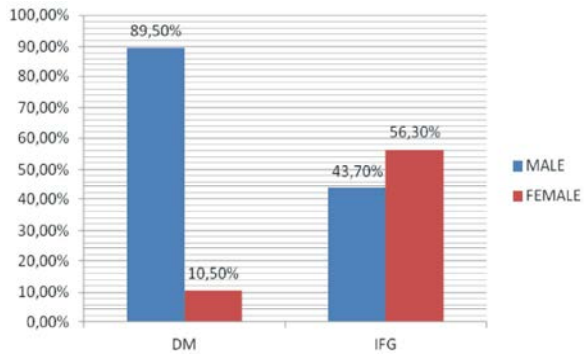

Fig. 1: Prevalence of DM and IFG by sex

school or higher education. Regarding occupational status, 86 (71.7%) respondents were self employed, 24 (20%) were government/ private employed, 7 (5.8%) were student and 3 (2.5%) were unemployed (Table 1).

Risk Factors Associated with TB Patients Screened for DM: The prevalence of previously known DM and that of having family history of DM among TB patients was 2.5% and all of them were male. Among TB patients having family history of DM 66.7% were diabetic while (33.3%) were non- diabetic (Table 2). Therefore, those with family history of diabetes were more prone to become diabetic. The prevalence of DM was 15.8% [95%CI: 9.20-22.45] among patients with pulmonary TB cases and all of them were in age group greater than 25years.

The prevalence of DM among the male was 89.5% and among the female was 10.5 %. (Fig. 1). Likewise, 70% of the participants were from urban areas and 30% from rural settings. DM was higher in urban residents (21.4%) than rural residents (2.8%). Newly diagnosed DM account for 84.2% of all patients tested positive for DM. Of the study subjects, 60 (50.0%) were sputum smear negative for AFB at baseline and DM was higher in smear positive subjects (25.0%) than smear negative (6.7%).

The prevalence of IFG among patients with active pulmonary TB was 32 (26.7%); which was higher in subjects from urban residence (68.8%) compared with those from rural areas (31.3%). The Prevalence of IFG was (56.3%) among women and (43.7%) among men.

Table 3: Seroprevalence of diabetes mellitus in relation to socio demographic characteristics and HIV among active tuberculosis study subjects at St. Peter hospital, 2014 (N=120)

Variables/Characteristics	No (%)	Diabetic cases no (%)	Chi square test value	P-value
Age				
≤24	14 (11.6)	0 (0)	4.2903	0.232
25-44	74 (61.7)	14 (18.9)		
45-64	25 (20.8)	3 (12.0)		
≥65	7 (5.8)	2(28.6)		
Sex				
Male	67 (55.8)	17(25.4)	10.3597	0.001*
Female	53 (44.2)	2 (3.8)		
Education				
No formal educated	37 (30.8)	3 (8.1)	2.7475	0.432
Grade 1-6	28 (23.3)	5 (17.9)		
Grade 7-12	43 (35.8)	8 (18.6)		
Diploma and above	12 (10)	3 (25.0)		
Marital status				
Single	44 (36.7)	9 (20.5)	1.8086	0.613
Married	71 (59.2)	10 (14.1)		
Widowed	2 (1.7)	0 (0.0)		
Divorced	3 (2.5)	0 (0.0)		
Residence				
Urban	84 (70.0)	18 (21.4)	6.5778	0.010*
Rural	36 (30.0)	1 (2.8)		
Occupation				
Self employed	86 (71.7)	12 (13.9)	5.3109	0.150
Gov. / pvt. Employed	24 (20)	7 (29.2)		
Student	7 (5.8)	0 (0.0)		
Unemployed	3 (2.5)	0 (0.0)		

Table 4: Seroprevalence of diabetes mellitus in relation to related risk Factors of the study subjects, St. Peter specialized hospital Addis Ababa, 2014.(N=120)

Characteristics	No (%)	Diabetic cases no (%)	Chi square test value	P-value
HIV/AIDS status				
HIV positive	63 (52.5)	10 (15.9)	0.0002	0.990
HIV negative	57 (47.5)	9 (15.8)		
Smoking				
Yes	18 (15)	5 (27.8)	2.2671	0.132
No	102 (85)	14 (13.7)		
Drinking alcohol				
Yes	58 (48.3)	12 (20.7)	1.9866	0.159
No	62 (51.7)	7 (11.3)		
Sputum smear test for AFB				
Positive	60 (50.0)	15 (25.0)	7.5664	0.006*
Negative	60 (50.0)	4 (6.7)		
History of diabetes				
Yes	3 (2.5)	2 (66.7)	5.9662	0.015*
No	117 (97.5)	17 (14.5)		
Habit of physical exercise				
Yes	65 (54.2)	12 (18.5)	0.7351	0.391
No	55 (45.8)	7 (12.7)		

Table 5: Multivariate analysis on seemingly significant predictors of DM in bivariate analysis, St. Peter specialized hospital Addis Ababa, 2014 (120)

Characteristics	Crude odds ratio (95% confidence interval)	P-value	Adjusted odds ratio (95% confidence interval)	P-value
Sex				
Female	1	0.005	1	0.032*
Male	8.67 (1.90-39.49)		5.61(1.16-27.03)	
History of diabetes				
No	1	0.049	1	0.057
Yes	11.76 (1.0-137.00)		24.59(.91-665.57)	
Sputum smear test for AFB				
Negative	1	0.010	1	0.029*
Positive	4.66(1.44-15.04)		4.52(1.16-17.51)	
Residence				
Rural	1	0.031	1	0.061
Urban	9.54(1.22-74.51)		8.74(.9-84.23)	

Socio Demographic Characteristics in Relation to Diabetes Mellitus: Bivariate logistic regression was used to identify possible explanatory (Independent) variables. As a result, sex (P=0.001) and place of residence (P = 0.010) were significantly associated with the occurrence of DM. On the other hand, age (P=0.232), educational status (P = 0.432), occupational status (P = 0.432) and marital status (P = 0.613), were not significantly associated with the development of DM (Table 3).

Risk Factors Associated with Diabetes Mellitus: Bivariate logistic regression of possible risk factors of DM showed that smear positive (P=0.006) and past history of DM (P=0.015) were significantly associated with the occurrence of DM. The rest, HIV sero-status (P=0.990), smoking (P=0.132), drinking alcohol (P=0.159) and habit of physical exercise (0.391) were not significantly associated with the occurrence of DM (Table 4).

Seemingly significant values (P ≤ 0.05) on socio-demographic characteristics and associated risk factors were taken to multivariate logistic regression. As a result only sex (P=0.032) and smear status (P=0.029) were significantly associated with the occurrence of DM.

On the other hand, past history of diabetes (P=0.057) and place of residence (P=0.061) were not significantly associated with the occurrence of DM. Men were about six times (AOR = 5.6; 95% CI = 1.16-27.03) more likely to develop DM than women. Patients with smear positive were also five times (AOR=4.5; 95% CI=1.16-17.51) more likely to develop DM than smear negative patients. (Table 5).

DISCUSSION

In this hospital based cross-sectional study the prevalence of DM was higher among patients with active PTB; it is six times higher than the estimated prevalence

of DM in Ethiopia (2-3%) [13]. Our finding is in line with reports of almost similar prevalence from Maryland, USA (14%), India, Bangalore (15.9%) and Mexico (17.8%) [14- 16]. And also reports of high prevalence from Pakistan (19.8%), India, Kerala (21%), Texas (27.8%) and southern Mexico (29.6%) [14, 17, 18]. Additionally there are reports of lower prevalence than our finding from Nigeria (1.9%), China (3.2%), India (5-5.8%), Tanzania (7.81%) and Uganda (8.5%) [15, 19-22]. The wide range of prevalence of DM in different studies might be due to the difference in socio-demographic characteristics of source populations in the localities studied.

The higher prevalence of DM among patients with TB was associated with male study subjects, urban dwellers, smear positive and HIV co-infected ones. The high prevalence of DM in smear positives was also comparable with studies in Texas (24.2%) and low prevalence (5.82%) from India [19, 23]. And also high prevalence of DM in the males was very close to the findings in India (90.9%) very low report from Ethiopia (11.1%) [24- 26]. The increased prevalence among male study subjects might be due to risk factors like drinking alcohol and smoking which are more widely practiced among men than women and are assumed to cause different metabolic disorders including DM [27]. The observed rise in the prevalence of DM in urban areas can be explained by rapid urbanization, overcrowded living conditions and the high HIV co-infection rate in the study areas [21].

This study also demonstrated the proportion of new cases of DM (84.2%) by screening for DM in patients with pulmonary TB. A similar study conducted in Tanzania, Gondar, Ethiopia and India showed high prevalence (61%-73%), (53%) and (9%-20%) of undiagnosed DM among new pulmonary TB cases respectively [17, 24, 25]. This high proportion of undiagnosed cases may indicate less awareness of DM by the public and lack of access to health care services for the diagnosis of DM [13, 17, 27]. Therefore, the finding of this research call for the implementation of active case finding of DM in patients diagnosed for TB and also for the integrating of TB and DM care programs. The overall proportion of IFG among TB cases was higher. The reason for this finding is not clear and could be a random occurring but in line with some of lower studies from Pakistan (2%) and USA (22%) [29, 30] and higher reports done in Gondar, Ethiopia (29.6%) Tanzania (37.6%) and Pakistan (41%) [25, 31, 32].

The prevalence of DM in patients with HIV co-infected active PTB cases was high. In line with this research, other studies indicated that the prevalence of TB cases to become diabetic was 4 times higher among HIV co-infected patients when compared with HIV negative TB patients [13, 33]. The increased prevalence of DM in HIV patients can contribute to the increased prevalence of active PTB.

Our study also demonstrated that among study participants having family history of DM 66.7% were diabetic. This observation may tell us there is a transfer of genetic makeup from family to their offspring. On the other hand we found 15% of smokers; of which male accounts for 88.9%. And this study demonstrated 48.3% of drunker; among these 77.6% were male.

High prevalence of DM was found amongst younger TB patients (25-44 years of age) and smear positive cases. In agreement with this finding, a study conducted in Mexican-American and Europeans revealed higher prevalence among younger people with incidence of TB background [17, 22 and 34]. Usually incidence of DM increases with age; but from our finding we have seen how much TB increases the chance of developing DM even at early ages. So this increased prevalence of TB-DM in the younger people will negatively affect TB control program and will become another burden to health service systems.

CONCLUSION

The prevalence of diabetes mellitus and impaired fasting glucose (IFG) among active pulmonary tuberculosis cases was higher compared to the published prevalence of DM in Ethiopia.

High prevalence of DM was found amongst younger TB patients (25-44 years of age); the increased prevalence of TB-DM in the younger people will negatively affect TB control program and will become another burden to health service systems.

Consent: All authors declare that ‘written informed consent was obtained from the patient for publication of this research article.

Competing Interests: There was no conflict of interest among the authors or with any other parties.

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