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High magnitude of diabetes mellitus among Active Pulmonary Tuberculosis Patients in Ethiopia

Assefa Getachew[1], Solomon Mekonnen[2*], Shiatye Alemu[3] and Hanan yusuf[3]

[1]Department of Radiology, College of Medicine and Health Sciences, University of Gondar, Ethiopia.
[2]Department of Physiotherapy, College of Medicine and Health Sciences, University of Gondar, Ethiopia.
[3]Department of Internal Medicine, College of Medicine and Health Sciences, University of Gondar, Ethiopia.

Authors' contributions

This work was carried out in collaboration between all authors. Authors SM and AG conceived and designed the study. Author SM analyzed the data and wrote the draft manuscript. Author AG commented on the final manuscript. Authors SA and HY commented on the manuscript. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aim: The main aim of this study was to determine the prevalence of diabetes mellitus in patients with active pulmonary tuberculosis at the University of Gondar Teaching Referral Hospital, northwest Ethiopia.
Study Design: A cross-sectional hospital-based study was performed using the WHO structured diabetic assessment protocol.
Place and Duration: The study included all active pulmonary tuberculosis patients visiting the University of Gondar Teaching Referral Hospital during the study period (October 2011 to November, 2012).
Methodology: We included 199 consecutive active pulmonary tuberculosis patients; 117 of these were male and 108 were urban dwellers. Analyses of fasting blood glucose level were carried out using blood samples collected by finger puncture. For testing significance, categorical data were compared using a chi-square test and expressed as

**Corresponding author: Email: solomekonnen@yahoo.com;*

proportion with a 95% confidence interval.
Result: The prevalence of diabetes was found to be 8.5 % [95%CI: 4.6– 12.5], which was higher (11.1%) among male than female participants (4.9%). Likewise, 10.2% of the patients were from urban and 6.6% from rural areas. The proportion of newly diagnosed diabetic cases was 52.9%, and all of them were between 25-44 years of age. The Prevalence of impaired fasting glucose was 29.6%. The prevalence of HIV co-infection in the study population was 28.6% [95%CI: 22.3 34.9] and Diabetes was 4 times higher among HIV co-infected patients than among HIV-negative tuberculosis patients. Of all patients with active tuberculosis, 146 (73.7%) were sputum smear negative for acid fast bacilli. The proportion of diabetes was 9.6% among smear positive and 8.2% among smear negative cases.
Conclusion: The prevalence of diabetes mellitus and pre-diabetes among active pulmonary tuberculosis cases was higher compared to the published prevalence of DM in the general population. Therefore, it is important to implement an active case detection of diabetes among tuberculosis patients.
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Keywords: HIV-co infection; IFG; TB-DOTS; TB/DM.

1. INTRODUCTION

Tuberculosis (TB) continues to be the leading killer of the bacterial diseases worldwide. In 2005 there were an estimated 8.8 million new cases of tuberculosis of whom more than 1.7 million died from the disease [1, 2]. According to the 2008 WHO report, Ethiopia ranks seventh among the world's 22 countries with a high tuberculosis burden [3]. In this tuberculosis (TB) endemic country, the total number of patients diagnosed to have diabetes mellitus (DM) is rising. In the year 2000, 2.5% of the Ethiopian people were estimated to have DM [3].

DM increases the risk for progression from latent TB infection to active TB disease, and complicates the treatment of active TB as it is hard to treat an infection in the face of poor glycemic control. A study from the US shows that data from different investigations consistently reveal that the OR of patients with active TB and DM ranges from 1.3 to 7.8 fold, indicating that DM clearly increases the risk of TB. Likewise, the number of excess cases of TB that is attributable to DM has already reached the number of TB cases attributable to HIV infection [4]. A study showed that the enhanced risk of metabolic syndrome with antiretroviral drugs could further predispose patients to diabetes, but evidence remains scarce. Long-term studies are needed to examine the effect of antiretroviral treatment on the rising burden of diabetes in Ethiopia [5].

WHO suspects that TB control is being undermined by a growing number of DM patients in the world, which currently stands at an estimated 285 million and is anticipated to reach 438 million by 2030[1, 6]. DM affects lower socioeconomic groups and ethnic minorities with a higher prevalence of TB. Hence, TB remains a major cause of mortality in developing countries, where the prevalence of DM is increasing rapidly. Despite the suggested significance of DM as a risk factor for TB, little is known about its contribution to the burden of TB in Ethiopia where both diseases are highly prevalent. [7-9]. Therefore, this study aims to assess the prevalence of DM and other TB risk factors such as HIV, smoking, and alcoholism on patients with active pulmonary TB.

2. METHODS

This study was conducted at Gondar University Hospital which serves as referral center for more than 5 million people in the surrounding catchment area. The hospital has DOTS (Directly Observed Treatment, short course) Follow-up Clinic organized for more about 13 years.

2.1 Study Subjects

This cross-sectional hospital-based study was conducted among patients with active pulmonary TB aged 15 years and above. All eligible subject with active pulmonary TB cases who visited the TB-DOTS of the hospital during the data collection period (October 2011 to August, 2012) were included.

2.2 Sampling

The samples size for the study was determined by assuming the prevalence of DM in patients with TB to be 15% [10] 80 % power to detect the difference, a 5% level of significance, and a 10% non-response rate. Accordingly the calculated final sample size of 168 was raised to 199 to increase the statistical power of the sample.

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. Culture was not available in the hospital. Therefore, culture test was not used for the diagnosis of TB. Sputum smear positive pulmonary TB was defined when 2 of the three morning sputum smear tests are positive for AFB or 1 of the 3 are positive with suggestive CXR and clinical features.

2.3 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[11]. 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. Subjects who were tested positive for DM and HIV infected were referred to the Chronic Illness Clinic for further care and treatment. Prevalence estimations of diabetes were made for all study subjects, and similar prevalence was determined based on HIV status, residence (for urban and rural), age, and sex among DM-TB cases directly from our study data. The prevalence estimation was made along with the 95% confidence interval (CI).

2.4 Body Mass Index

Weight and height of study subjects measured using standard measuring equipment at the DOTS clinic. Body mass index (BMI) calculated by dividing the weight by square of the height. BMI was used to define underweight (BMI < 18.00 kg/m^2), normal (BMI ≥ 18.00 and < 25.00 kg/m^2), overweight and obese (BMI ≥ 25.0 kg/m^2) for adults. A structured and pretested questionnaire was used to collect socio-demographic characteristics, clinical, laboratory, and chest X-rays (CXR) data.

2.5 Data Analysis

Double data entry procedure was implemented using EPI Info version 3.5.3 and Data exported to STATA version 11 for analysis. Data were reported as mean and standard deviation, and crude estimates were calculated using data for TB incidence and DM prevalence for the study population. For testing significance, categorical data were compared using a chi-square test and expressed as proportion with a 95% confidence interval. All significant tests were 2-sided; and the results were considered statistically significant at $P<0.05$. Logistic regression was applied to test the presence of association. Statistical analysis was performed using STATA version 11 software.

3. RESULTS

Of the total 199 active pulmonary TB cases, 117 (58.8%) were male, and 108 (54.3%) of them were urban dwellers. The mean age (±SD) of the study group was 33.9 (±13.9) ranging from 14 to 80 years.

Majority of the study subjects were in the age group between 25-44 years. In terms of occupational status, self-employees and students account for the highest proportion, 131(65.8%) (Table1).

The prevalence of DM was 8.5% [95%CI: 4.6, 12.5] among patients with pulmonary TB and all of them were in age group 25-44 years. The prevalence of DM among the male was 11.1 % [95%CI: 5.3, 16.9], and among the female 4.9% [95% CI: .2, 9.04]. Likewise, 10.2% [4.4, 15.9] of the participants were from urban areas, and 6.6% [95%CI: 1.4, 11.8] from rural settings (Table 3). Newly diagnosed DM account for nearly 53% of all patients tested positive for DM.

The prevalence of IFG among patients with active pulmonary TB was 29.6% [95%CI: 23.2, 36.0]; which was slightly higher in subjects from rural residence (34.1%) [95%CI: 24.2, 43.9] compared with those from urban areas 25.9% [95%CI: 17.6, 34.3]. The Prevalence of IFG was 31.7% [95%CI: 21.5, 41.9] among women and 28.2% [95%CI: 19.9 – 36.4] among men (Fig. 1).

HIV co-infection rate among the study population of active pulmonary TB cases was 28.6% [95%CI: 22.3, 34.9]. The proportion was 32.9% [95%CI: 22.6, 43.2] in women and 25.6% [95%CI: 17.6, 33.6] in men. HIV co-infection was higher (40.7%) in subjects from urban areas than in those from rural settings (14.3%). The occurrence of DM in HIV co-infected study subjects was 4 times higher than HIV-negative TB patients (OR 4.1, $P= .004$). The proportion of cigarette smokers was 3% and that of alcohol consumers was 4.6%. About 47

% of the study subjects were under weight, 50.3% normal weight, and 2.03 % overweight and/or obese Table 2.

The majority (72.5%) of the TB patients had TB symptoms for more than 3 weeks, and only 3.6 % for a week. Delayed diagnosis of pulmonary TB was observed among rural residents, and the difference was statistically significant (*p=.001*).

Of the study subjects, 147 (73.9%) were sputum smear negative for AFB at baseline, and DM was higher in smear positive subjects (9.6%) than smear negative (8.2%). Chest radiographic study was available for a number of patients at base line and among these 73.7% showed typical post-primary radiographic picture, .6% primary, 22.8% atypical, and 3% normal (Table 2).

Table 1. Distribution of socio-demographic variable by residence and sex at Gondar university hospital, North West Ethiopia, 2012

Characteristics	Urban		Rural		Total n (%)
	Male n (%)	Female n (%)	Male n (%)	Female n (%)	
Age					
≤ 24	24 (36.9%)	15 (34.9%)	15 (28.9%)	7 (17.9%)	61 (30.7%)
25-44	31 (47.7%)	21 (48.8%)	23 (44.2%)	20 (51.3%)	95 (47.7%)
45-64	6 (9.2%)	6 (13.9%)	10 (19.2%)	11 (28.2%)	33 (16.6%)
≥ 65	4 (6.2%)	1 (2.3%)	4 (7.7%)	1 (2.6%)	10 (5.03%)
Total	65 (32.7%)	43 (21.6%)	52 (26.1%)	39 (19.6%)	199
Education					
No formal schooling	18 (28.6%)	11(26.8%)	36 (72%)	35 (89.7%)	100 (51.8%)
Grade 1-6	3 (4.8%)	5 (12.2%)	2 (4%)	1 (2.6%)	11 (5.7%)
Grade7-12+1	18 (28.6%)	15 (36.6%)	6 (12%)	2 (5.1%)	41 (21.2%)
Diploma and above	24 (38.1%)	10 (24.4%)	6 (12%)	1 (2.6%)	41 (21.2%)
Total	63 (32.6%)	41 (21.2%)	50 (25.9%)	39 (20.2%)	193
Marital Status					
Never married	42 (64.6%)	19 (44.2%)	23 (44.2%)	5 (12.8%)	89 (44.7%)
Currently married	20 (30.8%)	9 (20.9%)	22 (42.3%)	26 (66.7%)	77 (38.7%)
Separated	3 (4.6%)	10 (23.3%)	7 (13.5%)	3 (7.7%)	23 (12%)
Widowed	0 (0.0%)	5 (11.6%)	0 (0.0%)	5 (12.8%)	10 (5.03%)
Total	65 (32.7%)	43 (21.6%)	52 (26.1%)	39 (19.6)	199
Occupational					
Gov employed	11 (16.9%)	4 (9.3%)	0 (0.0%)	0 (0.0%)	15 (7.5%)
self employed	27 (41.5%)	12 (27.9%)	40 (76.9%)	8 (20.1%)	87 (43.7%)
Student	23 (35.4%)	10 (23.3%)	9 (17.3%)	2 (5.1%)	44 (22.1%)
Homemaker	0 (0.0%)	14 (32.6%)	1(1.9%)	27 (69.2%)	42 (21.1%)
Retire	0 (0.0%)	0 (0.00%)	1 (1.9%)	0 (0.0%) 2	1 (.5%)
Un-employed	4 (6.1%)	3 (6.9%)	1 (1.9%)	(5.1%)	10 (5.1%)
Total	65 (32.7%)	43 (21.6%)	52 (26.1%)	39 (19.6)	199

Table 2. Health related characteristics of the study group distributions by sex at Gondar University hospital, Northwest Ethiopia, 2012

Characteristics	Total n (%)	Male n (%)	Female n (%)
FBG level			
70-109	123 (61.8)	71 (57.7)	52 (42.3)
110-125	59 (29.7)	33 (55.9)	26 (44.1)
≥ 126	17 (8.5)	13 (76.5)	4 (23.5)
Total	199	117 (59.1)	82 (40.9)
HIV/AIDS status			
HIV Positive	57 (28.4)	30 (52.6)	27 (47.4)
HIV Negative	142 (71.4)	87 (61.3)	55 (38.7)
Total	199	117 (59.2)	82 (40.8)
Smoking			
Yes	6 (3.0)	6 (100)	0 (.00)
No	192 (96.9)	111 (57.5)	82 (42.5)
Total	198	117 (59.1)	81 (40.9)
Drinking Alcohol			
Yes	9 (4.6%)	9 (100)	0 (.00)
No	190 (95.5)	108 (56.8)	81 (43.2)
Total	199	117 (59.1)	81 (40.9)
BMI (kg/m^2)			
< 18	96 (48.2)	55 (57.3)	41 (42.7)
18-24.9	99 (49.8)	60 (60.6)	39 (39.4)
25 and above	4 (2.0)	2 (50.0)	2 (50.0)
Total	199	117 (59.2)	81 (40.8)
Waist circumference			
<90	194 (97.5)	114 (58.7)	80 (41.2)
≥ 90	5(2.5)	3 (60.0)	2 (40.0)
Total	199	117(59.3)	82 (40.7)
Duration of TB Symptom			
≤ 1	9 (4.5)	4 (44.4)	5 (55.6)
2-3 weeks	48 (24.1)	34 (70.8)	14 (29.2)
> 3 week	142 (71.4)	79 (55.6)	63 (44.4)
Total	199	117 (60.1)	82 (39.9)
Sputum smear test for AFB			
Positive	52 (26.1)	30 (57.7)	22 (42.3)
Negative	147 (73.9)	87 (59.2)	60 (40.8)
Total	199	117 (58.8)	82(41.2)
Chest x-ray (CXR)			
Typical post prim	124 (62.3)	72 (58.1)	52 (41.9)
Primary	1 (.5)	1 (1.1)	0 (.00)
Atypical	38 (19.1)	18 (47.4)	20 (52.6)
Normal	5 (2.5)	2 (2.15)	3 (4.0)
No CXR	31 (15.6)	24 (77.4)	7 (22.6)
Total	199	117 (55.7)	82 (41.2)

Table 3. Socio-demographic characteristics and HIV status of study subjects with diabetes Mellitus in active pulmonary TB at Gondar referral Hospital of Gondar, North West Ethiopia (2013)

Variable	N (%)	Diabetic cases # *(%)*
Age in year		
≤ 24	61 (30.8)	0 (0.00)
25-44	94 (47.5)	13 (13.8)
45-64	33 (16.7)	4 (12.1)
≥65	0 (0.00)	0 (0.00)
Sex		
Male	117 (58.8)	13 (11,1)
Female	82 (41.2)	4 (4.9)
Residence		
Urban	108 (54.3)	11 (10.2)
Rural	91 (45.7)	6 (6.6)
HIV Status		
HIV positive	57 (28.6)	10 (17.5)
HIV Negative	142 (71.4)	7 (4.9)
Education		
No formal schooling	100(51.8)	9 (9.00)
Grade 1-12	52 (26.9)	3 (7.3)
Diploma and above	41 (21.2)	2 (4.9)
Marital Status		
Never married	89 (44.7)	3 (3.4)
Currently married	77 (38.7)	9 (11.7)
Separated	33 (16.6)	5 (15.2)

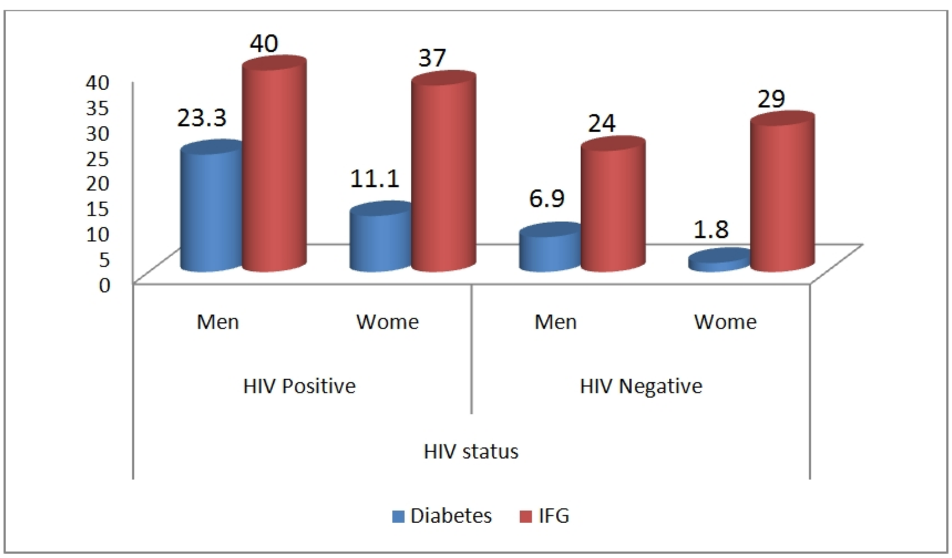

Fig. 1. Prevalence of diabetes mellitus and impaired fasting glucose by sex and HIV status among pulmonary active tuberculosis patient in Gondar University Referral Hospital, North West Ethiopia, 2012

4. DISCUSSION

In this institution-based cross- sectional study, we have found that the prevalence of DM was higher among patients with active pulmonary TB, which is almost three times higher than the estimated population prevalence of DM in Ethiopia [12]. Our finding is in line with reports of high prevalence from Mexico (25%), Tanzania (16.7%), India (14.8% - 44%), Indonesia (13.2%), Pakistan (9.5%), and China (12.4%) [1,13-16]. The wide range of prevalence of DM in different studies might be due to the socio-demographic characteristics of source populations in the localities studied. Previous literature supports that DM is an important risk factor for the occurrence of TB. [12,13,17].

The higher prevalence of DM among patients with TB was associated with male study subjects, urban dwellers, and HIV co-infected ones. The high prevalence of DM in the males was very close to the findings in Pakistan and India [13,18,19]. On the other hand, the prevalence of DM in urban areas was also comparable to that of other studies [1,18-20]. 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 that significant proportion of new cases of DM (50%) was detected by doing active screening for DM in patients with pulmonary TB. A similar study conducted in Kerala, India, showed a high prevalence of undiagnosed DM among new pulmonary TB cases. 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 [20,22]. This finding call for the implementation of active case finding of DM in patients diagnosed for TB and the integrating of TB and DM care programs. Similarly, the overall proportion of IFG among newly diagnosed pulmonary TB cases was higher than the report from Indonesia (3.7%), India (24.5%) and Guinea (31%) [14,18,23] and lower than that of a study done in Tanzania 37.6% [15].

The proportion of DM among HIV co-infected active pulmonary TB cases was high. In agreement with this finding, other studies showed that the prevalence of tuberculosis cases to become diabetic was 4 times higher among HIV co-infected patients compared with HIV-negative tuberculosis patients [15]. The huge prevalence of DM in HIV patients can contribute to the increasing prevalence of active pulmonary tuberculosis.

We found a high prevalence of DM amongst younger TB patients (25- 44 years of age), and more proportion of DM was found among the smear positive cases. In line with this finding, a study performed among non-North Americans and Europeans showed higher risk among younger people, with a high background of TB incidence [10,12,20]. The rising prevalence of DM/ TB burden in this group will adversely affect TB control programs and will become another burden to the health system.

This study contributes to the growing body of evidence on the importance of the TB/DM relationship. To our information, this is among the very few investigations that assessed the association between DM and TB in Ethiopia. The findings we report indicate that diabetes was high among tuberculosis patients. Since TB patients with DM have an increased risk of poor treatment out-come, it is important to launch a well-functioning chronic disease and TB control programs in countries like Ethiopia where the prevalence of HIV and TB epidemic is high.

5. CONCLUSION

The prevalence of diabetes mellitus and pre-diabetes among active pulmonary tuberculosis cases was higher compared to the published prevalence of DM in the general population at Gondar University Referral Hospital, and more than half of the DM cases were undiagnosed before the time of screening. Furthermore, the proportion of DM among HIV co-infected patients of newly diagnosed pulmonary TB cases was very high. Therefore, it is imperative to have active case detection of DM in patients with TB and active case detection of TB in patients with DM.

CONSENT

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

ETHICAL APPROVAL

The protocol and written consent was approved by the Institution review board (IRB) of the University of Gondar, Ethiopia. In addition, a written permission was obtained from the respective Hospital Director. For the sake of privacy and confidentiality no personal identifiers, such as names were collected.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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