

# Screening for diabetes among tuberculosis patients: a nationwide population-based study in Egypt

Mohsen Gadallah<sup>1</sup>, Wagdy Amin<sup>2</sup>, Magdy Fawzy<sup>2</sup>, Alaa Mokhtar<sup>2</sup>, Amira Mohsen<sup>3</sup>

1. Community, Environmental and Occupational Medicine. Faculty of Medicine - Ain Shams University, Cairo 11566 Egypt.
2. Ministry of Health and Population - Chest Directorate, National Tuberculosis Control Program, Cairo, Egypt.
3. National Research Center, Cairo, Egypt, Department of Community Medicine, Cairo, Egypt.

## Abstract

**Background:** The prevalence of type 2 diabetes mellitus (DM) is increasing rapidly in Egypt and considered one of the major health problems in the Eastern Mediterranean region.

**Objectives:** To measure the prevalence of diabetes and detect the undiagnosed cases of diabetes mellitus among patient with tuberculosis.

**Methods:** Study Design: Nationwide population-based study. To diagnose DM among TB patients, we used a fasting blood sugar level of  $\geq 126$  mg/dl and a post-prandial blood glucose test result of  $\geq 200$  mg/dl.

**Results:** Screening for DM among 1435 TB patients' with no history of DM detected 30 new cases of DM, with a case detection rate of 2.09%. The highest screening yields were among TB patients aged  $\geq 40$  years, females and those with pulmonary TB. The number needed to screen (NNS) TB patients for detecting one new case of DM was 48 while the lowest values were for older age (NNS=27) and females (NNS=29).

**Conclusion:** Older age and being females and those with pulmonary type of TB were more prone to the double burden of TB and DM. Identifying cases with double burden of diseases will improve the proper management of both diseases and prevent complications.

**Keywords:** Screening test, diabetes mellitus, tuberculosis.

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## Introduction

Diabetes mellitus (DM) affected 422 million adults and killed 5.1 million people. In 2013, there were an estimated 9.6 million incident cases of TB and 1.5 million TB-related deaths globally. It is projected that the number of people affected by DM will increase to 592 million by 2035,

and approximately 80% of these people live in low- and middle-income countries, where TB is endemic.<sup>1,2</sup> The association between TB and DM is re-emerging in particularly in low and low-middle income countries during the past decade. Many systematic reviews confirmed the significant evidence between TB and MD co-morbidity and they reported that DM patients have a three-fold greater risk of contracting TB than do non-diabetics (95% confidence interval [CI]: 2.3–4.3) while the prevalence of DM among TB patients ranged between 1.9% and 45% with median global value of 16%. The tremendous increase in the prevalence of DM in developing countries will reflect inversely on the successful control of TB especially in countries with high burden of both diseases.<sup>3-5</sup>

### Corresponding author:

Mohsen Gadallah,  
Community, Environmental and  
Occupational Medicine.  
Faculty of Medicine - Ain Shams University,  
Cairo 11566 Egypt.  
Email: mohsengadallah@gmail.com

In Egypt, the prevalence of DM among those aged from 15 to 64 years increased from 15.8% in 2005 to 17.2% in 2011-12. Accordingly, a large proportion of Egyptians will be exposed to high risk of acquiring TB. Moreover, in Egypt Gadallah et al<sup>6</sup> reported that patients with both TB and DM were more likely to develop complication than TB patients without DM. There is no national survey in Egypt to address the significant link between DM and TB. In this study, we describe the feasibility of implementing a screening program to screen TB patients for DM within all governmental TB control and management units. The objectives of this study were to measure the prevalence of known diabetes among TB patients, detect new cases of DM and to estimate the necessary number to screen TB patients to find a new case of DM.

## Methods

**Study design:** This was a nationwide population-based study.

### Study population:

TB patients (all forms) newly diagnosed and recorded in all TB management units in Egypt during the fourth quarter of 2012 (1745 patients) were included, and their diabetes status was determined. Only TB patients' aged  $\geq 18$  years were included in the study (1608 patients). Diagnosis of TB either pulmonary or extra pulmonary was based on the national tuberculosis control guidelines. Pulmonary TB (PTB) was diagnosed when at least two sputum smear examinations were positive for acid-fast bacilli (AFB) or one smear examination positive for AFB and x-ray chest showed radiographic abnormalities consistent with active TB as determined by a chest specialist. Extra pulmonary TB (EPTB) was made by identifying AFBs in organs other than lung diagnosed histologically and/or culture with clinical evidence of active EPTB.

### Diagnosis of DM:

Patients with TB were first asked whether they had DM. If the answer was yes (i.e., a self-reported history of taking anti-diabetic drugs after being diagnosed by a medical professional), then the patient considered to have an established case of DM (known DM). When the answer was no, they were screened using fasting blood glucose (FBG) and 2-hour blood glucose tests. Those with a FBG test result of  $\geq 126$  mg/dl and a post-prandial blood glucose (PPBG) test result of  $\geq 200$  mg/dl were considered positive for DM (newly detected DM). Blood glucose was

analyzed using semi-automated photometer 5010, manufactured by RIELE, GmbH & Co KG, Berlin-Germany, 2012.

### Data collection tool and variables:

Physicians working in all TB management units were trained to collect study data variables related to the study objectives from TB register and patient cards. In addition, a simple questionnaire was designed to collect data about the other study variables. Laboratory technician was responsible for withdrawing blood from TB patients and carried out the both FBG and PPBG. The key variables included: age, gender, place of residence, history of diabetes and type of TB.

### Operational definition of study variables and outcome:

**Known DM cases:** Are those TB patients with previous history of DM and under current treatment of diabetes.

**Screen Detection New Cases:** Are those TB patients with unknown DM status or gave no history of DM and but positive by screening test.

**Total prevalence:** All TB patients with known diabetes and the new detected cases by screening.

### Ethical approval

The protocol of the study was approved by the Institutional Review Board (IRB) of the faculty of medicine, Ain Shams University. All patient data were kept confidential. Informed consent was obtained from each patient included in the study after having been given a clear description of the study objectives. New diabetic patients detected by the screening were referred to specialized clinics for further management.

### Statistical analysis:

All data were analyzed using SPSS version 21. Chi-square test or Fisher's exact test were applied for qualitative variables. For all study variables; 95% CI were applied. For calculation of the number needed to screen (NNS) was calculated as the reciprocal of the case detection rate. Additional yield percent was calculated as follow number of new of DM detected by screening divided by total number of known and new cases of DM multiplied by 100. Multivariable logistic regression models were used for identifying the predictor variables associated with the total prevalence and screened detection new cases of DM among TB patients. A P value of  $\leq 0.05$  was considered significant.

## Results

### Screening for DM among TB patients

The total number of TB cases notified in the fourth quarter of 2013 was 1,745 patients. In this study only patient aged  $\geq 18$  years old were included. Of 1608 TB patients included in the study, 173 (10.76%, 95%CI=(9.34–12.37)

had previously been diagnosed with DM. Screening of the remaining 1435 TB patients detected 30 newly diagnosed cases of DM, with a screening detection rate of 2.09% (95%CI=1.47–2.97). The prevalence (known diabetics) and detection rates were re-calculated across the patient characteristics (tables 1 and 2).

**Table (1) Prevalence of known DM among TB patients**

	<b>Total sample</b>	<b>Known DM</b>	<b>Prevalence of known DM (95% CI)</b>
<b>Total</b>	1608	173	10.76 (9.34–12.37)
<b>Age</b>			
< 30	490	7	1.43 (0.69–2.92)
30–39	340	11	3.24 (1.82–5.70)
$\geq 40$	778	155	19.92 (17.27–22.87)
<b>Sex</b>			
Male	1132	102	9.01 (7.48–10.82)
Female	476	71	14.92 (12.00–18.40)
<b>Residence</b>			
Urban	847	94	11.10 (9.16–13.39)
Rural	761	79	10.38 (8.41–12.75)
<b>Site of TB</b>			
EPTB	373	26	6.97 (4.80–10.17)
PTB	1235	147	11.90 (10.21–13.87)

The highest prevalence of known DM (19.92%) was reported among older age ( $\geq 40$  years old) and among females (14.92%). Similarly, the highest screen detection rate was found among older age group (3.69%) and among females (3.46%).

After excluding previously diagnosed DM cases, the NNS to detect a new case of DM among TB patients was 48. The lowest NNS values were found among TB patients aged  $\geq 40$  years (NNS=27) and female TB patients (NNS=29), while the highest NNS value was reported among TB patients aged less than 30 years (NNS=483).

**Table (2) Screen detection rate of new cases of DM among TB patients**

	<b>Total no. screened for DM</b>	<b>New cases of DM</b>	<b>Screen detection rate (95% CI)</b>	<b>Additional yield (%)</b>	<b>Number Needed to Screen (NNS)</b>
<b>Total</b>	1435	30	2.09 (1.47–2.97)	14.8	48
<b>Age</b>					
< 30	483	1	0.21 (0.04–1.16)	12.5	483
30–39	329	6	1.82 (0.84–3.92)	35.3	55
≥ 40	623	23	3.69 (2.47–5.48)	12.9	27
<b>Sex</b>					
Male	1030	16	1.55 (0.96–2.51)	13.6	64
Female	405	14	3.46 (2.07–5.72)	16.5	29
<b>Residence</b>					
Urban	753	18	2.39 (1.52–3.83)	16.1	42
Rural	682	12	1.76 (1.01–3.05)	13.2	57
<b>Site of TB</b>					
EPTB	347	5	1.44 (0.62–3.33)	16.1	69
PTB	1088	25	2.30 (1.56–3.42)	13.7	44

Factors associated with known DM cases and new DM cases detected by screening among TB patients are displayed in tables 3 and 4. The results of the bivariate analyses showed that an age of 30–40 and ≥ 40 years old, the female gender and the presence of pulmonary TB (PTB) were significantly associated with known DM. The same variables remained significant after applying a multi-

variable logistic regression. As regards factors associated with screen detection rate, the bivariate analysis showed that only those in the age groups of 30–40 and ≥ 40 years old and the female gender were significantly associated with newly detected cases of DM. The same variables remained in the final model of the multivariate logistic analysis.

**Table (3) the relation between patient characteristics and the total prevalence of DM among TB patients**

Characteristic	Total prevalence of DM (n=203)			
	P value	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)
<b>Age</b>				
< 30®	-	-	-	-
30–39	0.005	3.17 (1.35–7.43)	0.004	3.56 (1.51–8.39)
≥ 40	< 0.001	17.87 (8.71–36.67)	< 0.001	19.78 (9.57–40.80)
<b>Sex</b>				
Male®	-	-	-	-
Female	< 0.001	1.77 (1.28–2.45)	< 0.001	2.7 (1.92–3.81)
<b>Residence</b>				
Rural®				
Urban	0.643	1.08 (0.79–1.48)	0.17	1.25 (0.91–1.71)
<b>Site of TB</b>				
EPTB®				
PTB	0.007	1.79 (1.17–2.78)	< 0.001	2.27 (1.45–3.54)

® Reference group

**Table (4) the relation between patient characteristics and new detection cases of DM among TB patients**

Characteristics	Newly detected DM cases (n=30)			
	P value	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)
<b>Age</b>				
< 30®	-	-	-	-
30–39	0.040	8.95 (1.07–74.71)	0.030	10.55 (1.26–88.66)
≥ 40	< 0.001	18.48 (2.50–137.30)	0.003	21.58 (2.89–161.30)
<b>Sex</b>				
Male®	-	-	-	-
Female	0.023	2.27 (1.10–4.69)	0.001	3.53 (1.63–7.64)
<b>Residence</b>				
Rural®	-	-	-	-
Urban	0.404	1.37 (0.65–2.86)	0.276	1.52 (0.72–3.21)
<b>Site of TB</b>				
EPTB®	-	-	-	-
PTB	0.331	1.61 (0.61–4.23)	0.106	2.32 (0.84–6.45)

® Reference group

## Discussion

This study is considered the first documented national-based survey for implementing bi-directional screening for DM and TB in Egypt. All patients with active TB (≥ 18 years) registered in the fourth quarter of 2012 from all

TB clinics/hospitals in Egypt had been subjected to DM screening. The total prevalence was 12.6%, which is still lower than the national figure obtained from the national stepwise survey in 2012 (17.2%). This lower prevalence rate among our TB patients might be explained by the

higher proportion of males in our study (70%) compared with the proportion of 51% in the study population of the Egypt stepwise survey. Another explanation for the low prevalence of DM among the study population is the method of DM diagnosis; in our study, we depended upon measuring both FBS and PPBS levels, while in the stepwise survey, only FBS was used. Similar to our results; Li et al<sup>7</sup> reported a DM prevalence of 12.4% among TB patients in China, while in contrast with our results, higher prevalence rates were reported in India and Ethiopia.<sup>8-10</sup> Moreover, the prevalence of DM was significantly associated with older age groups. In agreement to our results; many studies have found a significantly higher prevalence of DM among those aged  $\geq 40$  years.<sup>3,8-11</sup> Regarding the association between gender and the prevalence of DM among TB patients, the current study showed a significant higher prevalence of DM among females even after adjusting for other confounder factors. There is no consensus about sex and the prevalence of DM as some studies have reported a higher prevalence among males<sup>8,11,12</sup>, while other studies have reported the reverse<sup>10</sup> while many researches did not find any association.<sup>13-16</sup>

Our results revealed that the prevalence of DM was significantly higher among PTB patients than extra-pulmonary TB (EPTB) patients, which is consistent with other studies performed in India<sup>8,11,16</sup>, Ethiopia<sup>10</sup>, and Sri Lanka<sup>12</sup>. The association between PTB and DM might be related to the temporary elevation of blood sugar due to infection with TB. Because our study was cross-sectional, the existence of this temporal effect is uncertain and could not be determined. Therefore, it is recommended that future studies monitor blood sugar during the course of TB treatment to avoid a false-positive diagnosis of DM, if the screening is performed only at the beginning of the treatment.

The screening of TB patients with an unknown history of DM showed a case detection rate of 2.09%, yielding approximately a 15% increase in the prevalence of DM. The case detection rate was significantly higher among the female gender, those aged  $\geq 40$  years and those with PTB. In this study, in order to detect a new case of DM among TB patients, we needed to screen 48 patients. The NNS in the current study ranged between 27 (for patients aged  $\geq 40$  years) and 483 (for TB patients younger than 30 years). This finding is much higher than what was reported in other studies in India, Ethiopia, Sri Lanka, Kenya, Peru, Nigeria and China.<sup>8,10,12,14,17-19</sup> This difference might

be attributable to the prevalence of DM in the general population of each country, age composition differences and the methods used for DM diagnosis.

## Conclusion

The prevalence of DM among TB patients was quite lower than the national figure. The factors associated with the total prevalence of DM and the detection rate of new cases were older age and females and among those with pulmonary type of TB. The NNS was higher than many published articles.

There are some limitations of this study. The study sample used for screening TB patients for detection of diabetes among them was limited to patients seen in one quarter of the year. This study is considered a cross-sectional one with its disadvantage of temporal effect. Also, we did not measure the anthropometric parameters due to lacking of standardized weigh scales in most of study sites. Other limitations included lacking questions related physical exercise and family history of DM. The strengths of this study are; it is the first national base study to assess the prevalence of diabetes among TB patients and proved the feasibility to conduct such screening test for DM in all TB management clinics all over the country.

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## Conflicts of interests

The authors declare that they have no conflicts of interest concerning this article.

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