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A public-private model to scale up diabetes mellitus screening among people accessing tuberculosis diagnostics in Dhaka, Bangladesh

Kishor Kumar Paul^{a,b}, Yosra M.A. Alkabab^c, Md Mahfuzur Rahman^a, Shahriar Ahmed^a, Md Jobaer Amin^a, Md Delwar Hossain^d, Scott K. Heysell^c, Sayera Banu^{a,*}

^aProgramme on Emerging Infections, Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh

^bThe Kirby Institute, University of New South Wales, Kensington, New South Wales, Australia

^cDivision of Infectious Diseases and International Health, Department of Medicine, University of Virginia, Charlottesville, VA, USA

^dDepartment of Respiratory Medicine, BIRDEM General Hospital and Ibrahim Medical College, Dhaka, Bangladesh

Abstract

Background: Data are scarce regarding the prevalence of diabetes mellitus (DM) among tuberculosis (TB) patients in Bangladesh. This study was undertaken to estimate the number needed to screen (NNS) to identify a case of DM among those with TB symptoms and those with confirmed TB disease, and to identify factors predicting treatment outcomes of TB patients with and without DM.

Methods: Persons attending public–private model screening centres in urban Dhaka for the evaluation of TB were offered free blood glucose testing in addition to computer-aided chest X-ray and sputum Xpert MTB/RIF.

Results: Among 7647 people evaluated for both TB and DM, the NNS was 35 (95% confidence interval (CI) 31–40) to diagnose one new case of DM; among those diagnosed with TB, the NNS was 21 (95% CI 17–29). Among those with diagnosed TB, patients with DM were more likely to have cavitation on chest X-ray compared to those without DM (31% vs 22%). Treatment failure (odds ratio (OR) 18.9, 95% CI 5.43–65.9) and death (OR 2.08, 95% CI 1.11–3.90) were more common among TB patients with DM than among TB patients without DM. DM was the most important predictor of a poor treatment outcome in the classification analysis for TB patients aged 39 years and above.

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*Corresponding author at: Programme on Emerging Infections (PEI), Infectious Diseases Division (IDD), International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), 68, Shaheed Tajuddin Ahmed Road, Mohakhali, Dhaka 1212, Bangladesh. sbanu@icddr.org (S. Banu).

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijid.2020.01.001>.

Conclusions: A considerable burden of DM was found among patients accessing TB diagnostics through a public–private model in urban Bangladesh, and DM was associated with advanced TB disease and a high rate of poor treatment outcome.

Keywords

Screening for diabetes; Pulmonary TB with diabetes; CAD4TB; TB treatment outcome

Introduction

Worldwide, tuberculosis (TB) is the leading cause of death from a single infectious pathogen, and according to World Health Organization estimates, Bangladesh is among the 30 ‘high burden’ countries for TB (World Health Organization, 2018). The estimated incidence of all forms of TB in Bangladesh in 2016 was 221/100 000 population, giving rise to an estimated 360 230 new cases per year. Remarkably, only 223 921 cases were reported to the National Tuberculosis Control Program (NTP) in the same year. Concurrently, diabetes mellitus (DM) is also common in Bangladesh, affecting an estimated 8.4% of adults. A growing body of evidence suggests that people with DM are three times more likely to develop active TB than people without DM (Jeon and Murray, 2008), and when diagnosed, it has been suggested that patients with DM–TB are more likely to have a higher bacillary burden, take a longer time to clear their sputum culture of *Mycobacterium tuberculosis*, and suffer a higher mortality (Alisjahbana et al., 2007; Baker et al., 2011; Dooley et al., 2009; Jeon and Murray, 2008; Jimenez-Corona et al., 2013). These findings may be explained by biological variations in those with insulin resistance, which include a reduction in both the production and activity of components of innate and humoral immunity (Jeon and Murray, 2008; Kumar et al., 2013). Conversely, *M. tuberculosis* itself might aggravate glucose intolerance and hamper glycaemic control in people with DM, which furthers a poor on going immune response to *M. tuberculosis* containment (Dooley and Chaisson, 2009).

To address the co-epidemic of TB and DM, the Bangladesh national guidelines for the management of DM–TB now recommend DM screening for all adults diagnosed with TB (Hossain, 2014). In practice, however, DM screening is rarely done in current publicly funded directly observed therapy (DOT) facilities, which are the primary locations for all diagnosis and management strategies through the NTP. As a result, data are scarce regarding the prevalence of DM among TB patients and the TB treatment outcomes of those relatively few with dual diagnoses, and there are no guidelines for tailoring care for this important subpopulation. Therefore, we sought to fill these knowledge gaps within a specifically designed public–private partnership in order to capture patients presenting with TB symptoms throughout the health system in urban Dhaka, Bangladesh.

It was hypothesized that DM would be more common among those with confirmed TB disease, that DM-related TB would present with more advanced disease markers, and that analyses of a large cohort of patients across the health system would allow a more representative estimate of the number needed to screen (NNS) to identify a case of DM among those with TB symptoms and those with confirmed TB disease. This study was also

intended to provide policy direction regarding linkage of DM–TB patients to optimal dual disease care.

Materials and methods

Study setting

The study was conducted in three TB screening centres (TBSCs) in the Mohakhali, Dhanmondi, and Golapbagh neighbourhoods of urban Dhaka (Rahman et al., 2017), serving population centres totalling more than 12 million people (2011 census). While the average income of people living in these neighbourhoods is USD 176 per month, the majority typically access a private provider first for medical care. Within the developed public–private model, networked private providers (PPs), totalling 7712 in number, referred patients to the TBSCs for testing based on clinical suspicion. In addition to patients referred from PPs, smear-negative presumed TB cases were referred from public DOT facilities where only sputum microscopy was available as a TB diagnostic tool. The TBSCs were also open to walk-in clients with no referral history.

Screening procedure

At the TBSCs, all patients were asked about symptoms suggestive of TB disease. Patients with a cough for at least 2 weeks underwent digital chest X-ray. A Delft EZ DR X-ray system linked with Computer-Aided Detection for Tuberculosis (CAD4TB) version 3.07, a computer-aided reading software, was installed in each TBSC. CAD4TB identified shape and textural abnormalities in chest X-ray images to produce an abnormality score ranging from 0 (normal) to 100 (highly abnormal). A cut-off score of 63 was prespecified as correlative with TB disease, standardizing for abnormal lung images in the general population based on work from an earlier study in Dhaka (Rahman et al., 2017). In addition, a radiologist blinded to the CAD4TB score read all chest X-ray images and provided a standard radiology report. The words ‘cavitation’ or ‘cavity’ were then extracted from the radiologist’s report in order to provide further characterization between images from patients with and without DM.

Regardless of the CAD4TB abnormality score, all symptomatic individuals submitted a sputum sample and received a free Xpert MTB/RIF test. If the Xpert test failed, it was performed again to obtain a valid outcome if enough sample remained. In addition to Xpert MTB/RIF and chest X-ray, sputum microscopy was performed at the affiliated Mycobacteriology Laboratory at the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) when this test was specifically requested by the referring physician. Those who tested positive for Xpert MTB/RIF and/or were smear-positive for acid-fast bacilli (AFB) were considered bacteriologically positive TB patients. Xpert MTB/RIF test negative patients were followed up over the phone within one week to determine whether they were clinically diagnosed as having TB by the referring physician depending on symptom progression, chest X-ray findings, or other clinical suspicion. Walk-in patients with sputum Xpert MTB/RIF-negative and smear-negative (if performed) results were additionally assessed by trained physicians at TBSCs for any additional evidence that would prompt empiric TB treatment. Bacteriologically confirmed or clinically diagnosed TB cases

were followed up over the phone by the TBSC staff to collect data on anti-TB treatment initiation and smear conversion at 2, 5, and 6 months after treatment initiation.

All patients with symptoms of TB, regardless of bacteriological confirmation or clinical diagnosis, were offered free blood glucose testing with a commercially available blood glucose meter. The fasting blood glucose (FBG) or random blood glucose (RBG) level was measured for those who accepted testing. Those who had FBG ≥ 7 mmol/l or RBG ≥ 11.1 mmol/l were considered as having hyperglycaemia and were either tested for haemoglobin A1c (HbA1c) at the TBSC if they agreed (DM defined as HbA1c $\geq 6.5\%$), or otherwise confirmatory test data were collected from the patient and/or PP by phone. Patients on anti-diabetic medication, having raised HbA1c at the TBSC, and those diagnosed as diabetic by the referring PP were considered as diabetic.

Data analysis

De-identified data were analysed using statistical software package Stata 13.1 (StataCorp LP, USA). Demographic and clinical data along with TB diagnostic results were compared among all patients with and without DM and associations reported as odds ratios (OR) or mean differences with 95% confidence intervals (CI). Additional comparisons were made between those with and without DM among the subset with confirmed TB, including their TB treatment outcome. Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test where appropriate, and comparisons between continuous variables were performed using the independent *t*-test or Mann-Whitney *U*-test for those normally or non-normally distributed. All tests of significance were two-tailed. Additionally, the NNS to detect a new DM case was calculated using the following formula: all cases screened/new DM cases. To investigate the relationship between treatment outcomes and other independent variables, a binary treatment outcome was defined as 'good' if the patient was cured and/or the treatment was complete, and as 'poor' if the patient died or there was evidence of treatment failure. Treatment failure was defined as lack of sputum smear conversion or any positive culture for *M. tuberculosis* at 5 months after treatment initiation or beyond. Characteristics that have been associated with death or treatment failure in previous studies and those that were significant in the univariable analysis were categorically organized and then compared within a non-linear discrimination method, the Chi-square automatic interaction detection (CHAID), used for building classification trees and ascribing predictive weight.

Ethical approval

All participants provided informed written consent. The study protocol and consent forms were reviewed and approved by the Institutional Review Board at the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b).

Results

Characteristics of patients presenting to TBSCs tested for DM

During the study period (from July 2014 to October 2017), 46 382 patients presented to the three TBSCs and 7647 (16%) agreed to be tested with a blood glucose meter (Figure

1). Of those tested for blood glucose, 892 (12%) already had a history of DM and were on treatment, but an additional 192 (3%) were new diagnoses. The HbA1c percentage was determined for 27% (52/192) of newly diagnosed diabetic patients, and the mean HbA1c percentage was 9 with an interquartile range of 7.9 to 9.8. The NNS was 35 (95% CI 31–40) to diagnose one new case of DM (6755/192) among those presenting for evaluation of TB. Among those diagnosed with TB, the NNS was 21 (999/47, 95% CI 17–29), and for TB cases above 35 years of age, the NNS was 11 (431/41, 95% CI 8–14) to diagnose one new DM case (Table 1).

Characteristics of persons evaluated for TB according to DM status

Including those with a prior history of DM and new DM diagnoses, DM was common among both males and females presenting for TB evaluation, but on an average, diabetic patients were 10.7 years older (95% CI 9.7–11.8, $p < 0.001$) compared to non-diabetic patients (Table 2). As expected, FBG and RBG among diabetics were significantly higher compared to non-diabetic patients. Importantly though, people with DM were 1.9 (95% CI 1.6–2.3, $p = 0.001$) times more likely to be Xpert MTB/RIF-positive when compared with their non-diabetic counterparts. Rifampicin resistance was similarly distributed among diabetics and non-diabetics (3% vs 5%). Not only was the CAD4TB score of the digital chest X-ray higher for those with DM compared to non-DM patients among those being evaluated for TB (mean difference of 4.7, 95% CI 3.0–6.4, $p = 0.001$), but diabetic patients were also 1.4 (95% CI 1.2–1.6, $p = 0.001$) times more likely to have a CAD4TB score of 63 and were more likely to have cavitation (10% vs 6%, $p = 0.001$).

Characteristics of pulmonary TB patients according to their DM status

Two-hundred and fifty-two (23%) of those with DM were diagnosed as TB compared to 952 (15%) of those without DM ($p = 0.001$). TB patients with DM were more likely than TB patients without DM to be male (OR 1.43, 95% CI 1.04–1.97, $p = 0.027$), and similar to all patients presenting for evaluation, those confirmed with TB and DM were significantly older than TB patients without DM (mean age difference 10.4 years, 95% CI 8.2–12.6, $p < 0.001$). TB patients with DM were less likely to report unexplained weight loss, shortness of breath, and haemoptysis compared to those without DM (Table 3). In addition, among those positive for MTB/RIF, people with DM were significantly more likely to have a higher burden of *M. tuberculosis* DNA by the semi-quantitative read-out of the test. Rifampicin resistance status was similarly distributed (3% among those with DM vs 5% among those without DM). Differing from the cohort presenting for evaluation, when restricting to those with diagnosed TB only, there was no significant difference in CAD4TB score (mean difference of 2.58 with 95% CI 0.04–5.20) or CAD4TB score 63 (90% vs 88%), between those with and without DM, but the difference in cavitation persisted and was 1.59 times (95% CI 1.17–2.17, $p = 0.003$) more common among those with DM.

TB treatment outcomes

Treatment outcomes were obtained for 707 (75%) TB patients without DM and 207 (84%) TB patients with DM. Of the TB patients with DM, 131 (63%) were cured after treatment, 43 (21%) completed treatment, 16 (8%) experienced treatment failure, and 17 (8%) died before the completion of treatment. On the other hand, of TB patients without DM, 465

(66%) were cured, 210 (29%) completed treatment, three (1%) experienced treatment failure, and 29 (4%) died. On univariate logistic regression, it was found that treatment failure (OR 18.9, 95% CI 5.43–65.9, $p = 0.001$) and death (OR 2.08, 95% CI 1.11–3.90, $p = 0.022$) were more common among TB patients with DM compared to TB patients without DM. In an effort to understand the weight of prediction of all variables on the TB outcome, the characteristics of age, sex, DM status, smoking, presence of cavity on chest X-ray, TB diagnosis (bacteriological or clinical), and CAD4TB score were entered in the CHAID analysis without a validation cohort; three predictors (age, DM status, cavitory lesion) were selected by the CHAID routine for the classification tree. Tree analysis demonstrated that with the knowledge of age category and diabetes alone, 59 of 65 (90.8%) poor outcomes were predicted, while the addition of cavitory imaging accounted for 65 of 65 (100%) (Supplementary Material Figure S1). DM was associated with poor outcomes not only in those who were ≥ 55 years old (attributed in 25.9%; $p < 0.033$), but also in those who were between 39 and 55 years old (16.7%; $p < 0.004$).

Discussion

This prospective study appears to have involved the largest number of patients evaluated for DM in the context of diagnostics for TB, including both semi-quantitative molecular detection of bacterial burden in the sputum and computer-aided imaging of the chest for quantitative interpretation of pulmonary disease. Additionally, the public–private partnership design allowed recruitment of a highly representative sample of urban dwellers in Dhaka, the most populous city in Bangladesh. Not only was DM found to be more common in those referred for TB diagnostics than general population estimates for the country, it was significantly more common in those diagnosed with TB compared to those who were not diagnosed with TB. Among those diagnosed with TB, patients with diabetes also suffered significantly higher mortality and more treatment failure, indicating a lack of microbiological cure, than patients without DM.

The only other previous study of TB and DM diagnosis in Bangladesh was conducted from 2010 to 2011 and described the utility of screening for TB among patients admitted to a tertiary diabetes hospital in Dhaka (Rahim et al., 2012). The present study findings suggest that the corollary, screening for DM among people with symptoms of TB, was not only effective but applicable to an ambulatory population seeking healthcare in a mix of public and private clinics throughout the city. While many patients had been diagnosed previously with DM, the NNS for new cases with TB ($n = 21$) and for all people presenting for evaluation of TB ($n = 35$) indicated an acceptable use of healthcare resources and emphasize the importance of bundling high quality services for both communicable and chronic conditions at the point of entry to care (GBD 2016 Healthcare Access and Quality Collaborators, 2018). The NNS was significantly reduced when restricting to older age categories, offering a more targeted approach to intervention for resource allocation considerations.

The number of people prospectively evaluated at the TBSCs allowed the validation of previous assertions that DM–TB patients present with more advanced disease or are more likely to have lung cavities (Huang et al., 2017; Restrepo et al., 2007; Ugarte-Gil et

al., 2019). Yet while previous studies were retrospective and/or cases were selected from hospitalized patients with a bias towards severe illness (Chang et al., 2011; Huang et al., 2017; Perez-Guzman et al., 2001; Restrepo et al., 2007; Wang et al., 2009), the present study findings support that even in an outpatient setting, TB patients with DM have more advanced disease, as evidenced by a significantly higher proportion with bacteriological diagnosis, and among those with a positive Xpert MTB/RIF test, a higher bacterial load in the sputum. Relatedly, the computer-aided chest-imaging allowed not only rapid and systematic triage to Xpert MTB/RIF testing, but also found quantitatively more TB-like abnormalities in those with DM. In those with diagnosed TB, cavitory disease was indeed significantly more likely in patients with DM compared to those without, which confirms findings from other studies that were able to use more detailed computed tomography scans of the chest (Alkabab et al., 2018; Pande et al., 2016). While the diagnostic accuracy of the CAD4TB software requires further refinement (Pande et al., 2016; Rahman et al., 2017), these data suggest that DM diagnosis should further inform the artificial intelligence algorithms that produce the score.

While no comparable study exists for Bangladesh, the rates of death and treatment failure for DM–TB patients were higher than those in most reports from elsewhere, including South India (Jimenez-Corona et al., 2013; Mi et al., 2013; Viswanathan et al., 2014). Despite the understanding that patients with type 2 DM will likely be older than TB patients without DM and older age is a risk factor for mortality, the classification tree analysis demonstrated the independent weight of prediction of a poor treatment outcome. Our findings suggest that given the risk of a poor treatment outcome, patients with DM–TB in urban Dhaka are an ideal group in which to study the implementation of several recently promising approaches to improve care, such as modification of the anti-diabetic regimen to enhance host-directed therapy against TB (Degner et al., 2018; Zumla et al., 2015), or to augment pharmacokinetic exposure among DM–TB patients who may be more prone to anti-TB pharmacokinetic variability (Alkabab et al., 2017; Ghimire et al., 2016; Heysell et al., 2010; Pasipanodya et al., 2013; Pahl et al., 2014).

The study was subject to several limitations. Firstly, blood glucose level testing was voluntary for the individuals evaluated for TB at the TBSCs, and as a result a large number of individuals did not agree to be tested. While this was not originally anticipated, we suspect it was related to the patients' desire to avoid phlebotomy, and in general women and those in the lower age groups were slightly less likely to be screened for DM (Supplementary Material Table S1). Given that older age groups and men were more likely to screen positive for DM, we predict that the NNS would be higher than that calculated from the data among those agreeing to screening, but this further emphasizes the importance of designing strategies for screening, or repeat access to screening, among those in older age groups (Table 1). There was a greater proportion of men than women presenting for TB evaluation, and this trend remained for those diagnosed with TB. It has been noted in earlier studies in similar settings that women are less likely to seek healthcare for common illnesses compared to male household members (Pandey et al., 2002). Bangladesh national TB notification data also show that among the new pulmonary bacteriologically confirmed cases, the proportion of men is higher than women in all age groups except in children. Future interventions should seek to understand and ameliorate this disparity. Additionally, the final treatment outcome could not be verified in nearly a quarter of the

entire cohort as they were not followed for the extended period of time necessary to examine for potentially higher rates of relapse among those with DM or the proportion of those with transient hyperglycaemia resolving without treatment. These studies are now ongoing. Nevertheless, we believe the most important next steps in growing this public–private model should include metrics on the linkage and retention in care of TB patients shared by the NTP, private providers, and patient advocacy groups, and the development of horizontally integrated DM and TB management strategies.

In conclusion, a significant burden of DM exists among TB patients accessing healthcare through a public–private model in urban Bangladesh. The detection of DM was clinically meaningful and an independent predictor of poor treatment outcome. Further scale-up of the public–private model should focus on increasing the proportional uptake of DM screening, improving gender disparities in healthcare seeking behaviour, linkage and retention of DM–TB patients in care, and the implementation of research on individualized management including adjunctive metformin and therapeutic drug monitoring with dose adjustment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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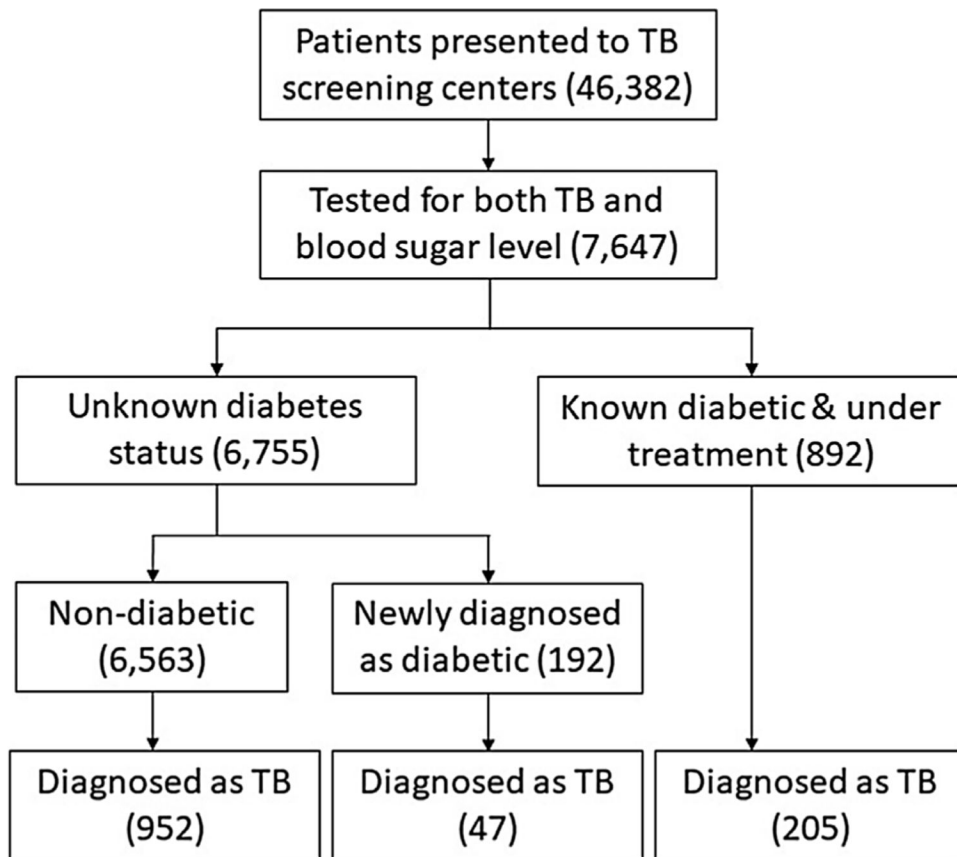


Figure 1. Flow diagram of presumed TB patients presenting to TB screening centres in Dhaka, Bangladesh, 2014–2017.

Table 1

Number needed to screen to identify one new case of DM among individuals presenting to three public–private model TB screening centres in Dhaka, Bangladesh, 2014–2017.

| Characteristics | Number tested | Number of new DM cases | NNS (95% CI) |
|--|---------------|------------------------|---------------|
| Patients presenting for evaluation of TB | | | |
| Sex | | | |
| Male | 4419 | 130 | 34 (29–40) |
| Female | 2336 | 62 | 38 (29–48) |
| Age group (years) | | | |
| 24 | 1104 | 8 | 139 (70–270) |
| 25–34 | 1651 | 27 | 61 (42–88) |
| 35–44 | 1238 | 41 | 30 (22–41) |
| 45–54 | 1101 | 42 | 26 (20–35) |
| 55–64 | 899 | 39 | 23 (17–31) |
| 65 | 762 | 35 | 22 (16–30) |
| Patients diagnosed as TB | | | |
| Sex | | | |
| Male | 689 | 40 | 17 (13–23) |
| Female | 310 | 7 | 44 (22–91) |
| Age group (years) | | | |
| 24 | 246 | 1 | 244 (44–1429) |
| 25–34 | 244 | 4 | 61 (24–156) |
| 35–44 | 155 | 13 | 12 (7–20) |
| 45–54 | 137 | 10 | 14 (8–25) |
| 55–64 | 117 | 11 | 11 (6–19) |
| 65 | 100 | 8 | 13 (7–24) |

DM, diabetes mellitus; TB, tuberculosis; NNS, number needed to screen; CI, confidence interval.

Table 2

Characteristics of individuals evaluated for TB according to their DM status presenting to three public–private model TB screening centres in Dhaka, Bangladesh, 2014–2017 ($N = 7647$).

| Characteristics | Without DM n = 6563 | With DM n = 1084 | p-Value |
|--|---------------------|------------------|---------|
| Sex, male, n (%) | 4289 (65) | 727 (67) | 0.271 |
| Age, years (mean \pm SD) | 40.8 \pm 16.4 | 51.6 \pm 13.6 | <0.001 |
| FBS, mmol (mean \pm SD) | 4.9 \pm 0.8 | 9.5 \pm 4.8 | 0.001 |
| RBS, mmol (mean \pm SD) | 5.7 \pm 1.4 | 12.3 \pm 5.7 | 0.001 |
| Xpert MTB/RIF positive, n (%) | 769 (12) | 224 (21) | 0.001 |
| Semi-quantitative burden reading in Xpert MTB/RIF, n (%) | | | |
| Low burden | 363 (48) | 84 (38) | Ref. |
| High burden | 399 (52) | 137 (62) | 0.010 |
| Xpert MTB/RIF rifampicin resistance status, n (%) | | | |
| Sensitive | 714 (93) | 215 (96) | Ref. |
| Indeterminate | 13 (2) | 2(1) | 0.400 |
| Resistant | 41 (5) | 7 (3) | 0.200 |
| CAD4TB score (mean \pm SD) | 67.6 \pm 25.5 | 72.3 \pm 24.0 | 0.001 |
| CAD4TB score ≥ 63 , n (%) | 3643 (55) | 677 (62) | 0.001 |
| Cavity on CXR, n (%) | 386 (6) | 104 (10) | 0.001 |
| Clinical diagnosis, n (%) | 173 (18) | 27 (11) | 0.800 |
| Pulmonary TB infection, n (%) | 952 (15) | 252 (23) | 0.001 |

TB, tuberculosis; DM, diabetes mellitus; SD, standard deviation; FBS, fasting blood sugar; RBS, random blood sugar; MTB, *Mycobacterium tuberculosis*; RIF, rifampicin; CAD4TB, Computer-Aided Detection for Tuberculosis; CXR, chest X-ray.

Table 3

Demographic and clinical characteristics of pulmonary TB patients according to DM status presenting to three public–private model TB screening centres in Dhaka, Bangladesh, 2014–2017 ($N=1204$).

| Characteristics | Pulmonary TB without DM n = 952 | Pulmonary TB with DM n = 252 | p-Value |
|---|---------------------------------|------------------------------|---------|
| Sex, n (%) | | | |
| Female | 303 (32) | 62 (25) | 0.027 |
| Male | 649 (68) | 190 (75) | |
| Age, years (mean \pm SD) | 37.7 \pm 16.6 | 48.1 \pm 12.4 | <0.001 |
| Age group (years), n (%) | | | |
| 24 | 245 (26) | 5 (2) | |
| 25–34 | 240 (25) | 26 (10) | 0.001 |
| 35–44 | 142 (15) | 63 (25) | <0.001 |
| 45–54 | 127 (13) | 76 (30) | <0.001 |
| 55–64 | 106 (11) | 49 (19) | <0.001 |
| 65 | 32 (10) | 33 (13) | <0.001 |
| Symptoms, n (%) | | | |
| Fatigue | 869 (91) | 232 (92) | 0.693 |
| Fever | 846 (89) | 222 (88) | 0.731 |
| Appetite loss | 765 (80) | 203 (81) | 0.944 |
| Cough for \geq 2 weeks | 632 (66) | 176 (70) | 0.299 |
| Unexplained weight loss | 705 (74) | 165 (65) | 0.007 |
| Night sweats | 394 (41) | 102 (41) | 0.794 |
| Shortness of breath | 250 (26) | 43 (17) | 0.002 |
| Haemoptysis | 147 (15) | 25 (10) | 0.026 |
| Current smoker | 192 (20) | 48 (19) | 0.671 |
| Diagnosed as TB by: | | | |
| GeneXpert MTB/RIF, n (%) | 769 (81) | 224 (89) | 0.005 |
| AFB microscopy, n (%) | 10 (1) | 1 (0.4) | 0.677 |
| Clinical diagnosis, n (%) | 173 (18) | 27 (10.7) | |
| Semi-quantitative burden reading in Xpert MTB/RIF, n (%) ^a | | | |
| Low burden | 363 (48) | 84 (38) | |
| High burden | 399 (52) | 137 (62) | 0.012 |
| Xpert MTB/RIF rifampicin resistance status, n (%) ^b | | | |
| Sensitive | 714 (93) | 215 (96) | |
| Indeterminate | 13 (2) | 2 (2) | 0.379 |
| Resistant | 41 (5) | 7 (3) | 0.173 |
| CAD4TB score, (mean \pm SD) | 84.9 \pm 17.7 | 87.4 \pm 14.6 | 0.053 |
| CAD4TB score \geq 63, n (%) | 690 (88) | 188 (90) | 0.264 |
| Cavity on CXR, n (%) | 209 (22) | 78 (31) | 0.003 |

TB, tuberculosis; DM, diabetes mellitus; SD, standard deviation; MTB, *Mycobacterium tuberculosis*; RIF, rifampicin; AFB, acid-fast bacilli; CAD4TB, Computer-Aided Detection for Tuberculosis; CXR, chest X-ray.

^aSemi-quantitative burden reading for 10 patients out of the 993 TB patients diagnosed by GeneXpert MTB/RIF (769 without DM + 224 with DM).

^bXpert MTB/RIF rifampicin resistance status for one patient out of the 993 TB patients diagnosed by GeneXpert MTB/RIF (769 without DM + 224 with DM).

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