Characteristics and treatment response in patients with tuberculosis and diabetes mellitus in New Delhi, India

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Diabetes mellitus (DM) is known to increase the risk of tuberculosis (TB) and adversely affect TB treatment outcomes. A descriptive study was carried out in registered TB patients screened for DM at Lok Nayak Hospital, New Delhi, India. Of 458 TB patients, 66 (14%) had DM. In those with dual disease, age ≥40 years, smear-positive pulmonary TB and recurrent TB were significantly more common. There was no effect of DM on TB treatment outcomes, although there was a trend towards smear non-conversion at 2 months. Screening for DM works well, and certain patient characteristics are more common in those with dual disease.

India, a middle-income country, has the highest tuberculosis (TB) burden in the world, with an estimated 2.3 million cases annually.[1] The country is experiencing urbanisation, ageing and changes in lifestyle, and these are associated with an escalating epidemic of diabetes mellitus (DM); in 2012, there were an estimated 63 million prevalent cases.[2] There is now good evidence that people with DM have 2–3 times the risk of developing active TB compared with those who do not have DM.[3,4] Not only may this lead to an increase in the TB burden, but patients with dual disease appear to have an increased frequency of adverse TB treatment outcomes, with delayed sputum culture conversion, an increased risk of death during anti-tuberculosis treatment and an increased risk of recurrent disease after successful completion of treatment.[5]

In 2012, a series of pilot studies was conducted in India on bi-directional screening for DM and TB in a routine setting, with aggregate data showing that screening in both directions was both feasible and effective.[6,7] No information, however, was presented on whether DM affects patient outcomes in a routine setting. We therefore decided to assess whether sputum smear conversion and treatment outcomes were affected by DM status in a hospital setting in Delhi, India.

METHODS

A descriptive study was carried out using the records and reports of India's Revised National TB Control Programme. The setting was a chest clinic at a tertiary care teaching hospital (Lok Nayak) in New Delhi, which has been implementing TB control activities for the last 10 years. The clinic has a catchment population of 0.5 million, and was one of the collaborating centres for the TB-DM bi-directional pilot project.[6,7] All adult TB patients diagnosed and registered from 15 February to 30 September 2012 were included in the study.

Patients were first screened verbally for known DM. In those with unknown DM status, blood tests were carried out using glucometers and test strips as previously described.[6] Patients were diagnosed with DM if fasting blood glucose was ≥ 126 mg/dl (7 mmol/dl), in line with World Health Organization guidelines.[8] Regardless of DM status, all TB patients received standardised TB treatment in accordance with national guidelines,[9] and were followed until the end of treatment. Treatment outcomes were monitored through registers and treatment cards, and reported in standard fashion according to the guidelines.[9] For the purpose of the study, treatment outcomes were categorised as successful (cured with negative sputum smear at the end of treatment, and treatment completed with no smears performed) and other (died, lost to follow-up, failed treatment, and transferred out with no outcome reported). All screening and treatment were provided free of charge.

The data were sourced from TB treatment cards, TB registers and TB-DM registers set up for the purpose of the pilot study. Data were extracted from the registers into paper-based forms and double entered into Epi-Data version 3.1 (EpiData Association, Odense, Denmark, http://www.epidata.dk). Patients were grouped according to whether or not they had DM, and categorical variables such as baseline characteristics and treatment outcomes were compared using the χ^2 test, with odds ratios and 95% confidence intervals as appropriate, with levels of significance set at 5%.

Ethics approval was obtained from the institutional ethics committee of Maulana Azad Medical College, New Delhi, and the International Union Against Tuberculosis and Lung Disease Ethics Advisory Group, Paris, France.

RESULTS

Of the 458 registered TB patients, 226 (49%) were male. The mean age of the patients was 32 years (interquartile range 20–42). Of 66 patients (14.5%) diagnosed with DM, 40 (60%) had a previous diagnosis. The baseline characteristics, sputum smear status during treatment and treatment outcomes for TB patients with and without DM are shown in the Table. In terms of baseline characteristics, age ≥ 40 years, smear-positive pulmonary TB (PTB) and recurrent TB were significantly more common in DM patients, while extra-pulmonary TB was significantly less common. There were no other differences. An increased proportion of patients with

TABLE Baseline characteristics, smear conversion and treatment outcomes of TB patients with and without diabetes registered at Lok Nayak Hospital, Delhi, India, in 2012

Characteristic	TB patients with DM (n = 66) n (%)	TB patients without DM (n = 392) n (%)	OR (95%CI)*
Sex			
Male	40 (61)	186 (47)	
Female	26 (39)	206 (53)	
Age, years			
<40	12 (18)	315 (80)	18.4 (9.3–36)†
≥40	54 (82)	77 (20)	
Disease classification			
Pulmonary smear-positive	38 (57)	151 (39)	2.2 (1.3–3.7)‡
Pulmonary smear-negative	17 (26)	80 (20)	
Extra-pulmonary	11 (17)	161 (41)	0.3 (0.1–0.6)†
Type of TB			
New	43 (66)	302 (77)	
Previously treated	23 (34)	90 (23)	1.8 (1.0–3.1)‡
HIV status			
Positive	0	17 (4)	
Negative	66 (100)	370 (94)	
Unknown	0	10 (2)	
Smoking status			
Smoker	9 (14)	49 (13)	
Non-smoker	57 (86)	343 (87)	
Sputum smear conversion			
End of intensive phase			
Converted	28 (74)	122 (83)	
Not converted	9 (24)	18 (12)	
Unknown	1 (2)	7 (5)	
End of treatment			
Converted	32 (88)	127 (91)	
Not converted	2 (6)	3 (2)	
Unknown	2 (6)	9 (7)	
Treatment outcomes			
Treatment success	58 (88)	362 (92)	
Other outcomes	8 (12)	30 (8)	

*OR only shown for comparisons where there were significant differences.
†$P < 0.001$.
‡$P < 0.05$.
TB = tuberculosis; DM = diabetes mellitus; OR = odds ratio; CI = confidence interval; HIV = human immunodeficiency virus.

DM who had their sputum smears examined did not experience smear conversion at the end of the initial phase of treatment, but this did not reach statistical significance when compared with patients who did not have DM. Final treatment outcomes did not differ between the groups.

DISCUSSION

In this observational study, it was feasible to routinely screen all TB patients for DM. Among patients with DM, there was a higher prevalence of older individuals and patients with smear-positive

PTB and recurrent TB. Older age might be expected, because type 2 DM disease tends to occur in older subjects. The reasons for the higher prevalence of PTB are unclear, but may be related to pulmonary microangiopathy and deficient activation of pulmonary macrophages, which are reported to occur in DM and may predispose patients to TB.[3] An increased risk of recurrent TB disease among DM patients has previously been reported.[5] In a recent prospective study in Mexico this association was confirmed, and was also shown to be due to reactivation of the same strain of *Mycobacterium tuberculosis* in 80% of cases and reinfection with a different strain in 20%.[10] More work is needed in India to understand the reasons for recurrent TB in patients with DM.

We found no significant effect of DM on sputum smear conversion or treatment outcomes, although an increased proportion of patients with DM remained sputum smear-positive at 2 months. Delays in sputum culture conversion have been reported in association with DM, although not consistently, and this also requires further study.[5]

The strength of the study was that it was conducted in a programme setting with no additional resources apart from government funds. Its limitations relate to any record review where data may be inaccurate and, in this study, the small sample group of patients with dual disease.

In conclusion, screening of TB patients for DM worked well in this tertiary hospital setting. The study also identified certain patient characteristics that may be more prevalent in those with DM, thus allowing targeting of screening if resources are constrained.

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On sait que le diabète sucré (DM) augmente le risque de tuberculose (TB) et influe de façon défavorable les résultats du traitement de la TB. On a mené une étude descriptive chez les patients TB enregistrés et dépistés pour DM à l'Hôpital Lok Nayak de New Delhi, Inde. Sur 458 patients TB, 66 (14%) souffraient de DM. Chez ceux atteints des deux maladies, un âge ≥40 ans, une TB pulmonaire à frottis positif et une rechute de TB sont significativement plus courants. Il n'y a pas d'effet du DM sur les résultats du traitement de la TB, quoiqu'il y ait une tendance vers la non-négativation du frottis à 2 mois. Le dépistage du DM fonctionne correctement et certaines caractéristiques du patient sont plus courantes chez ceux atteints des deux maladies.

Se conoce que la presencia de diabetes sacarina (DM) aumenta el riesgo de contraer la tuberculosis (TB) y ejerce un efecto desfavorable sobre el desenlace del tratamiento antituberculoso. Se llevó a cabo un estudio descriptivo de los pacientes tuberculosos registrados, en quienes se investigó el diagnóstico de DM en el Hospital Lok Nayak de Nueva Delhi en la India. De los 458 pacientes registrados con TB, 66 presentaban DM (14%). En los pacientes con ambas enferme-dades fue significativamente más frecuente que tuvieran una edad de ≥40 años, que padecieran TB pulmonar con baciloscopia positiva y recaídas de la TB. No se presentó ningún efecto de la DM sobre el desenlace terapéutico, aunque se observó una tendencia a la falta de conversión de la baciloscopia a los 2 meses de tratamiento. El cribado de la DM es eficaz y algunas características son más frecuentes en los pacientes que padecen ambas enfermedades.