High prevalence of undiagnosed diabetes among tuberculosis patients in peripheral health facilities in Kerala

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Setting: Two tertiary care hospitals and 12 peripheral health institutions (PHIs) in Trivandrum, Kerala, India.

Objective: To determine factors associated with the prevalence of diabetes mellitus (DM) among tuberculosis (TB) patients and examine differences in the proportion of new DM cases among TB patients diagnosed at tertiary care centres and PHIs.

Design: A descriptive study: TB patients diagnosed during March–September 2012 were screened for known DM. Those with unknown DM status were tested for random blood glucose and fasting blood glucose (FBG); FBG $\geqslant$ 126 mg/dl was diagnosed as new DM.

Results: Of 920 TB patients, 689 (72%) were male and the mean (standard deviation) age was 47.6 (16.4) years. Of these, 298 (32.4%) were diabetic: 235 (26%) had previously known DM and 63 (7%) were newly diagnosed. During the screening at PHIs and tertiary care hospitals, respectively 30/183 (16.4%) and 33/737 (4.5%) were newly diagnosed with DM (OR 3.71; 95%CI 2.17–6.32). Overall, age >50 years and pulmonary tuberculosis were independently associated with a higher prevalence of diabetes.

Conclusion: As nearly one in three TB patients had DM, we recommend that TB patients should be routinely screened for DM in Kerala. As the proportion of new DM was higher among TB patients diagnosed at PHIs, we would recommend that specific attention and investment be directed to PHIs.

India, the country with the highest number of tuberculosis (TB) cases in the world (an estimated 2.2 million cases in 2011),[1] also has a very high burden of diabetes mellitus (DM), with an estimated 63 million cases in 2012.[2] In India, 15% of pulmonary tuberculosis (PTB) cases have been estimated to be attributable to DM.[3] DM also affects TB treatment outcomes and may delay sputum conversion, increase case fatality rates during treatment, lead to increased failure rates in non-drug-resistant cases and also increase relapse rates of TB after successful completion of treatment.[4,5] Given this scenario, it has been felt that active screening for DM in TB patients may allow identification of previously undiagnosed DM and improve TB treatment outcomes through improved DM care.

Diabetes is common in Kerala, a state in South India with a population of 34.6 million, with an estimated community prevalence of 16–20%.[6,7] The state treated 25 917 TB patients in 2012, including all types of TB.[8] Kerala is known to have a high prevalence of DM in TB patients, with a recent study reporting a prevalence of 44%.[9]

As standardised procedures for DM screening among TB patients for use in hospitals and TB units (TUs)—a sub-district level tuberculosis programme management unit covering a population of 500 000, made up of varying numbers of peripheral health institutions (PHIs)—were not available in India, a monitoring tool linked to the TB registration and quarterly reporting system was developed and implemented, starting in multiple centres in India in 2012. The findings of this pilot study[10] showed that the screening procedures worked well, and the overall prevalence of DM in over 8000 screened TB patients was 13%. Trivandrum, in Kerala, was one of the sites that implemented screening at both hospital and field level in the TU, allowing for comparison of the yield from the different levels of screening.

This study aimed to determine factors associated with the diagnosis of DM during screening of TB patients under programme conditions. Specific objectives were to determine 1) the prevalence of DM, 2) the demographic and clinical factors associated with prevalence of DM, and 3) whether the yield of newly diagnosed DM was different in tertiary care facilities compared to that in PHIs.

METHODS

Study design

This descriptive study was part of a national level implementation project on bidirectional TB-DM screening performed within the routine health services in India in 2012.[10]

Study setting

The study was conducted in Trivandrum City in Kerala, a state in the south of India. In 2012, 1750 smear-positive TB patients were diagnosed and 2676 TB patients (including pulmonary smear-positive, pulmonary smear-negative and extra-pulmonary TB) were registered for treatment in Trivandrum district.[8] According to national guidelines,[11] TB patients are classified as PTB based on sputum smear examination for acid-fast bacilli (AFB) or, in those who are sputum smear-negative, by chest radiograph within 2 weeks of the negative result being obtained. Extra-pulmonary TB cases are diagnosed by the treating doctor based on a combination of radiology, histopathology, demonstration of AFB by smear or culture and/or clinical features. All TB patients are treated with a short-course,

fully intermittent (thrice weekly), standardised treatment regimen containing rifampicin throughout, delivered under direct observation.

The three centres that took part in the study in Trivandrum included two tertiary care hospitals and a TU consisting of 12 PHIs. The two hospitals were the Government Medical College Hospital, Trivandrum, and the Chest Disease Hospital, Pulayanarkotta. The Government Medical College Hospital is a 1916-bed, multi-specialty teaching hospital, with a daily out-patient load of 1800 and approximately 850 cases of TB diagnosed annually. The Chest Disease Hospital, Pulayanarkotta, which caters for patients with respiratory diseases, including TB, has 508 beds and a daily out-patient load of about 60; some 325 TB patients are diagnosed and treated there every year. As TB care in India is mainly domiciliary, TB patients are referred to peripheral centres to continue their treatment, and the hospitals provide in-patient care only for the management of complications or co-morbidities. The field-level programme management unit that participated in the study was the Trivandrum DTC (district TB centre) TU (covering a population of 0.5 million), which consists of 12 health care facilities, providing diagnosis of TB and directly observed treatment for TB patients. This unit registered 413 TB patients in 2012.

Trivandrum is the southernmost district of Kerala, with both a rural and an urban population. Patients are referred to the tertiary care hospitals from the PHIs or from private hospitals. Smaller PHIs are used by a predominantly rural population, whereas the tertiary care hospitals receive patients from both urban and rural areas. All of these hospitals provide free or subsidised care for patients. As a pulmonary care centre, the Chest Disease Hospital deals more with PTB, whereas the Government Medical College Hospital has various speciality departments providing care for extra-pulmonary TB patients.

Study participants

All TB patients aged ⩾15 years diagnosed consecutively at the two hospitals, or those registered for treatment at the Trivandrum DTC TU, between March and September 2012 made up the study population. The Chest Disease Hospital, Pulayanarkotta, started patient recruitment on 15 March 2012 and the Medical College Hospital, Trivandrum, on 19 March 2012. DTC Trivandrum TU started recruiting cases from 1 April 2012.

Data collection and analysis

The methods of screening, recording and reporting have been described in detail elsewhere.[10] Briefly, all TB patients were asked whether they had DM, and those with unknown DM status underwent random blood glucose (RBG) testing. If RBG was ⩾110 mg/dl, the patient was screened for fasting blood glucose (FBG). If FBG was ⩾126 mg/dl, DM was diagnosed. Venous blood samples were collected for blood sugar level measurement at the participating centre. Data on age, sex, smoking status (current smoker was defined as a person who smoked in the last month), RBG and FBG values were collected in the TB-DM register, the

study tool, by the field-level worker of the Revised National TB Control Programme (RNTCP), and were cross-checked by the District TB Officer of Trivandrum, the Medical Officer of the Medical College RNTCP cell and the principal investigator. The main outcomes for analysis were the number and proportion (with 95% confidence interval [CI]) of TB patients with a diagnosis of DM (previously known and newly diagnosed), stratified by age, sex, place of diagnosis and type of TB. Bivariate analysis was conducted to examine whether those factors were associated with the prevalence of DM. Odds ratios (OR) with 95%CI were used to measure associations. Multivariate analysis using logistic regression was conducted to calculate the adjusted OR. Only those variables that were statistically significant ($P < 0.05$) in bivariate analysis were considered for multivariate analysis. EpiData Version 3.5.3 (EpiData Association, Odense, Denmark) was used to analyse the data.

Ethics approval

The study was approved by the Institutional Ethics Committee of Government Medical College, Trivandrum. As this was a pilot project aiming to test the feasibility of DM screening among TB patients with a view to learning lessons for national scale-up approved by RNTCP authorities, the requirement for individual informed consent was waived by the Institutional Ethics Committee. All diagnosed DM patients were linked to DM care. Permission to use, report and publish the collected data in the pilot study was also obtained from the International Union Against Tuberculosis and Lung Disease Ethics Advisory Group, Paris, France.

TABLE 1   Demographic and clinical profile of TB patients screened and prevalence of DM among these by site, Trivandrum, Kerala, India, March–September 2012

Category	All patients n (%)	CDH n (%)	MCH n (%)	DTC TU n (%)	P value
Total	920 (100)	313 (100)	424 (100)	183 (100)	
Age, years					
>50	407 (44)	173 (55)	143 (34)	91 (50)	<0.01
⩽50	513 (56)	140 (45)	281 (66)	92 (50)	
Sex					
Male	670 (73)	264 (84)	274 (65)	132 (72)	<0.01
Female	250 (27)	49 (16)	150 (35)	51 (28)	
Current smoker					
Yes	370 (41)	117 (38)	174 (42)	79 (41)	0.29
No	531 (59)	194 (62)	236 (58)	101 (59)	
Type of TB					
Pulmonary	545 (59)	245 (78)	167 (39)	133 (73)	<0.01
Extra-pulmonary	375 (41)	68 (22)	261 (69)	50 (27)	
DM					
Yes	298 (32)	127 (43)	117 (28)	54 (30)	<0.01
No	622 (68)	186 (60)	307 (72)	129 (71)	
New DM (among DM cases only)					
New	63 (21)	27 (21)	6 (5)	30 (56)	<0.01
Previously diagnosed	235 (80)	100 (79)	111 (95)	24 (44)	

TB = tuberculosis; DM = diabetes mellitus; CDH = Chest Disease Hospital; MCH = Medical College Hospital; DTC TU = district TB centre TB unit (consisting of 21 peripheral health institutions).

TABLE 2 Factors associated with DM (previously and newly diagnosed) prevalence among TB patients, Trivandrum, Kerala, India, March–September 2012

Category	TB patients n	Patients with DM n (%)	OR (95% CI)	Adjusted OR (95%CI)*
Age, years				
>50	418	182 (45)	2.8 (2.1–3.7)†	2.5 (1.9, 3.3)†
≤50	530	116 (22)		
Sex				
Male	689	233 (34)	1.5 (1.1–2.1)†	1.0 (0.7, 1.5)
Female	259	65 (25)		
Type of TB				
Pulmonary	567	216 (38)	2.3 (1.7–3.1)†	1.9 (1.4, 2.7)†
Extra-pulmonary	383	82 (21)		
Current smoker				
Yes	377	144 (38)	1.6 (1.2–2.1)†	1.3 (0.96, 1.9)
No	546	152 (28)		
Site of diagnosis				
PHI	183	54 (30)	0.9 (0.6–1.2)	
Tertiary care	737	244 (33)		

*Adjusted for age, sex, type of TB and smoking status.
† $P < 0.05$.
DM = diabetes mellitus; TB = tuberculosis; OR = odds ratio; CI = confidence interval; PHI = peripheral health institution.

RESULTS

A total of 948 TB patients were screened in all three sites. Of these, 920 (97%) finished the entire screening process, completing all their required blood measurements. These 920 patients were included in the analysis. Of these, 670 (72%) were male and the mean (standard deviation) age was 47.8 (16.2) years. The median (interquartile range) age was 49 (37–59) years. The profile of the patients screened and the overall prevalence of DM among TB patients, desegregated by age, sex, smoking status and type of TB and for each site, are shown in Table 1. TB patients diagnosed at the Medical College Hospital had a higher proportion of extra-

TABLE 3 Factors associated with proportion of new DM among TB patients screened, Trivandrum, Kerala, India, March–September 2012

Category	TB patients n	Patients with newly diagnosed DM n (%)	OR (95%CI)	Adjusted OR (95%CI)*
Age, years				
>50	407	41 (10.1)	2.5 (1.5–4.3)†	2.2 (1.3, 3.8)†
≤50	513	22 (4.3)		
Sex				
Male	668	48 (7.2)	1.2 (0.7–2.2)	0.98 (0.5, 2.0)
Female	252	15 (6)		
Type of TB				
Pulmonary	545	50 (9.2)	2.8 (1.5–5.3)†	2.1 (1.1, 4.1)†
Extra-pulmonary	375	13 (3.5)		
Current smoker				
Yes	370	28 (7.6)	1.2 (0.7–1.9)	0.9 (0.5, 1.7)
No	531	35 (6.6)		
Site of diagnosis				
PHI	183	30 (16.4)	4.2 (2.5–7.1)†	3.7 (2.2, 6.4)†
Tertiary care	737	33 (4.5)		

*Adjusted for age, sex, type of TB, smoking status and site of diagnosis.
† $P < 0.05$.
DM = diabetes mellitus; TB = tuberculosis; OR = odds ratio; CI = confidence interval; PHI = peripheral health institution.

pulmonary TB, females and those aged ≤50 years. Of the 920 TB patients screened, 298 (32%) were diagnosed with DM. Of these, 63 (21%) were newly diagnosed DM cases, whereas 235 (79%) had previously known DM. The proportion of new DM was higher among TB patients diagnosed at PHIs compared to those at tertiary care hospitals.

Factors associated with a higher prevalence of DM among the TB patients are shown in Table 2. Age >50 years, male sex, PTB and current smoking were associated with higher prevalence of DM on bivariate analysis. In multivariate modelling, only age >50 years and PTB were found to be independently associated with DM.

Factors associated with the prevalence of new (previously undiagnosed) DM among the TB patients are shown in Table 3. Diagnosis in a PHI, age >50 years and PTB were found to be independently associated with new DM after multivariate modelling.

DISCUSSION

We found a high prevalence of DM among TB patients treated in Trivandrum; it was significantly higher among those aged >50 years and in those with PTB. The prevalence of DM among the TB patients was higher in Trivandrum than in the other sites that took part in the pilot study (personal communication, SS): the overall prevalence of diabetes in TB patients in the nationwide pilot was 13%,[10] whereas that in the Trivandrum centres was 32.4%.

More than three quarters of the TB patients with DM knew their DM status before the screening; however, this proportion was lower among TB patients screened at PHIs. Among the TB patients screened at peripheral TU level, more than half the cases of DM diagnosed were new cases. This probably indicates that patients reaching the major hospitals have multiple opportunities for screening before the diagnosis of TB, whereas patients diagnosed with TB at peripheral level are likely to miss a diagnosis of DM if they do not undergo active screening after TB diagnosis.

The high prevalence of DM among TB patients in Trivandrum could be explained by the high prevalence of DM in the general population in Kerala, which, as reported by previous studies among the adult population, is 16–20%,[6,7] and is much higher than in other states in India. TB patients in Kerala are also older than in other Indian states, which could be another reason for the high prevalence of DM in TB patients. The prevalence of TB is lower in Kerala than in the rest of the country.[12,13] Kerala also has a lower prevalence of human immunodeficiency virus (HIV) infection in the general population compared to other states of South India: the prevalence of HIV in the general population of India is 0.31% compared to 0.19% in Kerala.[14] DM could therefore be one of the main factors driving the TB epidemic in Kerala, unlike other high TB burden countries.[15]

A study looking at the prevalence of DM in TB patients in Kerala showed a high prevalence of DM, with 44% of TB patients having the disease.[9] However, this prevalence was determined by glycated haemoglobin (HbA1c) testing, which is not feasible in field conditions. The use of the HbA1c measurement could also be the reason for the higher diagnosis of DM in TB patients. This study also showed that almost half the DM patients diagnosed on screening were unaware of their DM status at the time of screening, and they would have remained undiagnosed if the screening had not been undertaken. Factors associated with a diagnosis of DM in TB patients in that study were male sex and age >50 years.

The strengths of this study are that a large number of TB patients were consecutively screened in the study sites in Trivandrum and are thus representative. Trivandrum was the only one

of two cities where screening was performed at both tertiary care hospital and PHI level, allowing a comparison to be made between the two different sites of screening of the yield and proportion of new DM diagnosed in the same population. Also, the use of a screening tool developed at national level allows for a comparison of the proportion of DM diagnosed in Trivandrum to that in other states in India. Possible limitations of the study include the lack of information on other possible confounding factors, as the information collected was limited to that included in the screening tool. Only patients notified to the RNCTP were included in the screening. There is a possibility that some patients, particularly those with extra-pulmonary TB being treated with individualised regimens outside the RNTCP, were not included in the study.

This study has major policy implications. First, it demonstrates the feasibility of screening for DM in TB patients using a standard screening tool. Second, it reiterates the high prevalence of DM in TB patients in Kerala, highlighting once again the importance of DM as a risk factor for TB in Kerala. Third, it demonstrates that screening for DM in TB patients at field level results in a higher proportion of previously undiagnosed DM patients being detected, which shows the importance of early screening of TB patients at field level. The RNTCP can also support India's non-communicable disease programme by early diagnosis of DM in a group of patients who would otherwise be undiagnosed, linking them to care and with a consequent reduction in morbidity and mortality. All of this requires close coordination between the RNTCP and the National Non-Communicable Disease Control Programme.

This study reinforces the view that DM screening in TB patients should be part of the minimum standard of care offered to all TB patients in Kerala and that it needs to be a high priority area for implementation. The state of Kerala has since taken a policy decision to screen all of its TB patients for DM. The government of India subsequently also made this a policy for the rest of the country. In addition, steps have been taken to link the RNTCP and the National Non-Communicable Disease Control Programme at PHI level in Kerala, allowing for DM screening and improved care of TB patients diagnosed with DM.

CONCLUSION

This study confirms the high prevalence of DM in TB patients in Kerala and that a significant proportion of DM patients may not be aware of their status; screening for diabetes is thus an urgent requirement and a minimum standard of care for TB patients, particularly at field level.

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Contexte : Deux hôpitaux de soins tertiaires et 12 institutions périphériques de santé (PHI) à Trivandrum, Kerala, Inde.

Objectif : Déterminer les facteurs en association avec la prévalence du diabète sucré (DM) chez les patients tuberculeux (TB) et examiner la différence des proportions de nouveaux DM entre les patients TB diagnostiqués dans les centres de soins tertiaires et dans les PHI.

Schéma : Etude descriptive. On a dépisté un diabète déjà connu chez les patients TB diagnostiqués pendant la période de mars à septembre 2012, et chez les patients dont le statut de DM était inconnu on a mesuré le glucose sanguin au hasard et le glucose sanguin à jeun (FBG) ; les sujets dont le FBG était ⩾ 126 mg/dl ont été diagnostiqués comme nouveaux cas de DM.

Résultats : Sur 920 patients TB, il y a eu 689 hommes (72%). Leur âge moyen était de 47,6 années (16,4). D'entre eux 298 (32,4%) étaient diabétiques ; 235 (26%) souffraient d'un DM déjà connu et 63 (7%) ont été nouvellement diagnostiqués. Dans les PHI, 30/183 (16,4%) ont été nouvellement diagnostiqués comme diabétiques au cours du dépistage et dans les hôpitaux de soins tertiaires 33/737 (4,5%) l'ont été également (OR 3,71 ; IC 95% 2,17–6,32). Au total, un âge >50 ans et la TB pulmonaire sont en association indépendante avec une prévalence plus élevée du DM.

Conclusion : La DM existe chez près d'un patient TB sur trois. Dès lors, nous recommandons le dépistage en routine du DM chez les patients TB de Kerala. La proportion de nouveaux cas de DM étant plus élevée chez les patients TB diagnostiqués dans les PHI, nous recommandons dès lors qu'une attention et un investissement spécifiques soient portés à ce problème dans les PHI.

Marco de referencia: Dos hospitales de atención terciaria y 12 centros periféricos de atención de salud de Trivandrum, en el estado de Kerala en la India.

Objetivo: Determinar los factores que se asocian con la prevalencia de diabetes (DM) en los pacientes aquejados de tuberculosis (TB) y examinar las diferencias en la proporción de casos nuevos de DM diagnosticados en los establecimientos de atención terciaria y en los centros periféricos de salud.

Métodos: Fue este un estudio descriptivo; se interrogó a los pacientes con diagnóstico de TB establecido entre marzo y septiembre del 2012 sobre el antecedente personal de DM y a los pacientes que desconocían su situación frente a la DM se practicaron pruebas de glucemia casual y glucemia en ayunas (FBG); el diagnóstico de un caso nuevo de diabetes se definió con una FBG ⩾ 126 mg/dl.

Resultados: De los 920 pacientes con TB, 689 eran de sexo masculino (72%) y la mediana de la edad fue 47,6 años (desviación estándar 16,4 años). De estos pacientes, 298 eran diabéticos (32,4%), de ellos 235 conocían su diagnóstico (26%) y se diagnosticaron 63 casos nuevos (7%). La proporción de casos nuevos diagnosticados en los centros periféricos fue de 30 en 183 pacientes (16,4%) y en los hospitales de atención terciaria fue de 33 en 737 (4,5%) (OR 3,71; IC95% de 2,17 a 6,32). En general, una edad >50 años y la presencia de TB pulmonar fueron factores asociados de manera independiente con una mayor prevalencia de DM.

Conclusión: Cerca de uno de cada tres pacientes TB presentaba DM; por esta razón se recomienda la detección sistemática de la DM en los pacientes con diagnóstico de TB en Kerala. La proporción de casos nuevos de DM fue mayor en los pacientes TB diagnosticados en los centros periféricos de atención sanitaria, por lo cual se preconiza prestar una mayor atención a este aspecto y realizar inversiones específicas en estos centros.