BMJ Open

Prevalence and factors associated with diabetes mellitus among tuberculosis patients in South India—a cross-sectional analytical study

Sathish Rajaa ,[1] Yuvaraj Krishnamoorthy ,[1] Selby Knudsen,[2] Gautam Roy,[3] Jerrold Ellner,[4] C Robert Horsburgh,[5] Natasha S Hochberg,[6,7] Padmini Salgame,[8] Govindarajan S,[9] Senbagavalli Prakash Babu,[3] Sonali Sarkar[3]

To cite: Rajaa S, Krishnamoorthy Y, Knudsen S, *et al*. Prevalence and factors associated with diabetes mellitus among tuberculosis patients in South India—a cross-sectional analytical study. *BMJ Open* 2021;**11**:e050542. doi:10.1136/bmjopen-2021-050542

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-050542).

Received 05 March 2021
Accepted 30 September 2021

For numbered affiliations see end of article.

Correspondence to
Yuvaraj Krishnamoorthy;
yuvi.1130@gmail.com

ABSTRACT

Objective To determine the prevalence and determinants of diabetes mellitus (DM) among tuberculosis (TB) patients and to assess the additional yield and number needed to screen (NNS) to obtain a newly diagnosed DM among TB patients.

Design We undertook a cross-sectional analysis of the cohort data under Regional Prospective Observational Research for Tuberculosis-India consortium. Newly diagnosed TB patients recruited into the cohort between 2014 and 2018 were included. Pretested standardised questionnaires and tools were used for data collection. Prevalence of DM among TB patients was summarised as proportion with 95% CI. Type II DM was diagnosed if random blood sugar level was >200 mg/dL or if the participant had a documented history of DM. NNS by blood glucose testing to diagnose one new DM case among TB patients was also calculated.

Setting Three districts of South India: Puducherry, Cuddalore and Villupuram

Subjects Newly diagnosed sputum smear positive pulmonary TB patients aged ≥16 years

Results In total, 1188 TB patients were included. Prevalence of DM among TB patients was 39% (95% CI: 36.2% to 41.8%). In unadjusted analysis, elderly TB, marital status, caste, gender, higher education level, household income and obesity had a significant association with DM. However, in adjusted analysis, only marital status (currently married aPR; 3.77 (95 CI: 2.20 to 6.49), widowed/separated/divorced aPR; 3.66 (95 CI: 1.96 to 6.83)) and body mass index category (normal weight aPR; 3.26 (95 CI: 2.55 to 4.16), overweight aPR; 3.86 (95 CI: 2.69 to 5.52), obesity aPR; 4.08 (95 CI: 2.81 to 5.94)) were found to be significant determinants. The number of TB patients needed to be screened to find a new DM case was 12.

Conclusion We found that one in three TB patients had coexisting DM. The number of TB patients needed to be screened to obtain a newly diagnosed DM patients was also determined. The study supports and highlights the need of RNTCP's effort in bidirectional screening of TB and DM.

Strengths and limitations of this study

- We systematically covered a majority of the newly diagnosed sputum smear positive pulmonary tuberculosis (TB) patients availing care from Revised National TB Control Program (RNTCP) or Directly Observed Treatment Short course (DOTS) centres in the study setting.
- We did not perform fasting and postprandial blood glucose test to confirm the diagnosis of diabetes mellitus among TB patients.
- The patients included in our study were diagnosed in public health facilities and not directly from the community. Hence, the sample may not be representative of all TB patients in the region.

INTRODUCTION

Of the 10.6 million annual tuberculosis (TB) cases occurring globally, India harbours one fourth.[1] A major health challenge faced recently worldwide is the double burden of communicable and non-communicable diseases.[2 3] This can be partly attributed to shared risk factors.[4 5] Despite, HIV infection being the most important risk factor for development of TB infection,[6] numerous other factors causing derangement of immunologic homeostasis, like diabetes mellitus (DM), alcoholism, tobacco use, malignancies, steroid therapy, stress, malnutrition and chronic renal failure can lead to active TB disease.[7 8] Coexistence of TB and DM is well documented in low-income and medium-income countries.[2 5 9]

Global incidence of DM is also on an increasing trend. In 2012, around 1.5 million people died from DM and its complications, with the highest mortality rates recorded in underdeveloped countries. A sedentary lifestyle, increased rice consumption, urbanisation and ageing has caused an escalation of DM epidemic among developing countries like India. Research from various settings has documented that around 12%–44% of TB

cases have coexisting DM,[10] and that DM triples the risk of active TB disease development.[11] This is postulated to be due to impairment in cell-mediated immunity which results in active TB disease and high relapse rates.[12] Lung damage in DM manifests as vascular complications, increased basal membrane thickness, decreased lung elasticity and neuropathy.[10 13] In addition to these, defects in cellular and humoural immunity pave way for several acute and chronic lung infections, including TB.[14 15] With 629 million people estimated to have diabetes by 2045, it is anticipated that TB incidence will also be amplified.[16] Unfortunately, the regions currently experiencing high TB burden will be affected the most, with a 163% increase expected for Africa and 84% for south-east Asia.[17] DM also escalates the risk of treatment failure, relapse and death among patients with TB.[18–20] There is a bidirectional relationship between TB and diabetes; the presence of long-term diabetes may trigger TB disease and affect the prognosis, while TB worsens the glycaemic control in TB-diabetes population.[20 21] Recently, there has been emphasis on identifying strategies to reduce the combined burden of DM and TB.

This double burden of TB and DM has recently emerged as an important public health problem in India highlighting the importance of screening TB patients for DM on a routine basis. The Central TB Division and the National non-communicable disease division jointly developed a framework called 'National Framework for joint TB-Diabetes collaborative activities'[22] which acts as a guidance tool for policymakers, programme managers and healthcare professionals in implementing TB–DM collaborative services.[22] It recommends screening all registered TB patients for diabetes and ensures comprehensive diabetes care and management among diagnosed TB cases. Such integrated efforts can augment early diagnosis and enhance good treatment outcomes. Nevertheless, there is paucity of evidence describing the burden and determinants of DM among TB patients, especially from South India. Hence, we undertook this study to determine the prevalence of DM among TB patients and factors associated with the same. We also assessed the additional yield and number needed to screen (NNS) to obtain a case of newly diagnosed DM among TB patients.

METHODS

Study setting and study population

We conducted a cross-sectional analysis of a large-scale ongoing cohort study under Regional Prospective Observational Research for Tuberculosis (RePORT)-India Consortium.[23] This study has two prospective observational cohorts: one with the participants having active pulmonary TB and the other where the household contacts of active pulmonary TB cases are included. For our analysis, we enrolled newly diagnosed pulmonary TB patients from cohort 1. The study was conducted by Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) in collaboration with Boston University Medical Campus and Rutgers University.

The study encompassed three districts from South India, namely Puducherry (population ~1.3 million), Villupuram (population ~3.5 million) and Cuddalore (population ~2.6 million). Enrolment started in May 2014 in Puducherry, August 2014 in Cuddalore and November 2015 in Villupuram and continued until 2019. The details of the study procedure have been reported elsewhere.[24–26]

One tuberculosis unit (TU) in Puducherry and two TUs each in Villupuram and Cuddalore were selected for recruitment of study participants. Service delivery at the subdistrict level was operational through the designated microscopy centres (DMCs) and the Peripheral Health Institutions with TUs as the nodal point. Under the programme, diagnosis and treatment were provided free of cost. Persons getting diagnosed with TB at the DMC's were referred to their nearby Primary Health Centre (PHC) for initiation of treatment after screening for comorbidities like type II diabetes, HIV, etc. The sociodemographic details, clinical course, medication adherence and comorbidity profile were maintained at the PHC and followed up using treatment cards.

We enrolled only the newly diagnosed sputum smear positive pulmonary TB patients (at least 1+acid fast bacilli)≥16 years from the selected districts. We excluded patients with a known history of TB disease or treatment, multidrug resistant TB and patients currently on TB treatment.

Ethics and consent

Written consent, and assent in addition to parents' consent (in case of participants<18 years of age), was obtained from all participants enrolled in the study. The study protocol was approved by the Institute Ethics Committee and Scientific Advisory Committee of JIPMER, and the Institutional Review Boards at Boston University Medical Campus and Rutgers-New Jersey Medical School.

Study procedure

A pretested semi-structured questionnaire was used to capture the sociodemographic characteristics such as age, gender, education, occupation, religion, caste and marital status. Karnofsky's score was used to assess functional impairment.[27] Participants were also enquired on alcohol use. Anthropometric measurements such as height and weight were measured for calculating the body mass index (BMI). A majority of the interviews was conducted in the clinic, and the rest in the participant's homes. Filled questionnaires were scanned and transferred to Boston University using the Verity TeleForm Information Capture System software V.10.8 (Sunnyvale, CA, USA), and it was read into a Microsoft Access (Seattle, WA, USA) database. Errors in the data entry process were reviewed and duly corrected by the onsite team in India.

Study definitions

A participant was classified as a hazardous alcohol user if they had reported drinking alcohol for about 2–3 times/week and had ≥3 drinks on a typical day; or 2–4 times/month and had ≥6 drinks in one sitting at monthly. BMI was categorised as underweight (<18.5 kg/m^2), normal (18.5–22.9 kg/m^2), overweight (23–24.9 kg/m^2) and obese (≥25 kg/m^2) based on Asian classification.[28] Diagnosis of active TB was made using sputum culture—positive for MTB either by solid or liquid culture. Type II DM was defined as a random blood sugar reading >200 mg/dL or a history of diabetes verified through medical records. Diagnosis of type II DM was made during the phase of enrolment and also during the course of treatment.

Statistical analysis

Data were extracted from the RePORT India consortium project database for the JIPMER site and analysed using Stata V.14.2 software. Continuous variables such as age were summarised as mean and SD or median (IQR) based on normality. Categorical variables were summarised as proportions. Prevalence of type II DM among TB patients was summarised as percentage with 95% CI. We used generalised linear model with Poisson distribution and a log-link to find the factors associated with type II DM among TB patients. Gender, education, occupation, marital status, religion, caste, Karnofsky score, obesity and alcohol use were considered as covariates. Factors with p value less than 0.2 in the univariable analysis were considered for multivariable analysis. Unadjusted and adjusted prevalence ratios (PR) were obtained from univariable and multivariable analysis. Variables with a p value less than 0.05 in the final model were considered as statistically significant. NNS by blood glucose testing to diagnose one new DM case was calculated by the following formula:

$$\text{NNS} = \frac{1}{\text{No. of newly diagnosed DM by glucose testing/ Number of TB cases screened (excluding known DM cases)}}$$

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting or dissemination plans of our research.

RESULTS

Sociodemographic, behavioural and anthropometric characteristics

A total of 1188 eligible TB patients were included during the study period. Sociodemographic, behavioural and anthropometric characteristics of the study participants are described in table 1. The mean (SD) age of the study participants was 44.5 (14.6) years. More than three-fourth (78.2%) of the participants were males; about 16% did not receive any formal education; more than three-fourth (75.9%) had a household income between 3000 and 10 000; majority (88.9%) were Hindus; three-fourth were employed; almost three-fourth (72.9%) were currently married and more than one-fourth (26.4%) belonged to

Table 1 Socio-Demographic characteristics of the study participants (n=1188)

Characteristics	Frequency	Percentage (%)
Age category (in years)		
<19	76	(6.4)
20–29	130	(10.9)
30–39	201	(16.9)
40–49	328	(27.6)
50–59	263	(22.1)
>60	190	(15.9)
Gender		
Female	258	(21.7)
Male	930	(78.3)
Educational status (n=1185)		
No formal education	189	(15.9)
Primary school	273	(23.0)
Secondary school	501	(42.3)
Higher secondary	222	(18.8)
Marital status		
Currently married	866	(72.9)
Never married	198	(16.6)
Widowed/divorced/separated	124	(10.5)
Religion (n=1186)		
Hindu	1054	(88.9)
Christian	78	(6.6)
Islam	54	(4.5)
Employment status (n=1187)		
Unemployed	105	(8.8)
Employed	893	(75.3)
Others	189	(15.9)
Caste (n=1170)		
OBC	861	(73.6)
SC/ST	309	(26.4)
Income (INR) (n=1162)		
<3000	136	(11.7)
3001–5000	448	(38.5)
5001–10 000	433	(37.3)
>10 000	145	(12.5)
Alcohol use		
Alcohol user	695	(58.5)
Non-drinker	493	(41.5)
Karnofsky Performance Scale		
Able to carry normal activity and work	348	(29.3)
Unable to work, able to live at home	840	(70.7)
BMI category* (n=1181)		
Underweight (<18.50 kg/m^2)	705	(59.7)
Normal (18.50–22.99 kg/m^2)	357	(30.2)
Overweight (23.00–24.99 kg/m^2)	64	(5.4)
Obesity (≥25.00 kg/m^2)	55	(4.6)

*Asia Pacific guidelines for obesity.
INR, Indian Rupees (₹).

SC/ST category. More than half (59.7%) of the participants were underweight; and about 58.4% were alcohol users. Performance status assessed by Karnofsky score showed that only 29.3% were able to carry out their normal activity without the requirement of special care.

Factors associated with DM among TB patients

Prevalence of DM among TB patients was 39% (95% CI: 36.2% to 41.8%). Of these patients, 33.2% had history of DM and 5.8% were newly diagnosed DM with Random Blood Sugar (RBS) more than 200 mg/dL. Table 2 shows the factors associated with DM among the study participants. In unadjusted analysis, elderly TB, marital status, caste, gender, higher education level, household income, obesity had a significant association with DM among TB patients. However, in adjusted analysis, only marital status and BMI category were found to be significant determinants. Obese TB patients had 4.08 times higher risk of having DM compared with underweight TB patients (aPR=4.08; 95% CI: 2.81 to 5.94). Patients who were separated/divorced/widowed (aPR=3.66; 95% CI: 1.96 to 6.83) and currently married (aPR=3.77; 95% CI: 2.20 to 6.49) had significantly higher risk of having DM compared with never-married TB patients.

Additional yield

Of the total 1188 eligible TB patients screened for DM, 463 (39%) had DM, of which 68 (14.7%) were newly diagnosed cases (additional yield by RBS screening). The number of TB patients needed to undergo blood glucose testing (excluding known case of DM patients from testing) to diagnose a new DM case was approximately 12.

DISCUSSION

The present study showed that 39% of newly diagnosed smear positive pulmonary TB patients had DM. We had an additional yield of nearly 15% by screening the cases with random blood glucose testing. The NNS to diagnose a DM case was 12. We also found that obese TB patients and those patients who were separated/divorced/widowed had significantly higher risk of having DM compared with those with normal BMI and unmarried patients.

The prevalence obtained in our study (39%) was observed to be five times higher than the burden among the general population (7.3%) of India.[29] Studies conducted around the world show wide variations in the burden of DM among TB patients ranging from 1.9% to 45%.[30] Systematic reviews on burden of DM among active TB patients showed the median prevalence in Asia and Indian subcontinent to be 17% and 19%, respectively, which were considerably less than our finding.[17 30] However, other studies conducted in South India (Puducherry: 29%; Tamil Nadu: 25.3%; Andhra Pradesh: 31%; Kerala: 32%; Karnataka: 35%) and neighbouring countries (Pakistan: 39%; China: 30%) showed findings comparable to our current study.[10 31–36] Reason for such higher burden maybe differences in lifestyle factors like increased consumption of rice as their staple diet, a higher proportion of elderly population and a higher burden of obesity/overweight in south India.[37] Data from the Prospective Urban Rural Epidemiological Study (PURE study) among 132 373 participants from 21 countries confirms a strong correlation between excess white rice intake and incident diabetes.[38] There were wide disparities observed in TB +DM burden across studies from other African and Asian countries.[39–43] Such differences could be attributed to the diversities in screening mechanisms and also due to variations in the actual burden of DM among the general population.

Nearly 15% of the DM patients were newly diagnosed, while rest of them were previously diagnosed with DM. Long-term or chronic DM could impair the adaptive and innate immune responses essential to counter TB proliferation.[44] In addition, similarities in risk factor profile between DM and TB, could have influenced the larger proportion of previously diagnosed DM among TB patients found in our study.

In our study, we found that 12 patients needed to be screened with random blood glucose for diagnosing one new DM case. This finding was lesser compared with the previous studies in India from Andhra Pradesh, and Gujarat, whereas it was found to be almost similar to other low middle-income settings such as Vietnam and Ethiopia.[45–48] This finding justifies and necessitates proper implementation of screening for DM among TB patients in India.

We found that marital status and obesity were significant determinants of DM among TB patients. Though marital status has not shown significant association in previous literature, several studies have shown a significant association between obesity and DM among TB patients, which are in line with our study findings.[32 36 49] Although an optimum status of nutrition or obesity may act as a protective factor in patients with TB,[50] the hyperglycaemia and distorted immunity outweighs this advantage and may lead to increased risk of TB treatment failure or mortality among DM patients. In addition, weight loss as a result of poor control of DM can lead to metabolic decomposition, thereby further increasing the risk of TB treatment failure and death.[51] One of our published studies on the impact of nutritional status and diabetes on TB found that active TB disease and its association with diabetes are higher among normal, overweight and obese adults, when compared with those who are undernourished.[52]

Another specific characteristic of obese TB patients that needs attention is the altered pharmacokinetics observed among them leading onto TB treatment failure.[53 54] This increased volume of distribution can cause a decrease in blood concentration of rifampicin and such patients might require alterations in dosage as per bodyweight. Optimal treatment of diabetes among TB cases should also be kept in mind, as poor glycaemic control is often linked with adverse TB outcomes, while host-directed metformin therapy is often associated with lesser TB mortality and better sputum conversion at end of intensive phase.[55 56]

Table 2 Association of sociodemographic, behavioural and anthropometric characteristics with diabetes mellitus among tuberculosis patients in South India (n=1188)

Characteristics	Total	Diabetes mellitus, n=463 (%)	Unadjusted prevalence ratio (95% CI)	Adjusted prevalence ratio (95% CI), n=1138	Adjusted p-value
Age categorisation (in years)					
<60	998	373 (37.3)	1	1	–
≥60	190	90 (47.4)	1.26 (1.00 to 1.59)	1.13 (0.86 to 1.48)	0.36
Gender					
Female	258	87 (33.7)	1	1	0.23
Male	930	376 (40.3)	1.19 (0.94 to 1.50)	1.18 (0.89 to 1.57)	–
Educational status					
No formal education	189	59 (31.2)	1	1	–
Primary	273	106 (38.8)	1.24 (0.90 to 1.71)	1.04 (0.72 to 1.51)	0.79
Secondary	501	227 (45.3)	1.45 (1.09 to 1.93)	1.18 (0.84 to 1.65)	0.32
Higher	222	71 (31.9)	1.02 (0.73 to 1.45)	1.24 (0.82 to 1.88)	0.29
Marital status					
Currently married	866	379 (43.7)	3.46 (2.31 to 5.20)	3.77 (2.20 to 6.49)	<0.001*
Never married	198	25 (12.6)	1	1	–
Widowed/separated/ divorced	124	59 (47.6)	3.76 (2.38 to 6.06)	3.66 (1.96 to 6.83)	<0.001*
Employment					
Unemployed	105	38 (36.2)	1	{Not included in the model}	
Employed	893	375 (42)	1.16 (0.83 to 1.62)		
Others	189	50 (26.4)	0.73 (0.26 to 0.49)		
Alcohol use					
Yes	695	267 (38.4)	0.96 (0.79 to 1.15)	{Not included in the model}	
No	493	196 (39.7)	1		
BMI category†					
Underweight	705	141 (20.0)	1	1	–
Normal	357	222 (62.2)	3.09 (2.50 to 3.81)	3.26 (2.55 to 4.16)	<0.001*
Overweight	64	49 (76.5)	3.82 (2.77 to 5.27)	3.86 (2.69 to 5.52)	<0.001*
Obesity	55	48 (87.3)	4.33 (3.12 to 6.01)	4.08 (2.81 to 5.94)	<0.001*
Caste					
OBC	861	356 (41.3)	1	1	–
SC/ST	309	100 (32.3)	0.78 (0.62 to 0.97)	0.90 (0.70 to 1.16)	0.42
Karnofsky's Performance Scale					
Able to carry normal activity and work	348	146 (41.9)	1	{Not included in the model}	
Unable to work, able to live at home	840	317 (37.9)	0.90 (0.74 to 1.09)		
Income (INR)					
<3000	136	41 (30.1)	0.77 (0.55 to 1.08)	0.80 (0.54 to 1.20)	0.28
3001–5000	448	174 (38.8)	1	1	–
5001–10 000	433	164 (37.8)	0.97 (0.78 to 1.20)	0.87 (0.68 to 1.10)	0.26
>10 000	145	79 (54.5)	1.40 (1.07 to 1.83)	1.11 (0.82 to 1.51)	0.47

Employment, alcohol use, Karnofsky's Performance Scale were not included into the model as the p value was more than 0.20.
*P-value statistically significant (<0.05).
†Asia Pacific guidelines for obesity (BMI >25.0 kg/m^2).

This study has several strengths. We comprehensively covered a vast majority of newly diagnosed sputum smear positive pulmonary TB patients accessing care at RNTCP/DOTS centres from the study setting. The large sample size, data quality assurance through double data entry and validation, and the use of standardised and validated questionnaires such as Karnofsky score are added advantages to the study.

Despite the strengths, we had a few limitations. We did not perform fasting and postprandial blood glucose test to confirm the diagnosis of DM among TB patients. Hence, we cannot differentiate our study finding from other causes of high random blood sugar like stress induced hyperglycaemic. As this was conducted as a part of large-scale cohort study on TB patients, we could not assess important factors related to DM such as diet, physical activity, family history of DM or other chronic conditions.

As the patients in our study were selected from three contiguous districts of South India, the generalisability of the results may be limited to similar settings. Since our study was based on the data obtained from public health facilities, the sample may be biased towards those with positive health seeking behaviour, and not be representative of all the TB patients in the community. Finally, since this was a cross-sectional analysis, causal inferences cannot be made between demographic, anthropometric or behavioural factors,and DM.

In spite of these limitations, our study has several programmatic implications. First, we provide baseline information on the burden of likely DM among TB patients, with a larger sample size. We have identified specific target groups requiring additional attention through focused interventions. We have also estimated the number of TB patients needed to screened to diagnose a new DM case. Our findings urge an effective implementation of the bidirectional screening strategy under RNTCP, as this rising and unidentified DM epidemic among TB patients is likely to affect our targets of WHO End TB strategy. More intensive-specific public health strategies are the need of the hour, for better implementation of preventive care and effective provision of comprehensive health. As the long-term prognosis of patients with TB and diabetes depend on diabetes treatment success, effective management of diabetes and regular active screening for its complications and TB relapse should be ensured even after completion of TB treatment.

Author affiliations
[1]Jawaharlal Institute of Postgraduate Medical Education, Puducherry, India
[2]Department of Infectious Diseases, Boston Medical Center, Boston, Massachusetts, USA
[3]Department of Preventive and Social Medicine, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, Puducherry, India
[4]Department of Medicine, Rutgers New Jersey Medical School, Newark, New Jersey, USA
[5]Boston University, Boston, Massachusetts, USA
[6]Section of Infectious Diseases, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, USA
[7]Department of Epidemiology, Boston University School of Public Health, Boston, Massachusetts, USA
[8]Rutgers University Newark, Newark, New Jersey, USA
[9]Directorate of Health Services, State TB cell, Puducherry, India

Acknowledgements The authors would like to acknowledge the work done by the field and office staff of the Indo-US TB project under the Department of Preventive & Social Medicine, JIPMER. The authors would like to extend heartfelt gratitude to each of the participant from the study sites.

Contributors Conceived and designed the study: YK and SR. Data management and extraction: SPB. Analysed the data and wrote the paper: SR and YK. Provided comments and inputs to revise the manuscript: SK, GR, GS, JE, CRH, NSH, PS, SPB and SS. Guarantors: SR, YK and SS

Funding This work was supported by in whole or in part with Federal funds from the Government of India's (GOI) Department of Biotechnology (DBT), the United States National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Office of AIDS Research (OAR), and distributed in part by CRDF Global. The contents of this publication are solely the responsibility of the authors and do not represent the official views of the DBT, the NIH or CRDF Global.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The study protocol was approved by the Institute Ethics Committee and Scientific Advisory Committee of JIPMER, and the Institutional Review Boards at Boston University Medical Campus and Rutgers-New Jersey Medical School.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data are available on reasonable request.

ORCID iDs
Sathish Rajaa http://orcid.org/0000-0002-6103-420X
Yuvaraj Krishnamoorthy http://orcid.org/0000-0003-4688-510X

REFERENCES

1 World Health Organization. *Global tuberculosis report 2019*. Geneva, Switzerland: WHO, 2019.
2 Zheng C, Hu M, Gao F. Diabetes and pulmonary tuberculosis: a global overview with special focus on the situation in Asian countries with high TB-DM burden. *Glob Health Action* 2017;10:1264702.
3 Kapur A, Harries AD. The double burden of diabetes and tuberculosis - public health implications. *Diabetes Res Clin Pract* 2013;101:10–19.
4 Imai C, Hashizume M. A systematic review of methodology: time series regression analysis for environmental factors and infectious diseases. *Trop Med Health* 2015;43:1–9.
5 Remais JV, Zeng G, Li G, *et al*. Convergence of non-communicable and infectious diseases in low- and middle-income countries. *Int J Epidemiol* 2013;42:221–7.
6 Rieder HL. *Epidemiologic basis of tuberculosis control. International Union against tuberculosis and lung disease*. Paris: IUATLD-162, 1999.
7 Sester M. Tuberculosis in immunocompromised host. *Respir Med* 2010:200–8.
8 Solovic I, Sester M, Gomez-Reino JJ, *et al*. The risk of tuberculosis related to tumour necrosis factor antagonist therapies: a TBNET consensus statement. *Eur Respir J* 2010;36:1185–206.
9 Sil A, Patra D, Dhillon P, *et al*. Co-Existence of diabetes and TB among adults in India: a study based on national family health survey data. *J Biosoc Sci* 2021;53:758–72.
10 Viswanathan V, Kumpatla S, Aravindalochanan V, *et al*. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. *PLoS One* 2012;7:e41367.

11 Syed Ahamed Kabeer B, Sikhamani R, Swaminathan S, *et al*. Role of interferon gamma release assay in active TB diagnosis among HIV infected individuals. *PLoS One* 2009;4:e5718.
12 Mburu JW, Kingwara L, Ester M, *et al*. Prognostic factors among TB and TB/DM comorbidity among patients on short course regimen within Nairobi and Kiambu counties in Kenya. *J Clin Tuberc Other Mycobact Dis* 2018;12:9–13.
13 Caner B, Ugur O, Bayraktar M, *et al*. Impaired lung epithelial permeability in diabetics detected by technetium-99m-DTPA aerosol scintigraphy. *J Nucl Med* 1994;35:204–6.
14 Atac G, Sevim T, Gungor G. The factors influencing time to sputum smear and culture conversion among patients with pulmonary tuberculosis. *Toraks Dergisi* 2001;2:16–20.
15 Iqbal N, Irfan M, Jabeen K, *et al*. Chronic pulmonary mucormycosis: an emerging fungal infection in diabetes mellitus. *J Thorac Dis* 2017;9:E121–5.
16 International Diabetes Federation. *IDF diabetes atlas*. 8th edition, 2017. http://www.diabetesatlas.org/IDF_Diabetes_Atlas_8e_interactive_EN/
17 Noubiap JJ, Nansseu JR, Nyaga UF, *et al*. Global prevalence of diabetes in active tuberculosis: a systematic review and meta-analysis of data from 2·3 million patients with tuberculosis. *Lancet Glob Health* 2019;7:e448–60.
18 Guariguata L, Whiting DR, Hambleton I, *et al*. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract* 2014;103:137–49.
19 Huangfu P, Pearson F, Ugarte-Gil C, *et al*. Diabetes and poor tuberculosis treatment outcomes: issues and implications in data interpretation and analysis. *Int J Tuberc Lung Dis* 2017;21:1214–9.
20 Pavlović JM, Pavlovic AD, Bulajić MV, *et al*. Prevalence of diabetes mellitus (DM) in tuberculosis (TB) patients: clinical and radiologic features in the TB-DM association based on a five-year hospital study. *Infez Med* 2018;26:22–7.
21 Aftab H, Christensen DL, Ambreen A, *et al*. Tuberculosis-Related diabetes: is it reversible after complete treatment? *Am J Trop Med Hyg* 2017;97:1099–102.
22 Ministry of Health and Family welfare. Government of India. *National framework for joint TB-Diabetes collaborative activities. director General of health services*, 2017.
23 Hamilton CD, Swaminathan S, Christopher DJ, *et al*. Report international: advancing tuberculosis biomarker research through global collaboration. *Clin Infect Dis* 2015;61Suppl 3:S155–9.
24 Van Ness SE, Chandra A, Sarkar S, *et al*. Predictors of delayed care seeking for tuberculosis in southern India: an observational study. *BMC Infect Dis* 2017;17:1–9.
25 Hochberg NS, Sarkar S, Horsburgh CR, *et al*. Comorbidities in pulmonary tuberculosis cases in Puducherry and Tamil Nadu, India: opportunities for intervention. *PLoS One* 2017;12:e0183195.
26 Hoyt KJ, Sarkar S, White L, *et al*. Effect of malnutrition on radiographic findings and mycobacterial burden in pulmonary tuberculosis. *PLoS One* 2019;14:e0214011–11.
27 Karnofsky Performance Status. [Internet]. Available: https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=44156
28 WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157–63.
29 Anjana RM, Deepa M, Pradeepa R, *et al*. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. *Lancet Diabetes Endocrinol* 2017;5:585–96.
30 Workneh MH, Bjune GA, Yimer SA. Prevalence and associated factors of tuberculosis and diabetes mellitus comorbidity: a systematic review. *PLoS One* 2017;12:e0175925.
31 Raghuraman S, Vasudevan KP, Govindarajan S, *et al*. Prevalence of diabetes mellitus among tuberculosis patients in urban Puducherry. *N Am J Med Sci* 2014;6:30–4.
32 Padmalatha P, Hema K. Study on prevalence of diabetes mellitus in tuberculosis patients attending a tertiary care hospital in Guntur, Andhra Pradesh. *Indian J Basic Applied Med Res* 2014;4:494–8.
33 Jali MV, Mahishale VK, Hiremath MB, *et al*. Diabetes mellitus and smoking among tuberculosis patients in a tertiary care centre in Karnataka, India. *Public Health Action* 2013;3:51–3.
34 Nair S, Kumari AK, Subramonianpillai J, *et al*. High prevalence of undiagnosed diabetes among tuberculosis patients in peripheral health facilities in Kerala. *Public Health Action* 2013;3:S38–42.
35 Aftab H, Ambreen A, Jamil M, *et al*. High prevalence of diabetes and anthropometric heterogeneity among tuberculosis patients in Pakistan. *Trop Med Int Health* 2017;22:465–73.
36 Mi F, Jiang G, Du J, *et al*. Is resistance to anti-tuberculosis drugs associated with type 2 diabetes mellitus? A register review in Beijing, China. *Glob Health Action* 2014;7:24022.
37 Ghosh K, Dhillon P, Agrawal G. Prevalence and detecting spatial clustering of diabetes at the district level in India. *J Public Health* 2020;28:535–45.
38 Bhavadharini B, Mohan V, Dehghan M, *et al*. White rice intake and incident diabetes: a study of 132,373 participants in 21 countries. *Diabetes Care* 2020;43:dc192335.
39 Thapa B, Paudel R, Thapa P, *et al*. Prevalence of diabetes among tuberculosis patients and associated risk factors in Kathmandu Valley. *SAARC J Tuber Lung Dis HIV/AIDS* 2015;12:20–7.
40 Kottarath M, Mavila R, V. A, *et al*. Prevalence of diabetes mellitus in tuberculosis patients: a hospital based study. *Int J Res Med Sci* 2015;3:2810–4.
41 Ade S, Affolabi D, Agodokpessi G, *et al*. Low prevalence of diabetes mellitus in patients with tuberculosis in Cotonou, Benin. *Public Health Action* 2015;5:147–9.
42 Faurholt-Jepsen D, Range N, PrayGod G, *et al*. Diabetes is a risk factor for pulmonary tuberculosis: a case-control study from Mwanza, Tanzania. *PLoS One* 2011;6:e24215.
43 Haraldsdottir TL, Rudolf F, Bjerregaard-Andersen M, *et al*. Diabetes mellitus prevalence in tuberculosis patients and the background population in Guinea-Bissau: a disease burden study from the capital Bissau. *Trans R Soc Trop Med Hyg* 2015;109:400–7.
44 Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLoS Med* 2008;5:e152.
45 Achanta S, Tekumalla RR, Jaju J, *et al*. Screening tuberculosis patients for diabetes in a tribal area in South India. *Public Health Action* 2013;3:43–7.
46 Dave P, Shah A, Chauhan M, *et al*. Screening patients with tuberculosis for diabetes mellitus in Gujarat, India. *Public Health Action* 2013;3:29–33.
47 Hoa NB, Phuc PD, Hien NT, *et al*. Prevalence and associated factors of diabetes mellitus among tuberculosis patients in Hanoi, Vietnam. *BMC Infect Dis* 2018;18:603.
48 Workneh MH, Bjune GA, Yimer SA. Prevalence and associated factors of diabetes mellitus among tuberculosis patients in south-eastern Amhara region, Ethiopia: a cross sectional study. *PLoS One* 2016;11:e0147621.
49 Tiroro S. The magnitude and associated factors of tuberculosis among diabetic patients at Tikur Anbessa specialized teaching hospital in Addis Ababa, Ethiopia. 2015. mph thesis. Addis Ababa university. Available: http://etd.aau.edu.et/bitstream/123456789/7590/1/Sisay%20Tiroro.pdf
50 Leung CC*et al*. Lower risk of tuberculosis in obesity. *Arch Intern Med* 2007;167:1297–304.
51 Wang Q, Ma A, Han X, *et al*. Prevalence of type 2 diabetes among newly detected pulmonary tuberculosis patients in China: a community based cohort study. *PLoS One* 2013;8:e82660.
52 Kubiak RW, Sarkar S, Horsburgh CR, *et al*. Interaction of nutritional status and diabetes on active and latent tuberculosis: a cross-sectional analysis. *BMC Infect Dis* 2019;19:627.
53 Babalik A, Ulus IH, Bakirci N, *et al*. Plasma concentrations of isoniazid and rifampin are decreased in adult pulmonary tuberculosis patients with diabetes mellitus. *Antimicrob Agents Chemother* 2013;57:5740–2.
54 Nijland HMJ, Ruslami R, Stalenhoef JE, *et al*. Exposure to rifampicin is strongly reduced in patients with tuberculosis and type 2 diabetes. *Clin Infect Dis* 2006;43:848–54.
55 Mahishale V, Avuthu S, Patil B, *et al*. Effect of poor glycemic control in newly diagnosed patients with smear-positive pulmonary tuberculosis and type-2 diabetes mellitus. *Iran J Med Sci* 2017;42:144–51.
56 Yu X, Li L, Xia L, *et al*. Impact of metformin on the risk and treatment outcomes of tuberculosis in diabetics: a systematic review. *BMC Infect Dis* 2019;19:859.