Original Article

DOI: 10.7860/JCDR/2022/55850.16712

Microbiology Section

Intensive Case Finding of Tuberculosis and Diabetes Mellitus-Bidirectional Screening of Patients Attending a Tertiary Teaching Hospital in Rural Telangana, India

KIRANMAI SANNITHI[1], T ASHITA SINGH[2], NEELIMA ANGALI[3], RAGHURAM PRASAD[4], RAJIVE KUMAR SUREKA[5]

BY-NC-ND

ABSTRACT

Introduction: Tuberculosis (TB) is a communicable disease of global public health threat. Poor and vulnerable populations are mainly affected with it. In association with Diabetes Mellitus (DM), TB may get worsen as increased relapse rates, delayed sputum culture conversion, increase in the case fatality rates etc. Conversely, TB may increase the incidence of DM, and worsen glycaemic control in diabetes patients.

Aim: To study the effectiveness of bidirectional screening for TB and DM in rural hospital.

Materials and Methods: A cross-sectional cohort study conducted at Medicine and Pulmonology department of MediCiti Institute of Medical Sciences (MIMS) for a period of nine months in June 2019-February 2020. All TB patients were screened for DM and vice versa. All TB patients were followed-up for treatment outcome of TB and all DM patients were followed-up for glycaemic control. Relative risk was calculated using incidence of outcome or control of disease in TB with DM patients to TB patients and DM with TB patients to DM patients.

Results: Of 256 TB patients, 38 (14.8%) were TB with DM cases. All 256 patients were followed-up for TB treatment outcome, 100% TB patients without DM had recovery, whereas 97.3% TB patients with DM had recovery after two months of therapy. Relative risk of DM on TB outcome was 0.97. Of 256 DM patients screened, 9 (3.5%) had been newly diagnosed with TB. All 256 people were followed-up for impact on glycaemic control. Relative risk of TB on glycemic control was 1.87.

Conclusion: Bidirectional screening would potentially improve care and prevention of TB and DM.

Keywords: Glycaemic control, Pulmonary tuberculosis, Relative risk, Treatment outcome

INTRODUCTION

The TB is the major infectious disease among five infectious killers globally. TB is a communicable disease which remains as a global public health threat, mainly affecting population in developing countries. Every year, more than 9 million people become sick with this infectious disease, and approximately 2 million die because of it. TB in India contributes to one-fourth of the global burden. The prevalence of TB in India is 24 lakh cases [1]. Telangana notification rate is 192 per one lakh population. Access to TB diagnosis and treatment is a major concern in people with TB residing in rural areas as it may get delayed [2]. Hence it is essential to understand the epidemiology for appropriate interventions. In recent decades, with the increasing prevalence of DM cases in the world along with TB, the association is re-emerging as a public health priority [3]. The connection of DM and TB is more significant in developing countries where TB is indigenous and the prevalence of DM is on rise [4].

National Tuberculosis Elimination Programme (NTEP) in India has also taken steps towards prevention of TB through the 3Is project. TB co-morbidities, especially Human Immunodeficiency Virus (HIV), Diabetes and Tobacco have been prioritised [5]. These risk groups are to be considered for screening TB. Guidelines are already existing for detecting TB in people living with HIV (PLHIV) and for screening their contacts and in people with DM [6].

The primary objective of TB screening is to ensure early detection of TB and to initiate treatment promptly, with an eventual aim of reducing the incidence of improper treatment outcomes and other adverse ill-effects of TB, as well as helping to decrease the TB transmission. Hospital outpatient and inpatient departments and primary healthcare centres are the preferred sites and groups for screening TB as described by the NTEP. DM, a chronic metabolic disease is growing in number globally, particularly in places where burden of TB is also high. In association with DM, TB may get worsen as increased relapse rates, delayed sputum culture conversion, increase in the case fatality rates etc. even on completion of treatment [7]. With the increase in the number of people with diabetes, care and control of TB may be compromised; chiefly in areas with high burden of these diseases [8]. The risk increases on delay in the diagnosis. Systematic screening can be advantageous for both the groups.

Theoretically, DM and TB may complicate each other at many levels. TB infection may advance fast in people with dual burden than without [7]. Conceivably, people with DM will be more prone to TB than non diabetic people leading to an increased risk of latent TB infection, but there is a feeble evidence. The clinical picture of TB in people with diabetes may change and latest diagnostic algorithms may be needed. Diabetes may quicken the appearance of drug-resistant TB, especially multidrug resistant TB (strains of TB resistant to two first line drugs, rifampicin and isoniazid) among those receiving TB treatment, although the proof is narrow [9]. Reciprocally, TB may increase the incidence of DM, and exacerbate improper glycaemic control in diabetes patients [10]. Moreover, TB drugs may have drug interactions with the treatment of diabetes, and diabetes may impede with the action of certain antiTB medication.

The interaction between TB and DM should be well documented. So, the World Health Organisation (WHO) and the International Union against Tuberculosis and Lung Disease (The Union) in 2011 developed a collective structure for treatment and control of TB and DM that proposed countries to take up few endeavours,

such as bidirectional screening for TB and DM [11]. Though this is one of the recommendations of NTEP there is limited evidence on implementation and the outcomes of bidirectional referrals [12]. Studies on diabetes in TB patients in India are very limited and have used different techniques and criteria [13]. This study also aligns to the recommendation from the NTEP, to screen for prevalence of TB in people with DM in medium and high-TB burden places with an average TB prevalence exceeding 100/100,000 population.

With many benefits of early detection and intensive case finding, the present study was aimed for intensive case finding of TB and DM by bidirectional screening and also to identify the effect of TB and DM on their outcome and control in the present study.

MATERIALS AND METHODS

A cross-sectional screening and prospective cohort study was conducted at Medicine, Chest and TB outpatient departments of MIMS for a period of nine months in June 2019-February 2020. Subjects were recruited from patients visiting MIMS located in Medchal mandal one of the rural parts of Medchal Malkajgiri District in Telangana State, India. This hospital serves all patients with communicable and non communicable diseases. This is the teaching hospital with about 700 bedded inpatient facilities. The present study was approved by Ethical committee of MIMS. Ethical committee approval number was EC/16/IV/2k17/(1/27).

Sample size calculation: Prevalence of DM and TB co-morbidities is considered at 20% as the prevalence of DM in TB population ranged from 1.9-45% with a precision of 0.05 and Z score of 1.96 [14,15]. A probability of 5% (alpha), at which results were considered statistically significant, 95% power was applied. The sample size derived for both the groups based on the above measures was 256 each from Medicine, and chest and TB department, respectively. 10% were also added to the sample size for follow-up study. A total of 564 patients were screened and 512 patients were included in the study.

Inclusion criteria: All newly registered TB patients and all newly diagnosed or previously known DM patients with no previous history of TB of age >18 years attending the outpatient department were included after taking informed consent.

Exclusion criteria: In the DM patients group, known TB patients were excluded to avoid duplication. Patients who were lost to follow-up were also excluded from the study.

A total of 256 DM patients from Medicine department and 256 TB patients from TB and chest department of age >18yrs were studied and followed-up by the end of the study after exclusion and lost to follow-up. A total of 52 patients were excluded.

Various objectives of the study, methodology used, benefits and probable risks of present study were explained to the participants. As the study was done in rural population, research assistant had taken adequate care to ensure confidentiality as each participant had been given unique identification numbers without using names and was questioned individually (in their local language) in the examination area of the outpatient unit to ensure privacy and obtained written informed consent. The investigators and research staff signed a copy of confidentiality agreement form before study initiation. Administrative approval from the State TB Cell, Telangana was obtained for conducting the study.

Study Procedure

Potential participants for the study were identified by the physicians in the Medicine, Chest and TB outpatient departments. Data collection was done using a close-ended questionnaire given to the patients. The questionnaire has variables pertaining to age, social (based on kuppuswamy scale-education, income and occupation) and demographic information, symptoms for DM and TB, medication used, diagnosis of TB/DM, treatment outcomes. The questionnaire was done in Telugu or English, according to the convenience of the participant, by a research assistant who was trained and expert in the respective languages. The questionnaire was pretested by conducting a pilot testing with 20 patients and necessary changes were made and the questionnaire was validated by ethical committee. All registered TB cases were screened for DM both with symptoms and blood glucose screening. A higher Random Blood Sugar (RBS) (>200 mg/dL)/Fasting Blood Sugar (FBS) (126 mg/dL) prompted the investigator for Haemoglobin A1c (HbA1c) screening, value of more than 6.5% was diagnosed as DM [16].

HbA1c test: Glycohaemoglobin is a haemoglobin-glucose complex to which glucose gets bound to haemoglobin. Procedure was initiated by collecting whole blood samples in vacutainer tubes containing EDTA and mixed thoroughly. The minimum volume (1 mL) required for analysis was taken directly from this collection tubes and loaded into the Glycohaemoglobin analyser. Results were given as % HbA1c [17].

All registered diabetic patients from Medicine department intensive case finding of TB was done. Intensified Case Finding (ICF) is a screening activity used for earlier detection of probable TB patients in a given population. Patients with any of the four symptoms (4s positive) suggestive of TB were subjected for Sputum examination and/or chest X ray or CBNAAT (if extra pulmonary TB suspected) for TB diagnosis.

Case finding procedures

- 4s symptoms suggestive of TB: 4 symptom screening-cough >2 weeks, prolonged fever, loss of weight, loss of appetite [18].
- Chest X-ray posteroanterior view: Pneumonic consolidation± lymphadenopathy. Miliary TB (Classic miliary TB is defined as millet like (1-5 mm) seeding of TB bacilli appearing on chest radiography [19]) or pleural effusion or pulmonary oedema are other radiological findings of TB.
- Cartridge Based Nucleic Acid Amplification Test (CB-NAAT) is a molecular method of detection of genes for *Mycobacterium* and also rifampicin resistance within two hours. The test was performed as per instructions [CEPHEID, Sunnyvale, CA, USA]. The procedure was done by adding sampling reagent (containing NAOH and isopropanol) and the sample in the ratio of 2:1 and incubated at room temperature for 15 minutes with shaking intermittently. Into each cartridge, 3 mL of this treated sample was taken and inserted in the module of CBNAAT machine. After an automatic process for 1hr and 50 min, results were displayed on the monitor [20].

Once sputum or X-ray or CBNAAT or clinically diagnosed as positive for TB, the patients were sent to Directly Observed Treatment Short course (DOTS) centre, where treatment and further follow-up was done.

Both the groups were followed-up by the Research assistants after the intensive phase of TB treatment and after two months of antidiabetic therapy by contact over phone or home visit. The level of glycaemic control was compared between cohort of DM patients with TB and cohort of DM patients without TB by testing HbA1c levels in blood. Sputum smear conversion after intensive phase was compared between cohort of TB patients having DM and cohort of TB patients not having DM.

STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 16.0. Categorical variables were depicted as counts (proportions) and Chi-square test was used

for comparing categorical variables. A p<0.05 was considered statistically significant. Relative risk was calculated using incidence of outcome or control of disease in TB with DM patients to TB patients and DM with TB patients to DM patients, respectively.

RESULTS

A total of 512 patients, 256 TB and 256 DM patients, respectively were studied for characteristics after excluding 52 patients. Among them Male TB patients were 152 (59.4%), higher in number when compared to female TB patients who were 104 (40.6%). DM prevalence in TB was slightly higher among males 25 (16.4%) than females 13 (12.5%). Similarly, Male DM patients, 147 (57.4%) were higher in number than female DM patients, 109 (42.6%). Prevalence of TB was also high in males 9 (6.1%) compared to females 0 in DM group.

Characteristic features of TB patients and DM patients like age, sex, social and demographic factors, symptoms (DM symptoms in TB and TB symptoms in DM) and medication were compared with the characteristics of TB with DM and DM with TB patients, respectively as shown in [Table/Fig-1]. Significant p-value (<0.05%) was noticed in variables such as age and symptoms.

Clinical categorisation of TB patients and DM prevalence in them are shown in [Table/Fig-2]. Higher DM prevalence is shown in pulmonary TB 32 (84.2%) than in extrapulmonary TB patients 5 (13.2%) and military TB patients 1 (2.6%).

Screening for DM in TB patients: The results of screening of DM in TB patients are summarised in [Table/Fig-3]. A total of 256 TB patients registered under the study were screened for DM by RBS. Among them 37 (14.4%) people had RBS >200 mg/dL. Of the 256 patients, 27 (10.5%) were known DM patients and 229 (89.5%) patients had unknown diabetic status. Among the 27 (10.5%) known DM patients, 14 (51.9%) patients had RBS >200mg/dL, in them 12 (44.4%) had HbA1C>6.5. In the remaining 229 (89.5%) patients, 13 (5.7%) had RBS>200mg/dL, among them 11 (4.8%) had HbA1C>6.5%. Therefore, 11 newly identified and the 27 (10.5%) known DM cases, a total of 38 (14.8%) TB with DM patients was sent to the medicine OPD for DM care. All 256 TB cases were followed-up after two months of initiation of ATT drugs.

Intensive case finding of TB in DM patients: A total of 256 DM patients, have been screened for symptoms of TB and also sent for X-ray, of which 42 (16.4%) patients were diagnosed as presumptive TB basing on symptoms and in them 28 (10.9%) showed X-ray findings of TB. All 42 (16.4%) presumptive TB patients were sent to the TB clinic for further diagnosis and treatment. Among them 7 (16.7%) were smear positive and 2 (4.8%) were diagnosed with extrapulmonary TB. The results of screening for TB in DM patients are summarised in [Table/Fig-4].

The 9 (3.5%) DM patients confirmed with TB were started on ATT drugs.

TB group				DM group			
Variables	Total no. of TB patients n (%)	TB patients having DM n (% to total)	p-value (Chi-square test)	Variables	Total no. of DM patients n (%)	DM patients having TB n (% to total)	p-value (Chi-square test)
Total	256	38 (14.8)		Total	256	9 (3.5)	
Age, years							
≥48	99 (38.7)	28 (28.3)	0.0001	≥48	169 (66)	8 (4.7)	0.15
<48	157 (61.3)	10 (6.4)		<48	87 (34)	1 (1.1)	
Sex							
Male	152 (59.4)	25 (16.4)	0.45	Male	147 (57.4)	9 (6.1)	-
Female	104 (40.6)	13 (12.5)		Female	109 (42.6)	0	
Residence							
Urban	17 (6.6)	2 (11.8)	0.76	Urban	28 (10.9)	2 (7.1)	0.27
Rural	239 (93.4)	36 (14.9)		Rural	228 (89.1)	7 (3.1)	
Social status							
Upper	0	0	-	Upper	6 (2.3)	0	-
Upper Middle	2 (0.8)	1 (0.5)		Upper Middle	14 (5.5)	0	
Lower middle	68 (26.5)	8 (11.8)		Lower middle	115 (44.9)	4 (3.5)	
Upper lower	121 (47.3)	18 (14.9)		Upper lower	89 (34.8)	3 (3.4)	
Lower	65 (25.4)	11(16.9)		Lower	32 (12.5)	2 (6.3)	
Symptoms							
Symptomatic	39 (15.2)	27 (69.2)	<0.0001	Symptomatic	42 (16.4)	8 (19.0)	<0.0001
Polyuria	25 (9.8)	25 (100)		Cough>2wks	36 (14.1)	06 (16.7)	
Polydipsia	11 (4.3)	09 (81.8)		Fever>2wks	14 (5.5)	04 (28.6)	
Polyphagia	02 (0.8)	0		Chest pain	08 (3.1)	02 (25.0)	
Unexplained weight loss	21 (8.2)	19 (90.5)		Weight loss	16 (6.25)	07 (43.6)	
Asymptomatic	217 (84.8)	11 (0.05)		Enlarged glands	02 (0.8)	02 (100)	
				Asymptomatic	214 (83.6)	1 (0.05)	
Medication							
Cat 1 ATT drugs	256 (100)	38 (14.8)	-	Metformin	256 (100)	8 (3.5)	-
Cat 2 ATT drugs	0	0		Glimiperide	240 (93.8)	8 (3.3)	
Others	0	0		Insulin	8 (3.1)	4 (50)	
				Others	2 (0.8)	0	

[Table/Fig-1]: Characteristics of the tuberculosis patients and diabetes patients.

Clinical characteristics	TB patients (n=256) n%	TB with DM patients (n=38) n%
Pulmonary tuberculosis	206 (80.5)	32 (84.2)
Extrapulmonary tuberculosis	48 (18.8)	5 (13.2)
Miliary tuberculosis	2 (0.8)	1 (2.6)

[Table/Fig-2]: Clinical categorization of TB patients and DM prevalence among them.

S. No.	Indicator	n=256
1.	Patients with TB studied	256
2.	Patients screened for RBS (Random Blood Sugar) in study	256
3.	Patients with known diabetes status	27
4.	Patients with unknown DM status	229
5.	Patients with RBS >200 mg/dL among the participants	37/256
6.	Patients with HbA1C >6.5 among all the participants	23/256
7.	Patients with HbA1C >6.5 among known DM status	12/27
8.	Patients with newly diagnosed DM	11
9.	Patients with TB and DM sent to the medicine OPD for DM care	38 (14.8%) (27known+11new)
10.	Patients with TB and DM reached DM care	38 (100%)

[Table/Fig-3]: Screening of TB patients for DM.

S. No.	Indicator	n=256
1.	Patients screened for TB symptoms	256
2.	Patients sent for X-ray	256
3.	Patients with symptoms of TB	42
4.	Patients with X-ray findings	28
5.	Patients referred to the TB clinic	42 (16.4%)
6.	Patients showed smear positive for TB	7
7.	Patients diagnosed with extrapulmonary TB	2
8.	Patients with confirmed TB	9 (3.5%)
9.	Patients receiving ATT treatment	9

[Table/Fig-4]: Screening of DM patients for TB.

Treatment outcomes of TB patients on follow-up: The results of the 512 patients came follow-up for treatment outcome in TB patients and glycaemic control in the DM patients separately are summarised in [Table/Fig-5]. A total of 256 TB patients came for follow-up, among them only one patient had not recovered from TB (had smear positive after the intensive phase). The patient was a known Diabetic and had improper glycaemic control. So, 218 (100%) of 218 TB patients without DM had recovery, whereas 37 (97.3%) of the 38 TB patients with DM were recovering after two months of ATT therapy. Relative risk of DM on TB outcome was 0.97.

Follow-up of DM patients for glycaemic control and impact of TB: 256 DM patients came for follow-up after two months, the glycaemic control was tested by means of HbA1C. The results of glycaemic control and impact of TB are summarised in [Table/Fig-5]. Of the 256 DM patients tested for HbA1C after two months, 115 (48%) had HbA1C >6.5%. Of them, 8 (7%) were DM with TB patients. Of the 9 (3.5%) DM patients with TB, 8 (88.8%) had impaired glycaemic control which was more compared to 107 (46.6%) showed improper glycaemic control among 247 (96.5%) DM without TB patients. Relative risk of TB on glycaemic control was 1.87. Tuberculosis showed significant effect on glycaemic control in DM with TB patients.

S. No.	Indicator	Total TB patients n=256	TB with DM n=38	TB without DM n=218
	Tuberculosis patients group follow-up:			
1.	Patients with TB followed-up after 2 months	256	38 (14.8%)	218 (85.2%)
2	Patients on treatment for TB who showed recovery on follow-up	255	37 (97.3%)	218 (100%)
3.	Patients on treatment for TB shown smear positive on follow-up	1	1	0
4.	Patients who were defaulters (who left the treatment)	0	0	0

S. No.	Indicator	Total DM patients n=256	DM with TB n=9	DM without TB n=247
	Diabetes patients group follow-up:			
1.	Patients with DM followed-up after two months	256	9 (3.5%)	247 (96.5%)
2.	Patients on treatment showing improper glycaemic control	115	8 (88.8%)	107 (46.6%)
3.	Patients on treatment showing proper glycaemic control	141	1	140

[Table/Fig-5]: Follow-up of tuberculosis patients group and diabetes patients group.

DISCUSSION

The finding of the study provides valuable insights into TB-DM prevalence and the impact of each other on treatment outcome. First, bidirectional screening was implemented for TB and DM. All TB patients were screened for DM and vice versa. The reason why all participants registered could be screened was close proximity of TB clinics and Medicine department in a tertiary care centre. But, when follow-up was done to know the impact on treatment outcome of TB and DM, there were drop outs because of the loss or change in contact number of the patients. To overcome this 10% more patients were screened so that number of patients studied and follow-up remains the same in both the groups.

About 14.8% TB patients registered for the study had DM. Nearly 2/3rd of all identified DM patients were known diabetic. According to literature, the DM prevalence in TB patients varies from a maximum of 29% in Puducherry to a minimum of 6.1% in Kashmir valley [21,22]. A large metacentric study found 13% prevalence of DM among TB across India [23]. The present study was in correlation with other studies, but showing slightly less prevalence than studies conducted at other places of South India where it is from 12.1% in Bangalore to 29% in Puducherry [24-27]. As this study was conducted in a rural area, there were less number of cases reported; this may be due to more physical activity in people living in rural area compared to the people in urban areas. However prevalence has regional variations, which may also be one reason [26].

In TB patients screened, higher median age patients noted who had diabetes, similar findings in Prakash BC et al., study which showed high TB with DM were seen in >40 years and study by Menon VU et al., identified that the prevalence of diabetes by age showed an increase in number after age of 50 [24,25]. Present study showed association with hyperglycaemia was higher with pulmonary TB showed similarity to other studies [27]. In a case-control study in the United States, patients having pulmonary TB had a higher prevalence of DM than the patients having extrapulmonary TB [28].

There are various mechanisms described by which TB can initiate DM. The pressure caused by TB on the body leads to increased hormonal level such as increase in cortisol which in turn increase blood sugars; and also due to let out of different cytokines, chemokines and tubercular proteins may lead to dysfunction of pancreas. This may be due to the deposition of amylin within the pancreas or may be due to entry by the Mycobacteria into pancreas [29-30].

In present study, nearly 16.4% of DM patients screened had symptoms suggestive of TB. This was higher than in general population, as it was evaluated as 2-3% of patients had TB symptoms [31,32]. Present study found only few TB cases (3.5%), may be due to adequate glycaemic control in patients attending tertiary care centre there could be a low risk of TB in them [33]. Other reason for the low detection rate may be due to nonperformance of CBNAAT or Acid Fast Bacilli (AFB) culture for smear negative cases. Inspite of this, these results are correlating with other studies done in DM clinics all over India [34].

Infections are common when there is impaired glucose tolerance, TB is common among them.

The relative risk of DM on TB treatment outcome of TB patients was noted in the study as 0.97. This can be due to absence of unrecovered patients in the control group (TB without DM). Nine studies assessed the effect of DM on prolonged positivity of TB bacilli at 2-3 months of treatment, among them six study groups in different studies have expressed relative risks (RRs) of >2 [35-38] and three studies stated RRs of <1 [7,36,39]. Relative risks of improper recovery of TB was ranging from 2.95 in Hispanics, 1.31 in non Hispanic Whites, and 0.93 in non Hispanic Black patients [36].

The impact of TB on glycaemic control is clearly noticed in the present study as 88.8% of DM patients had impaired glycaemic control where as 46.6% of DM patients without TB had impaired glycaemic control. This results correlates with the study by Krishnappa D et al., [27]. Relative risk noted as 1.87 in present study. The treatment of the DM is affected may be because of the hampering of drug efficacy or increased survival of the Mycobacteria or due to antitubercular drugs used for TB [40].

Limitation(s)

Long-term studies with bigger sample size are needed to determine the relationship of these chronic diseases in detail.

CONCLUSION(S)

The present study reports that DM and TB have bidirectional relationship. Considering the increasing burden of DM, particularly in areas with highly prevalent TB, these studies will be helpful for intensive case finding. Interdepartmental collaborative activities would also potentially improve care and prevention.

REFERENCES

[1] Central TB division, Ministry of Health and Family welfare, National Tuberculosis elimination Programme Annual report. India TB report 2020. March 2020, pg11-17. http://www.tbcindia.gov.in accessed August 2020.

[2] Storla DG, Yimer S, Bjune GA. A systematic review of delay in the diagnosis and treatment of tuberculosis. BMC Public Health. 2008;8(1):15.

[3] Restrepo BI. Convergence of the tuberculosis and diabetes epidemics: Renewal of old acquaintances. Clin Infect Dis. 2007;45(4):436-38.

[4] American Diabetes Association, Standards of medical care in diabetes. Diabetes Care. 2020;43(Suppl 1):S1-12.

[5] RNTCP at a glance. Central TB division, Ministry of Health and Family Welfare, March 2014, Available: http://uttarkashi.nic.in/Dept/Health/RNTCP/RNTCP.pdf. Accessed August 2020.

[6] Mansuri S, Chaudhari A, Singh A, Malek R, Viradiya, R. Prevalence of diabetes among tuberculosis patients at urban health centre, Ahmedabad. Int J Scientific Study. 2015;3(4):115-18.

[7] Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Ottamani SE, et al. The impact of diabetes on tuberculosis treatment outcomes: A systematic review. BMC Med. 2011;9:81.

[8] Viswanathan V, Kumpatla S, Aravindalochanan V, Rajan R, Chinnasamy C, Srinivasan R, et al. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. PLoS ONE. 2012;7(7):e41367.

[9] Liu Q, Li W, Xue M, Chen Y, Du X, Wang C, et al. Diabetes mellitus and the risk of multidrug resistant tuberculosis: A meta-analysis. Sci Rep. 2017;7:1090.

[10] Başoğlu OK, Bacakoğlu F, Cok G, Sayiner A, Ateş M. The oral glucose tolerance test in patients with respiratory infections. Monaldi Archives for Chest Disease. 1999;54:307-10.

[11] International Union against Tuberculosis and Lung Disease, World Health Organization. Collaborative framework for care and control of tuberculosis and diabetes. WHO/HTM/TB/2011.15. Geneva, Switzerland: WHO, 2011: pp 40.

[12] National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), Revised National Tuberculosis Control Programme (RNTCP), Directorate General of Health Services, Ministry of Health & Family Welfare. National framework for joint TB-Diabetes collaborative activities. New Delhi, India: Government of India; 2017. https://tbcindia.gov.in/WriteReadData/National%20framework%20for%20joint%20TB%20diabetes%2023%20Aug%202017.pdf.

[13] Kumar A, Members of Tuberculosis-Diabetes Study Group. Screening of patients with tuberculosis for Diabetes Mellitus in India. Tro Med Int Health. 2013;18(5);636-45. Doi: 10.1111/tmi.12084.

[14] Ade S, Affolabi D, Agodokpessi G, Wachinou P, Faihun F, Toundoh N, et al. Low prevalence of diabetes mellitus in patients with tuberculosis in Cotonou, Benin. Public Health Action. 2015;5(2):147-49.

[15] Nasa JN, Brostrom R, Ram S, Kumar AMV, Seremai J, Hauma M, et al. Screening adult tuberculosis patients for diabetes mellitus in Ebeye, Republic of the Marshall Islands. Public Health Action. 2014;4(Suppl 1):S50-52.

[16] Harries AD, Satyanarayana S, Kumar AM, Nagaraja SB, Isaakidis P, Malhotra S, et al. Epidemiology and interaction of diabetes mellitus and tuberculosis and challenges for care: A review. Public Health Action. 2013;3(1):03-09.

[17] Torke NS, Boral L, Nguyen T, Chakrin A, Kimball D. Comparison of four methods for Glycohemoglobin (HbA1c) determination. Clin Chem. 2005;51:A242-43.

[18] Getahun H, Kittikraisak W, Heilig CM, Corbett EL, Ayles H, Cain KP, et al. Development of a standardised screening rule for tuberculosis in people living with HIV in resource-constrained settings: individual participant data meta-analysis of observational studies. PLoS Medicine. 2011;8(1):e1000391.

[19] Sharma SK, Mohan A, Sharma A, Mitra DK. Miliary tuberculosis: New insights into an old disease. Lancet Infectious Diseases. 2005;5(7):415-30.

[20] Xpert MTB/RIF implementation manual: Technical and operational 'how-to'; practical considerations. World Health Organization 2014; ISBN: 978 92 4 150670 0 (NLM classification: WF 310).

[21] Vasudevan KP, Govindarajan S, Chinnakali P, Panigrahi KC, Raghuraman S. Prevalence of diabetes mellitus among tuberculosis patients in urban Puducherry. N Am J Med Sci. 2014;6(1):30-34.

[22] Zargar AH, Khan AK, Masoodi SR, Laway BA, Wani AI, Bashir MI, et al. Prevalence of type 2 diabetes mellitus and impaired glucose tolerance in the Kashmir valley of the Indian subcontinent. Diabetes Res Clin Pract. 2000;47:135-46.

[23] India Tuberculosis-Diabetes Study Group. Screening of patients with tuberculosis for diabetes mellitus in India. Tro Med Int Health. 2013;18(5):636-45.

[24] Prakash BC, Ravish KS, Prabhakar B, Ranganath S, Naik B, Satyanarayana S, et al. Tuberculosis-diabetes mellitus bidirectional screening at a tertiary care centre, South India. PHA. 2013;3(S1):S18-22.

[25] Menon VU, Kumar KV, Gilchrist A, Sugathan TN, Sundaram KR, Nair V, et al. Prevalence of known and undetected diabetes and associated risk factors in central Kerala-ADEPS. Diabetes Res Clin Pract. 2006;74:289-94.

[26] Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian council of medical research-INdia DIABetes (ICMR-INDIAB) study. Diabetologia. 2011;54:3022-27.

[27] Krishnappa D, Sharma SK, Singh AD, Sinha S, Ammini AC, Soneja M. Impact of tuberculosis on glycaemic status: A neglected association. Indian J Med Res. 2019; 149(3):384-88.

[28] Antony SJ, Harrell V, Christie JD, Adams HG, Rumley RL. Clinical differences between pulmonary and extrapulmonary tuberculosis: A 5-year retrospective study. J Natl Med Assoc. 1995;87:187-92.

[29] Schwartz P. Amyloid degeneration and tuberculosis in the aged. Gerontologia. 1972;18: 321-62.

[30] Broxmeyer L. Diabetes mellitus, tuberculosis and the mycobacteria: Two millenia of enigma. Med Hypotheses. 2005;65:433-39.

[31] Directorate General of Health Services, Ministry of Health & Family Welfare. Training module for medical practitioners. Revised National TB Control Programme. New Delhi, India: Government of India, 2010. http://www.tbcindia.nic.in/pdfs/Training%20Module%20for%20Medical%20Practitioner.pdf Accessed August 2020.

[32] Santha T, Garg R, Subramani R, Chandrasekaran V, Selvakumar N, Sisodia RS, et al. Comparison of cough of 2 and 3 weeks to improve detection of smear-positive tuberculosis among out-patients in India. Int J Tuberc Lung Dis. 2005;9:61-68.

[33] Leung CC, Lam TH, Chan WM, Yew WW, Ho KS, Leung GM, et al. Diabetic control and risk of tuberculosis: A cohort study. Am J Epidemiol. 2008;167:1486-94.

[34] Jain MK, Baghel PK, Agrawal R. Study of impaired glucose tolerance in pulmonary tuberculosis. Indian J Community Med. 2006;31:117-14.

[35] Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: A systematic review of 13 observational studies. PLoS Medicine. 2008;5(7):e152.

[36] Pablos-Mendez A, Blustein J, Knirsch CA. The role of diabetes mellitus in the higher prevalence of tuberculosis among Hispanics. Am J Public Health. 1997;87:574-79.

[37] Perez A, Brown HS 3rd, Restrepo BI. Association between tuberculosis and diabetes in the Mexican border and non-border regions of Texas. Am J Trop Med Hyg. 2006;74:604-11.
[38] Alisjahbana B, Sahiratmadja E, Nelwan EJ, Purwa AM, Ahmad Y, Ottenhoff TH, et al. The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis. Clin Infect Dis. 2007;45:428-35.
[39] Dooley KE, Tang T, Golub JE, Dorman SE, Cronin W. Impact of diabetes mellitus on treatment outcomes of patients with active tuberculosis. Am J Trop Med Hyg. 2009;80:634-39.
[40] Niazi AK, Karla S. Diabetes and tuberculosis: A review of the role of optimal glycemic control. J Diabetes Metab Disord. 2012;11:28.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Microbiology, MediCiti Institute of Medical Sciences, Hyderabad, Telangana, India.
2. Assistant Professor, Department of Microbiology, MediCiti Institute of Medical Sciences, Hyderabad, Telangana, India.
3. Assistant Professor, Department of Microbiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.
4. Assistant Professor, Department of General Surgery, Mallareddy Medical College for Women, Hyderabad,Telangana, India.
5. Professor, Department of Microbiology, MediCiti Institute of Medical Sciences, Hyderabad, Telangana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Raghuram Prasad,
Assistant Professor, Department of General Surgery, Mallareddy Medical College for Women, Suraram, Telangana-500055, Hyderabad, India.
E-mail: hod.rajive_microb@mims.edu.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 01, 2022
- Manual Googling: May 16, 2022
- iThenticate Software: Jun 03, 2022 (25%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: NTEP authority for providing support with OR research grant (2016).
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 22, 2022**
Date of Peer Review: **Apr 13, 2022**
Date of Acceptance: **May 17, 2022**
Date of Publishing: **Aug 01, 2022**