Introduction

Tuberculosis (TB) remains a worldwide global public health problem. Nearly, one-third of world’s population is infected with *Mycobacterium Tuberculosis* and about 10% of them are at risk of developing active form of the disease in their lifetime depending on the interaction of the epidemiological triad. India has the largest number of TB cases, in 2015, out of total global annual incidence of 9.6 million TB patients 2.2 million were estimated from India. According to annual status report 2016 of Revised National Tuberculosis Control Programme (RNTCP), in 2015, prevalence of TB is 195/lakh and incidence rate is 167/lakh Population.

The incidence of DM is increasing worldwide, and emerging as a major health problem in developing countries where the

ABSTRACT

**Context:** Tuberculosis (TB) and diabetes mellitus (DM) remains a worldwide global public health problem. About 95% of patients with TB live in the low and middle-income countries and more than 70% of patients with DM also live in the same countries, especially in South East Asia. Screening for diabetes in patients with TB will not only ensure early case detection but also better management of diabetes and will lead to better TB treatment outcome. **Aims:** This study aims to determine the prevalence and its associated factors of diabetes and prediabetes among diagnosed cases of TB patients registered under Revised National Tuberculosis Control Programme (RNTCP) in Bhopal city. **Settings and Design:** The current study was a longitudinal follow-up study conducted among registered TB patients under RNTCP in all 5 TB units of Bhopal District. **Subjects and Methods:** Participants were contacted and interview was conducted after obtaining consent using predesigned and pretested Performa during October 2013–September 2014. **Statistical Analysis Used:** Continuous variable were summarized as frequency, mean, and standard deviation. All variables were analyzed using Chi-square test of significance; *P* < 0.05 was taken as statically significant. **Results:** Out of the total 662 TB patients, 352 were male and 310 were female. Out of the total, 82 (12.39%) patients were diagnosed as diabetic and 108 (16.3%) were prediabetic. significant association found with six variables which are age, sex, body mass index, type of TB, Category of TB, and smoking. **Conclusion:** This study shows feasibility and importance of screening of TB patients.

**Keywords:** Associated factors, diabetes, tuberculosis

Introduction

Tuberculosis (TB) remains a worldwide global public health problem. Nearly, one-third of world’s population is infected with *Mycobacterium Tuberculosis* and about 10% of them are at risk of developing active form of the disease in their lifetime depending on the interaction of the epidemiological triad. India has the largest number of TB cases, in 2015, out of total global annual incidence of 9.6 million TB patients 2.2 million were estimated from India. According to annual status report 2016 of Revised National Tuberculosis Control Programme (RNTCP), in 2015, prevalence of TB is 195/lakh and incidence rate is 167/lakh Population.

The incidence of DM is increasing worldwide, and emerging as a major health problem in developing countries where the

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prevalence of TB is high.\textsuperscript{[3]} In 2015, the International Diabetes Federation estimated that about 415 million people worldwide have diabetes mellitus (DM) and this number is expected to rise to 642 million by 2040.\textsuperscript{[4]}

Available reports suggest that 95\% of patients with TB live in the low- and middle-income countries and more than 70\% of patients with DM also live in the same countries, especially in South East Asia.\textsuperscript{[5]}

The Indian Council of Medical Research–National study reported that there are 62.4 million people with Type 2 diabetes and 77 million people with prediabetes in India, these numbers are projected to increase to 101 million by the year 2030.\textsuperscript{[6]} Nationwide surveillance study of DM had found that the prevalence of known Type 2 DM (T2DM) in urban areas was 7.3\% and the prevalence of known T2DM was 3.2\% in peri-urban/slum areas.\textsuperscript{[7]}

Diabetes accounts for 14.8\% (range 7.1\%–23.8\%) of pulmonary TB and 20.2\% (8.3\%–41.9\%) of smear-positive TB as per a study conducted in India in 2000.\textsuperscript{[8]} Systematic review of studies conducted at multiple settings showed that screening of patients with TB for DM also yielded high prevalence of diabetes ranging from 1.9\% to 35\%.\textsuperscript{[9]}

Currently, both TB and diabetes are of global public health importance due to converging epidemic of both communicable and noncommunicable diseases.

Diabetes and TB may affect each other at many levels, among active TB patients; diabetes may adversely affect TB treatment outcomes and increasing the risk of relapse, death rate and multidrug resistance. Screening for diabetes in patients with TB can help in early case detection and management of diabetes and will lead to better TB treatment outcome.\textsuperscript{[0,10]}

The World Health Organization and International Union against TB and lungs disease in collaboration with National TB Control Programme developed a collaborative framework for care and control of diabetes and TB which emphasizes the routine implementation of bi-directional screening of two diseases and recommends the surveillance of diabetes among TB in all countries in primary health-care settings.\textsuperscript{[11]} However, screening methods, recording and reporting for the two diseases in routine health-care settings have not been well determined, and operational research is needed for better information in this field.

The current study was conducted with rationale that there is no such data regarding prevalence, associated factors for diabetes and TB comorbid condition, outcome assessment of TB with diabetes, exist in the whole of central India including Bhopal city. This is a Pioneer research work in concerned public health area conducted in central India and will foster the background for management of patients with comorbidity and also lay the foundation for further research.

Aims
This study aims to determine the prevalence of diabetes and prediabetes among diagnosed cases of TB registered under RNTCP in Bhopal District.

To identify the factors associated with the occurrence of diabetes among diagnosed cases of TB registered under RNTCP in Bhopal District.

Subjects and Methods

Study settings and design
The infrastructure of RNTCP bhopal district consist of 5 TB treatment and supervision units (TU), 1 per 5 lakh population. Furthermore, these 5 TU have 24 operational Designated Microscopy Centers (DMC) for identification and management of TB patients. The current study was a facility-based longitudinal follow-up study conducted on registered cases of TB in Bhopal equal or above the age of 18 years who gave their consent.

Study duration
The study was undertaken from October 1, 2013, to September 30, 2014, for 1 year.

Study subjects
All the patients aged 18 years and above with an established diagnosis of TB registered in TUs during the study period were considered as the targeted population. Further, the consent was obtained from the sampled patients. Moreover, patients of Type 1 diabetes and seriously ill patients such as TB meningitis and septicemia and pregnant patients were excluded from the study.

Data collection method
The current study was a facility-based longitudinal follow-up study conducted on registered cases of TB in Bhopal equal or above the age of 18 years who gave their consent from October 2013 to September 2014.

The study was planned and conducted as in following steps:

Line listing
A list of all TB patients of age 18 years or above who were on DOTS therapy at that time was made using TB register under RNTCP in Bhopal District.

Sampling
The current study was planned using simple random sampling strategy with randomization of all listed patients using random number table.

Interview and investigation
The day of DOTS therapy ascertain for all selected patients. Further participants were contacted, and the interview was conducted after
obtaining consent using predesigned and pretested pro forma which consisted of three basic sections, first section consisting of socio-demographic profile including age, sex, weight, height, education, occupation economic status, and history of any addiction. The second section consisted of assessment of TB status of patients including type of TB, category, and duration of treatment. The third section consisted of blood glucose level including both fasting and random blood glucose level of patients, history of diabetes, family history of diabetes, and treatment history of diabetes. The participants with already diagnosed DM on treatment were confirmed by their records. The time allotted for this was four months.

**Sampling method and sample size**

**Null hypothesis**

The prevalence of diabetes among TB patients is equal to that found in general population (8%).

**Alternate hypothesis**

The prevalence of diabetes among TB patients is significantly more (11%) than that found in general population.

There are four factors on which sampling strategy was based in the current study:

1. The level of significance for the current study related with null hypothesis ($H_o = \alpha = 0.01$) [99% confidence interval (CI) to minimize Type 1 error]
2. The desired level of the power ($1-\beta$) for the current study was kept 80%
3. According to null and alternate hypothesis clinically significant difference between the two proportions was estimated to be 3%
4. According central limit theorem, all the measures of central tendency and spread of variables normally distributed in the study population.

Based on the above factors, the formula for determining of sample size as follows: (Dawson, Beth; Trapp, Robert G.200).[12]

\[
N = \left( \frac{Z_{\alpha} \sqrt{\pi_0 (1 - \pi_0)} - Z_{\beta} \sqrt{\pi_1 (1 - \pi_1)}}{\pi_1 - \pi_0} \right)^2
\]

Here,

$N$ - Desired sample size

$Z_{\alpha} \cdot$ Two-tailed value of area under normal curve related with $H_o = 2.58$ as per 99% CI

$Z_{\beta} \cdot$ One-tailed value of area under normal curve related to alternative hypothesis and direction of result desired with power of 80% = −0.84

$\pi_0 \cdot$ Estimated prevalence of diabetes for the general population (8%)

$\pi_1 \cdot$ Estimated minimum prevalence of diabetes in TB patients is 11%

$\pi_1 - \pi_0 \cdot$ Clinical significance difference

\[
N = 600 \text{ approx.}
\]

**Operational definition**

**Diabetes and prediabetes**

According to the American Diabetes Association:

Diabetes – Fasting blood sugar level ≥126 mg/dl.

Random blood glucose level ≥200 mg/dl in patients with classical symptom of hyperglycemia.

Prediabetes – Fasting blood sugar level between 100 and 125 mg/dl.

**Statistical analysis used**

Data were entered into Microsoft Excel 2007 and analyzed using Epi Info™ language en-US version 7.2.1.0. (Atlanta, Georgia, US). Continuous variable was summarized as frequency, mean, and standard deviation. All variable were analyzed using Chi-square test of significance; $P < 0.05$ was taken as statically significant. Multivariate logistic regression analysis was done of variables found to be significant in univariate analysis by Chi-square test.

**Ethics approval**

Ethical approval received from Institutional Ethical Committee of Gandhi Medical College, Bhopal. Informed consent was obtained from patients before conducting the interview and also for follow-up.

**Results**

A total of 662 TB patients were interviewed using pretested questionnaire and assess for their blood glucose level. Out of the total 662 TB 352 were male (mean age 39.35), and 310 were female (mean age 33.47). Out of the total, 82 (12.39%) patients were diagnosed as diabetic, and 108 (16.3%) were prediabetic.

Table 1 shows the different risk factors associated with diabetes in TB patients, male TB patients (15.05%) were found to be significantly more associated with diabetes as compare to female patients (9.35%) [Figure 1]. Diabetes among TB patients was reported higher among patients with age more than 50 years (6.3%) as compare to patients with age <50 years (37.2%) and the difference was statically significant ($P < 0.0001$). In the current study, the prevalence of diabetes among TB was more among lower socioeconomic status patients (14.0%) as compare to middle (12.7%) and upper (2.7%) socioeconomic status patients though the difference was not significant ($P = 0.17$).
The prevalence of diabetes among illiterate TB patients was more (15.8%) than literate TB patients (12.02%) although the difference was not statistically significant ($P = 0.78$). TB patients having body mass index (BMI) $>$25 were found to be having more prevalence of diabetes (27.58%) as compare to patients with BMI $<$25 (8.12%). Smoker TB patients having more diabetes (17.09%) as compare to nonsmokers (9.81%) and the difference was statistically significant ($P < 0.001$). Alcoholic TB patients having more diabetes (14.1%) as compare to nonalcoholic patients (12.01%) but the difference was not significant ($P = 0.56$).

Out of total 662 TB patients, 69.7% were pulmonary TB and 30.3% were extrapulmonary TB and pulmonary TB patients (15.3%) had more prevalence of diabetes as compare to extrapulmonary TB (5.5%) and the difference was statistically significant ($P = 0.0001$). In the current study, 24.6% Type II treatment category TB patients had diabetes as compare to 9.5% of Type I treatment category TB patients and the difference was found to be statistically significant ($P < 0.001$).
Table 2: Predictors with their relative contribution in multivariate logistic regression models

| Predictor variable | B (predictor coefficient) | S.E. | Chi square value | OR (95% CI) | P      |
|--------------------|---------------------------|------|------------------|-------------|--------|
| Age                |                           |      |                  |             |        |
| >50 years          | 2.227                     | 0.291| 58.58            | 9.275       | 0.0001 |
| <50 years          |                           |      |                  | 5.24-16.407 | 0.833  |
| Sex                |                           |      |                  |             |        |
| Male               | -0.079                    | 0.374| 0.45             | 0.92        | 0.444-1.92 | 0.011 |
| Female             | 0.833                     | 0.748| 0.295            | 2.112       | 1.186-3.761 | 0.694 |
| BMI                |                           |      |                  |             |        |
| >25                | 0.444                     | 0.148| 1.55             | 1.159       | 0.55-2.42 | 0.054 |
| <25                | 0.444                     |       | 3.72             | 2.04        | 0.989-4.42 | 0.0001 |
| Smoking            |                           |      |                  |             |        |
| Yes                | 0.148                     | 0.365| 15.22            | 3.275       | 1.80-5.942 |       |
| No                 |                           |      |                  |             |        |
| Type of TB         |                           |      |                  |             |        |
| Pulmonary          | 0.705                     | 0.304| 15.22            | 3.275       | 1.80-5.942 |       |
| Extra pulmonary    |                           |      |                  |             |        |
| Treatment category of TB |          |      |                  |             |        |
| II                 | 1.186                     | 0.304| 15.22            | 3.275       | 1.80-5.942 |       |
| I                  |                           |      |                  |             |        |
| Constant           | -3.980                    | 0.405|                  | 0.19        | 0.0001 |

Table 1 shows a summary of univariate analysis showing statistically significant association with six variables which are age, sex, BMI, type of TB, category of TB, and smoking. Further, these six variables are eligible for multivariate logistic regression which was subsequently analyzed and showing that age of the TB patients is the most significant predictor of diabetes followed by treatment category, BMI, and Type of TB, respectively [Table 2].

Discussion

In the present study, we found a high prevalence of DM among the TB patients (12.39%) treated in Bhopal; and it was significantly higher among those with age > 50 years, male gender, smokers, patients having high BMI range (>25), Type II treatment category and those with pulmonary TB as compared to age <50, female gender, nonsmokers, BMI range <25, Type I treatment category, and extrapulmonary TB.

In the present study, the prevalence of diabetes among TB patients was 12.4%, and that of prediabetes was 16.3%. Similar results were reported in earlier studies by Singla et al., Raghuraman et al., Khanna et al., Kumar et al., 2013 and Balakrishnan et al. Zhang et al. 2009, with 25%, 29%, 14.5%, 13%, 44%, and 9.5%, respectively, prevalence of diabetes among TB patients.

This study found a significantly higher prevalence of DM in older TB patients. Similar finding has been reported by studies from other parts of India and other countries. This study also reported the higher association of DM and PTB, which is also reported in many studies including those by Zhang et al. and Gupta and Shah. This study has reported significant association between male gender and diabetes in TB, which is supported by that reported in the study conducted in South India.

In the current study, diabetes among TB was more among lower socioeconomic status patients (14.0%) as compared to middle (12.7%) and upper (2.7%) socioeconomic status patients though the difference was not significant (P = 0.17). Similar result also found in a study of Adriana Perez shows that diabetes and TB associated with lower socioeconomic status as compare higher economic status.

The result of the current study shows that diabetes among alcoholic TB patients to be more (14.14%) as compare to nonalcoholic patients (9.81%), and the difference was not significant (P = 0.56%). Similar result seen earlier study shows that alcohol consumption was found to be a risk factor for diabetes in TB patients.

The present study shows that diabetes was more common among TB patients with BMI more 25 (27.58%) as compare to those with BMI <25 (8.12%) and the difference was statistically significant (P = 0.001). Similar result was seen earlier by Raghuraman et al., which shows that the BMI of the TB patients with diabetes was higher when compared to TB without diabetes (18.92 ± 4.83 vs. 17.39 ± 4.23).

In the current study, we found that diabetes among TB was significantly more among Type II category TB patients as compare to Type I treatment category TB. Finding of this study was supported by the earlier study.

In the current study, we found that smoker TB patients have significantly more diabetes (17.09%) as compared to nonsmoker TB patients (9.81%) (P = 0.0001). Similar result was found in the earlier study.

This study emphasize the feasibility of screening of TB patients for diabetes as we implemented screening within the routine
health system with existing staff. In our study, higher proportion of previously undiagnosed DM patients being detected, this shows the importance of early screening of patients with TB and will enable us to manage these patients in the early phase. Prediabetes diagnosed at early phase so that primary prevention methods may be initiated timely. As we higher burden of both TB and DM in our country, we need better information, recording and monitoring system to guide us in managing this comorbidity, and we need to strengthen the care of these patients in our existing health services.

Conclusion
Our study had several strengths. First, we used large sample size with appropriate sampling design so that sample should be representative of whole district. Second, we conduct study with existing staff of RNTCP. There were a few limitations such as previous documentation of blood sugar, were not verified. Meantime for sugar testing and disease duration was not same for each TB patients.

The study has several programmatic implications as results of the current study emphasizes that National TB Control Programme in collaboration with NCD program should have special provision for screening, diagnosis, and management of DM among TB patients.

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Conflicts of interest
There are no conflicts of interest.

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