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Original Article

Community Section

Treatment Outcome of Tuberculosis in Patients with Diabetes under RNTCP in a Tertiary Care Centre, Chengalpattu, India: A Prospective Cohort Study

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ABSTRACT

Introduction: Diabetes increases the risk of Tuberculosis (TB) by three times, and this bidirectional association is currently one of the major concerns. A stronger evidence base is required to clarify the impact of Diabetes Mellitus (DM) on the treatment outcome of TB.

Aim: To compare the treatment outcome among diabetic and non diabetic patients on Category-I TB treatment based on the Revised National Tuberculosis Control Program (RNTCP). Also, to assess the various factors influencing the treatment outcome of TB among diabetic patients.

Materials and Methods: A prospective cohort study was conducted on 75 newly diagnosed TB patients enrolled for Category-I treatment Department of Pulmonary Medicine, Chengalpattu Medical College, Chengalpattu, Tamil Nadu, India, between October 2018 to November 2019. All patients with TB underwent blood glucose screening at treatment initiation and were categorised into two groups: with diabetes and without diabetes. Demographic details, family history of DM, smoking, alcohol consumption, and clinical profile were collected using a semi-structured questionnaire and followed-up for six months to assess their treatment outcome. The treatment outcome was compared statistically based on diabetes status using the Chi-square test.

Results: The mean age of the study population was 49.9±0.5 years, with the majority being male 56 (74.7%). More than half of the study population belonged to a low socio-economic status. Among the study population, 42 (56%) were diabetic, with a mean blood glucose level of 242.7±80.5 mg/dL. Eighty-two percent had Pulmonary TB, with a 68% smear positivity rate among diabetic patients. In terms of treatment outcome, 44 (58.7%) were cured, 15 (20%) completed treatment, 10 (13.3%) were lost to follow-up, and 6 (8%) expired during the treatment course.

Conclusion: Smear positivity and pulmonary TB were predominant among patients with diabetes. Treatment completion was lower, and mortality was higher among diabetic patients with TB.

Keywords: Blood glucose, Diabetes mellitus, *Mycobacterium tuberculosis*, Revised national tuberculosis control program

INTRODUCTION

Tuberculosis (TB) is a communicable disease that remains a global public health threat, primarily affecting populations in developing countries [1]. India, as a developing country, has the highest number of TB cases in the world, with about 2.3 million cases per year. Despite efforts to reduce the incidence of TB, it still poses a significant public health concern, especially when combined with Diabetes Mellitus (DM) [2]. TB is more prevalent in individuals with compromised immune systems, and the increasing prevalence of DM in high TB burden countries can negatively impact TB control efforts [3]. Approximately 95% of TB patients and 70% of diabetes patients live in low- and middle-income countries, particularly in Southeast Asia [4].

The global rise in diabetes poses a significant challenge in the fight against TB. India, known as the world's TB capital, accounts for approximately one-quarter of the global TB burden. Patients with both TB and DM are more likely to experience poor treatment outcomes, such as treatment ineffectiveness, patient mortality, and increased risk of TB recurrence. Furthermore, there is growing evidence that diabetes is a risk factor for both new and reactivated TB cases. Diabetes is associated with 10% of all TB cases worldwide [5]. The prevalence of DM and TB is projected to reach 438 million by 2030, with more than 80% of adult cases occurring in newly developed or developing countries [6].

Screening TB patients for diabetes can facilitate early detection and treatment of DM, which can improve TB treatment outcomes [7]. Previous cross-sectional studies have investigated factors associated with the outcomes of TB and DM [8,9]. However, this study aims to prospectively identify factors related to diabetes and TB treatment outcomes. It will provide further support for the importance of evaluating DM in TB patients without a pre-existing diagnosis to effectively manage TB-DM co-morbidity within the RNTCP setting.

The null hypothesis (Ho) posits that there would be no difference in the treatment outcomes of patients with both TB and diabetes. Conversely, the alternative hypothesis (H1) suggests that there would be a difference in treatment outcomes. Therefore, this study aims to assess the treatment outcome of TB in patients with diabetes, compare the treatment outcomes between diabetic and non diabetic patients receiving Category-I TB treatment under RNTCP, and evaluate various factors influencing the treatment outcomes of TB among diabetic patients.

MATERIALS AND METHODS

A prospective cohort study was conducted on TB cases registered under the RNTCP in the Department of Pulmonary Medicine, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India, from October 2018 to November 2019. Ethical clearance for the study was obtained from the Institutional Ethical

Committee (IEC) of Chengalpattu Government Medical College (No. IEC- CMC/Approval/22/2018 dated 25/6/2018). Written informed consent was obtained from all participants before their enrollment.

Inclusion criteria: All newly registered TB patients who were microbiologically confirmed through sputum smear and all newly diagnosed or previously known DM patients with no history of previous TB were included in the study. The age criterion for inclusion was >18 years. Diabetes was defined as having a Random Blood Sugar (RBS) >200 mg/dL or Fasting Blood Sugar (FBS) >126 mg/dL or Postprandial Blood Sugar (PPBS) >200 mg/dL [10,11].

Exclusion criteria: Patients who were seriously ill, Human Immunodeficiency Virus (HIV) positive, had chronic kidney disease, were on TB retreatment, paediatric TB cases, pregnant mothers, and multidrug-resistant TB patients were excluded from the study.

Sample size: The study population was selected using purposive sampling based on eligibility criteria. Only patients who could be followed-up in the chest medicine department were included, while those referred to other TB units were excluded. Out of 92 patients enrolled for Category-I treatment under the RNTCP during the first six months, 75 were considered for the study after necessary exclusions. The study population was followed weekly during the intensive phase and monthly during the continuation phase.

Data collection: Primary data was collected using a semi-structured proforma that included variables such as socio-demographic status, medical history of any chronic illness, personal history of smoking and alcohol consumption, past history and treatment history of TB, and diabetes status [12]. These data were collected before treatment initiation. Physical examination and investigations, including fasting and postprandial blood sugar levels, were conducted. Patients were followed-up for six months from the start of treatment to assess their treatment outcome.

Treatment outcomes: A TB patient with bacteriologically confirmed TB at the start of treatment and negative in the last month of treatment who tested smear or culture negative in the last month of treatment or atleast one previous occasion was considered cured. A patient was considered to have completed treatment if they finished treatment without evidence of failure, but with no record of sputum smear or culture results in the last month of treatment either due to tests not being done or results being unavailable, and tested negative on atleast one previous occasion. Treatment failure was defined as a patient's sputum smear or culture being positive at month five or later during treatment. Default was defined as a patient receiving anti-TB treatment for more than one month but not taking anti-TB drugs for two or more consecutive months after treatment initiation. Loss-to-follow-up was defined as patients who did not start treatment or whose treatment was interrupted for two consecutive months or more.

STATISTICAL ANALYSIS

Data analysis was performed using Statistical Package for Social Science (SPSS) version 25.0. The findings of patients with TB and DM were compared to those with TB without DM. Categorical variables were presented as counts (proportions), and the Chi-square test was used to compare these variables. A p-value <0.05 was considered statistically significant.

RESULTS

Among the 75 study participants, the mean age of the study population was 49.9±0.5 years. The percentage of males affected with TB was higher (74.7%) compared to females (25.3%). A greater percentage of the patients were illiterate and belonged to low and middle socio-economic status. The prevalence of diabetes among the study population was 42 (56%). Of these, 32 (78%) had undergone treatment within the past five years. The majority 62 (82.7%) had pulmonary TB, while 13 (17.3%) had extrapulmonary TB [Table/Fig-1].

Variables	TB patients (N=75)	
	With diabetes n=42 (%)	Without diabetes n=33 (%)
Age group (years)		
<50	16 (7.5)	22 (92.5)
>50	26 (70.3)	11 (29.7)
Gender		
Male	35 (62.5)	21 (37.5)
Female	7 (36.8)	12 (63.2)
Education status		
Illiterate	16 (61.5)	10 (38.5)
Literate	26 (53.1)	23 (46.9)
Socio-economic status[$]		
Lower	7 (30.5)	16 (69.5)
Middle	24 (66.7)	11 (33.3)
Upper	11 (62.5)	6 (37.5)
Family history of DM		
Family history present	10 (83.3)	2 (16.7)
Family history absent	32 (50.7)	31 (49.3)
Smoking status		
Smoking present	20 (83.3)	4 (16.7)
Smoking absent	22 (43.1)	29 (56.9)
Alcohol status		
Alcohol intake present	25 (62.5)	15 (45.5)
Alcohol intake absent	17 (48.6)	18 (51.4)
Site of TB		
Pulmonary TB	41 (66.1)	21 (33.9)
Extrapulmonary TB	1 (7.7)	12 (92.3)
Smear status		
Smear positive	34 (54.8)	28 (45.2)
Smear negative	8 (61.5)	5 (38.5)

[Table/Fig-1]: Characteristics of tuberculosis patients by diabetes status.
[$]: Socio economic scale based on Modified BG Prasad; TB: Tuberculosis; DM: Diabetes milletus

The random blood sugar values were 242.7±80.5 mg/dL and 170.5±8.6 mg/dL for TB patients with and without DM, respectively (p-value <0.001). There was a significant difference in the mean and standard deviation of Fasting Blood Sugar (FBS) and Postprandial Blood Sugar (PPBS) among TB patients with and without DM (p-value <0.001). The mean duration of smoking was higher in TB patients with DM compared to TB patients without DM [Table/Fig-2].

Name of the variable	Diabetics with TB Mean±SD	TB without diabetes Mean±SD	p-value
Age (years)	49.5±10.2	38.5±12.6	0.0001
Weight (kg)	50.5±14.5	53.2±9.8	0.356
Fasting blood sugar	152.5±9.2	98.3±10.7	0.001
Post prandial blood sugar	232.7±13.5	159.5±12.8	0.001
Random blood sugar	242.7±80.5	170.5±8.6	0.001
Duration of smoking (years)	6.9±9.67	3.2±1.6	0.04
Duration of alcohol (years)	5.38±12.7	4.4±2.8	0.561

[Table/Fig-2]: Descriptive statistics of study variables.

The majority of the population exhibited signs and symptoms such as cough with expectoration 59 (78.7%), weight loss 41 (54.7%) [Table/Fig-3].

Signs and symptoms	n (%)
cough with expectoration	59 (78.7)
weight loss	41 (54.7)
evening rise in temperature	42 (56)
Anorexia	32 (42.7)

Dyspnea	21 (28)
chest pain	14 (18.7)
Haemoptysis	8 (10.7)

[Table/Fig-3]: Signs and symptoms of tuberculosis in the study participants (n=75).

Out of the 75 TB patients, 44 (58.7%) were cured, 15 (20%) completed treatment, 10 (13.3%) were lost to follow-up, and 6 (8%) expired during the treatment period. There was no significant difference in the treatment outcomes between TB patients with and without DM [Table/Fig-4].

	TB with diabetes n (%)	TB without diabetes n (%)	Total N (%)	Chi-square
Cured	28 (63.63%)	16 (36.37%)	44 (100%)	χ^2=4.599, df=3 n=75, p=0.204
Treatment completed	7 (46.6%)	8 (53.5%)	15 (100%)	
Lost to follow-up	3 (30.0%)	7 (70.0%)	10 (100%)	
Died	4 (66.6%)	2 (33.4%)	6 (100%)	
Total	42 (56%)	33 (44%)	75 (100%)	

[Table/Fig-4]: Treatment outcome of tuberculosis in the study participants (n=75).

Binary logistic regression was performed to determine the independent predictors of treatment outcome. Age above 50 years, gender, smear positivity, alcohol consumption, and smoking were found to be statistically significant in the univariate analysis. Age, family history, and smoking were identified as independent risk factors for diabetes in TB patients in the binary logistic regression analysis [Table/Fig-5].

Variable	Diabetic tuberculosis n (%)	Crude OR (95% CI)	p-value	Adjusted OR (95%CI)	p-value
Age >50 years	26 (70.3%)	4.255 (1.906-4.473)	0.001	1.255 (1.106-2.23)	0.02
Male	35 (62.5%)	3.013 (1.906-4.473)	0.002	2.15 (0.906-2.13)	0.4
Education status literate	16 (16.5%)	1.97 (0.08-1.31)	0.31	1.01 (0.7-1)	0.57
Socio-economic status lower	31 (74%)	3.75 (0.86-4.8)	0.09	2.3 (0.97-3.2)	0.3
Site of TB Pulmonary TB	41 (66.1%)	2.15 (0.7-1.2)	0.07	1.7 (0.9-1.45)	0.13
Smear positivity	34 (54.8%)	2.071 (1.15-3.065)	0.05	0.22 (.056-3.78)	0.6
Alcoholic history (yes)	25 (62.5%)	2.67 (1.427-5.078)	0.003	1.2 (0.82-1.065)	0.7
Smoking history (yes)	20 (83.3%)	4.170 (1.056-8.515)	0.004	2.010 (1.056-3.78)	0.02
Family history (yes)	20 (83.3%)	2.451 (1.184-1.105)	0.02	1.0875 (1.05-1.32)	0.05

[Table/Fig-5]: Univariate and multivariable regression analysis showing factors associated with the presence of diabetes in tuberculosis patients.

DISCUSSION

According to statistics from the World Health Organisation (WHO), diabetes triples a person's chance of getting TB, and it may be a factor in 15% of TB infections worldwide [13]. In this study, out of 75 patients, 74.7% were male and 25.3% were female. TB was more prevalent among the age group of 45-60 years and least prevalent among those below 30 years and above 75 years, which was consistent with previous studies [3,14].

Married patients had better treatment outcomes compared to single patients, which was consistent with findings from Siddiqui AN et al., [15]. A significant percentage of the study subjects had a family history of TB and a family history of anti-TB treatment. A higher proportion of patients with TB and DM were illiterate and unemployed, indicating a poor socio-economic and demographic status, which was consistent with findings from Mukhtar F and Butt ZA [16].

In this study, 82.7% had pulmonary TB and 17.3% had extrapulmonary TB. Pulmonary TB was more common among patients with DM compared to extrapulmonary TB. Most patients were diagnosed with DM either at the time or just before initiating TB treatment. Siddiqui AN et al., also found a higher prevalence of PTB compared to EPTB among TB patients with DM [15].

The study by Viswanathan V described higher pretreatment sputum positivity among diabetics compared to non diabetics, but this was not statistically significant. In contrast, the present study found that pretreatment sputum positivity was higher among patients with DM compared to those without DM, and this difference influenced treatment outcome [14].

The present study also found differences in smear positivity between DM and non DM patients, contradicting the findings of Siddiqui AN et al., [15]. Signs and symptoms such as chest pain, dyspnoea, fever, and weight loss were found to influence treatment outcomes in TB patients with and without DM, while cough, anorexia, and haemoptysis had a lesser extent of influence.

Previous studies have also shown a high prevalence of diabetes among TB patients and have identified DM as a risk factor for TB [17-20]. However, some studies, including Ranganath TS and Shivaraj BM, have found no significant impact of DM on TB treatment outcomes, which aligns with the findings of the present study [3].

Limitation(s)

Limitations of this study include the exclusion of multidrug-resistant TB patients, which limits the assessment of drug susceptibility in TB patients with DM. The treatment outcomes were mainly based on sputum smear results, and the study could not evaluate the relationship between impaired glycaemia, diabetes, and pulmonary TB. Additionally, the severity of DM and its association with TB treatment outcomes could not be evaluated.

CONCLUSION(S)

The present study concludes that TB patients with DM are more likely to have sputum smear-positive pulmonary TB compared to sputum smear-negative pulmonary TB and extrapulmonary TB. However, the presence of DM does not adversely affect TB treatment outcomes and was not statistically significant. Therefore, the treatment of TB-DM patients can follow the same guidelines as TB patients without DM. Furthermore, integrating DM prevention and control strategies into the TB control program, and vice versa, can aid in the early diagnosis and management of DM complications. It is important to maintain strict glycaemic control, especially during the initial intensive phase of TB treatment, for better outcomes in patients with DM.

Future studies should focus on the long-term evolution of DM control and its impact on TB treatment outcomes.

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