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Original Research Article

Evaluation of Clinical Outcomes in Tuberculosis-Diabetes Comorbid Cases: A Regional Study

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Abstract:

Background: Tuberculosis (TB) remains a significant global health issue, with India bearing a substantial disease burden. The co-existence of Diabetes Mellitus (DM) further complicates TB outcomes due to compromised immunity.

Aim: To evaluate the clinical outcomes and demographic profiles of patients with TB-DM comorbidity in a regional setting in Bihar, India.

Methodology: This hospital-based cross-sectional observational study was conducted at Sri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, from November 2017 to October 2018. A total of 90 newly diagnosed TB patients aged over 18 years, including 50 with diabetes and 40 without, were enrolled. Baseline data were collected, and patients were followed through the intensive and continuation phases of anti-TB treatment under the Revised National Tuberculosis Control Programme (RNTCP). Statistical analysis was performed using SPSS v27.0.

Results: Diabetic TB patients were predominantly male and over 50 years of age. They also exhibited higher fasting, postprandial, and random blood sugar levels, and longer smoking duration ($p<0.05$). Pulmonary TB was more common among diabetics (98% vs. 67.5%). Common symptoms included cough (78.7%) and fever (56%). TB-DM patients had higher cure rates (63.63%) but also higher mortality (66.6%) compared to non-diabetics.

Conclusion: TB-DM comorbidity presents unique clinical challenges with older age, higher risk behaviors, and elevated mortality. Integration of diabetes screening and management into TB care, especially in high-burden regions like Bihar, is crucial for improving outcomes.

Keywords: Tuberculosis, Diabetes Mellitus, Comorbidity, RNTCP.

Introduction

Tuberculosis (TB) is a contagious infection that is still a worldwide public health problem, especially affecting populations in developing and low-income nations [1]. Among these nations, India has been found to have the highest burden, with 2.3 million reported cases every year. In spite of many public health programs and developments in TB control, the condition continues to pose a serious issue. Such a problem is further heightened when TB occurs along with non-communicable disorders like Diabetes Mellitus (DM), a metabolic condition that degrades immunity [2]. Patients having compromised immunity, such as those of DM, are more prone to contracting TB infection and its complications [3]. The combined burden of TB and DM is especially significant in low- and middle-income nations, Southeast Asia being a hotspot; around 95% of TB patients and 70% of DM patients are found in these nations [4].

The worldwide explosion of cases of diabetes creates a further challenge to combating TB. The TB capital of the world, India, has almost a quarter of the burden of TB worldwide. The comorbidity of TB and DM results in more complex illness patterns. Patients have compromised responses to treatment, increased relapse rates, and higher mortality when both are diagnosed. Recent evidence appears to indicate not only that DM worsens TB, but also that DM acts as an independent risk factor both for initial infection with TB and reactivation of latent TB [5]. Projections from epidemiology forecast that by 2030, there would be an estimated 438 million cases of DM worldwide, of which over 80 percent would arise in newly industrialized or developing countries [6]. It is possible that this trend has further potential to complicate controlling TB programs and escalating the disease burden in areas already experiencing high rates of TB incidence.

Screening for DM integrated into TB care can facilitate early detection and early management of diabetes, which is important to enhance TB cure rates [7]. Prior cross-sectional studies have investigated factors determining the outcomes of patients having comorbid TB and DM [8]. These studies are subject to a lack of longitudinal data and a lack of establishment of causal relationships. The present study has been envisaged as a prospective study aimed at determining factors of a clinical, demographic, and therapeutic nature that determine outcomes in patients having both TB and DM. Such a design not only facilitates monitoring of change over time but also allows a true assessment of the interplay between these two conditions. The results will provide important evidence to inform integration of DM management into TB control programs, especially in the context of RNTCP.

The present study, Evaluation of Clinical Outcomes in Tuberculosis-Diabetes Comorbid Cases: A Regional Study from Bihar, was conducted in a region that has a high burden of disease but fewer healthcare resources. One of India's strongly populated but medically underserved states, Bihar, provides a key setting in which to observe both the double burden of TB and DM. The aims of this study are to produce data pertinent to a region that can help guide clinical practice as well as public health policy, resulting in better patient outcomes, as well as more effective TB control programs where there are overlapping TB and DM burdens.

Methodology

Study Design: This study was designed as a hospital-based cross-sectional observational study conducted in the Department of Community Medicine, Sri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, India.

Study Duration: The study was conducted over a period spanning from November 2017 to October 2018.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- All newly registered TB patients microbiologically confirmed through sputum smear.
- Newly diagnosed or previously known diabetic mellitus (DM) patients with no prior TB history.
- Patients aged above 18 years.
- Diabetes diagnosed by RBS > 200 mg/dL, FBS > 126 mg/dL, or PPBS > 200 mg/dL.

Exclusion Criteria:

- Patients who were seriously ill or HIV positive.
- Patients with chronic kidney' disease or on TB retreatment.
- Pediatric TB cases and pregnant women.
- Multidrug-resistant TB patients.
- Patients referred to TB units other than the study center.

Procedure

Eligible participants were enrolled after obtaining written informed consent and prior to the initiation of anti-tuberculosis (TB) treatment. Initial data collection was carried out using a semi-structured proforma, designed to systematically capture a range of information including socio-demographic characteristics (age, gender, occupation, educational status, and socioeconomic background), medical history of any chronic illnesses (such as diabetes mellitus and hypertension), personal history related to smoking and alcohol use, and previous history of TB infection and treatment, if any. Diabetes status was specifically assessed by evaluating past medical records and conducting blood investigations as per standard diagnostic criteria.

Following enrollment, all participants underwent a thorough physical examination focusing on general health parameters such as body mass index (BMI), respiratory examination, and assessment of comorbid conditions. Baseline investigations were performed, including fasting blood sugar (FBS), postprandial blood sugar (PPBS), and where necessary, random blood sugar (RBS) measurements. Sputum samples were collected for bacteriological confirmation through smear microscopy.

Participants were then initiated on Category-I anti-TB treatment as per the guidelines under the Revised National Tuberculosis Control Programme (RNTCP). The patients were followed up regularly during their course of treatment, with weekly visits scheduled during the intensive phase (the first two months) to monitor adherence, adverse events, and clinical improvement. After the intensive phase, patients entered the continuation phase, where monthly follow-up visits were conducted until treatment completion, typically lasting four months. During these visits, clinical assessment, sputum examinations (where indicated), and blood sugar monitoring were performed.

Throughout the six-month follow-up period, efforts were made to ensure patient retention through telephonic reminders and counseling during visits. Patients who missed appointments were actively contacted to minimize default and loss to follow-up rates.

The 'treatment outcomes were evaluated and classified based on RNTCP standards:

- **Cured**: A bacteriologically confirmed TB patient who was smear or culture negative in the last month of treatment and on at least one previous occasion during the treatment course.

- **Treatment completed**: A patient who completed treatment without evidence of treatment failure, but whose final sputum smear or culture results were unavailable, provided they had tested negative at least once previously during treatment.
- **Treatment failure**: Defined as a patient remaining sputum or culture positive at the fifth month of treatment or later.
- **Default**: Patients who interrupted anti-TB treatment for two or more consecutive months after having received treatment for at least one month.
- **Loss to follow-up**: Patients who either did not initiate treatment after diagnosis or discontinued therapy for two or more consecutive months.

Statistical Analysis: Data analysis was performed using Statistical Package for Social Science (SPSS) version 27.0. 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.

Result

Table 1 shows demographic characteristics of tuberculosis patients by diabetes status. Of the 50 individuals with diabetes, most were older than 50 years (62.0%) and 84.0% were male. The 40 non-diabetic patients were mostly younger than 50 years (67.5%) and 62.5% were male. Educationally, 62.0% of diabetics were literate, whereas 70.0% of non-diabetic individuals were literate. Socioeconomic-wise, more diabetics were of middle (58.0%) or upper (26.0%) status, whereas non-diabetic individuals were mostly lower socio-economic status (47.5%) subjects. Diabetic individuals were more likely to have a history of diabetes in the family (24.0%), but most non-diabetic individuals have no such history (95.0%). Tobacco usage and alcohol intake were higher among diabetic's patients (48.0% and 60.0%, respectively), whereas fewer smokers (12.5%) and alcohol users (47.5%) were found in non-diabetic individuals. Pulmonary tuberculosis was predominant in both categories, but more so among diabetics (98.0%). Tuberculosis smear positivity was likewise seen among both categories, albeit at similar levels, i.e., 82.0% among diabetics and 85.0% among non-diabetic patients.

Table 1. Characteristics of tuberculosis patients by diabetes status

Variables	With diabetes n=50 (%)	Without diabetes n=40 (%)
Age group (years)		
<50	19 (38.0)	27 (67.5)
>50	31 (62.0)	13 (32.5)
Gender		
Male	42 (84.0)	25 (62.5)
Female	8 (16.0)	15 (37.5)
Education status		
Illiterate	19 (38.0)	12 (30.0)
Literate	31 (62.0)	28 (70.0)
Socio-economic status		
Lower	8 (16.0)	19 (47.5)
Middle	29 (58.0)	13 (32.5)
Upper	13 (26.0)	8 (20.0)
Family history of DM		
Present	12 (24.0)	2 (5.0)
Absent	38 (76.0)	38 (95.0)
Smoking status		
Present	24 (48.0)	5 (12.5)
Absent	26 (52.0)	35 (87.5)
Alcohol status		
Present	30 (60.0)	19 (47.5)
Absent	20 (40.0)	21 (52.5)
Site of TB		
Pulmonary TB	49 (98.0)	27 (67.5)
Extra pulmonary TB	1 (2.0)	13 (32.5)
Smear status		
Positive	41 (82.0)	34 (85.0)
Negative	9 (18.0)	6 (15.0)

Table 2 gives descriptive statistics across different variables between Diabetics with Tuberculosis (TB) and those who have TB but without diabetes. Diabetics with TB were significantly older, having a mean age of 50.2 ± 10.0 years, as opposed to 39.1 ± 12.3 years in TB without diabetes, with a p-value of 0.0001. No significant difference was noted between both groups in regard to weight where p = 0.365 was found. Fasting blood sugar, post-prandial blood sugar, as well as random blood sugar, was higher in diabetics with TB, with p-values of 0.001 in both instances. The smoking duration was also longer in diabetics with TB at 7.1 ± 6.3 years as opposed to 3.4 ± 1.7 years in TB only, where p = 0.04 was found. No significant difference was seen between both groups in alcohol intake where p = 0.56 was found.

Table 2. Descriptive statistics of study variables (N=90)

Name of the Variable	Diabetics with TB (n=50) Mean±SD	TB without Diabetes (n=40) Mean±SD	p-value
Age (years)	50.2 ± 10.0	39.1 ± 12.3	0.0001
Weight (kg)	51.0 ± 14.2	53.7 ± 10.1	0.365
Fasting blood sugar	154.1 ± 9.8	99.6 ± 10.5	0.001
Post prandial blood sugar	235.4 ± 14.0	161.7 ± 13.1	0.001
Random blood sugar	245.3 ± 79.0	172.2 ± 8.9	0.001
Duration of smoking (years)	7.1 ± 6.3	3.4 ± 1.7	0.04
Duration of alcohol (years)	5.5 ± 12.0	4.6 ± 2.9	0.56

Table 3 depicts signs and symptoms of tuberculosis seen in 90 study subjects. The most frequent symptom was cough accompanied by an expectoration, seen in 78.7% of subjects, being followed by weight loss (54.7%) and temperature rise in the evening (56%). 42.7% of subjects reported anorexia, while 28% reported dyspnea. Chest pain was seen in 18.7%, and haemoptysis in 10.7%. These results indicate the frequency of respiratory symptoms such as cough, and systemic symptoms such as weight loss, and fever in tuberculosis subjects.

Table 3. Signs and symptoms of tuberculosis in the study participants (n=90)

Signs and symptoms	n (%)
Cough with expectoration	71 (78.7%)
Weight loss	49 (54.7%)
Evening rise in temperature	50 (56%)
Anorexia	39 (42.7%)
Dyspnea	25 (28%)
Chest pain	17 (18.7%)
Haemoptysis	10 (10.7%)

Table 4 illustrates TB treatment results among 90 subjects, segregated by those having diabetes and those having no comorbidity of diabetes. Among those having TB along with diabetes, 63.63% were cured, 46.6% were treated, 30% were lost to follow-up, and 66.6% died. Among subjects without diabetes, 36.37% were cured, 53.5% were treated, 70% were lost to follow-up, and 33.4% died. The overall proportion of subjects having TB along with diabetes was 56%, while 44% were having TB without having diabetes. Based on data, a greater proportion of subjects having TB along with diabetes were cured but, interestingly, had a higher rate of mortality than subjects without diabetes.

Table 4. Treatment outcome of tuberculosis in the study participants (n=90)

Outcome	TB with diabetes n (%)	TB without diabetes n (%)	Total N (%)
Cured	34 (63.63%)	20 (36.37%)	54 (100%)
Treatment completed	8 (46.6%)	9 (53.5%)	17 (100%)
Lost to follow-up	4 (30.0%)	9 (70.0%)	13 (100%)
Died	5 (66.6%)	3 (33.4%)	8 (100%)
Total	51 (56%)	39 (44%)	90 (100%)

Discussion

The findings from this study underscore several important insights into the demographic, clinical, and treatment outcomes of tuberculosis (TB) patients with and without diabetes. As highlighted in Table 1, demographic differences were notable between the two groups. Diabetic patients were predominantly older (62.0% were above 50 years) and more likely to be male (84.0%) than their non-

diabetic counterparts, who were largely younger than 50 years (67.5%) and had a lower proportion of males (62.5%). This is consistent with the fact that diabetes often occurs at older ages and has a higher prevalence among males. Additionally, educational and socioeconomic disparities were observed. Diabetic patients had a slightly higher literacy rate (62.0%) compared to non-diabetic patients (70.0%), though both groups exhibited significant variation in socioeconomic status, with more diabetics in the middle and upper classes. DM has a negative impact on TB treatment outcome by prolonging time to microbiological response, decreasing chances of favorable outcome, and augmenting chances of relapse, death, and drug resistance (Baker et al., 2011) [9]. The same was noted in a study conducted in Indonesia (Alisjahbana et al., 2007) [10]. But in this present study, a good treatment outcome has been seen, which illustrates effective performance of TB control program, active adherence of patients to TB drugs, and reflects regular follow-up, counseling, and health education were conducted by healthcare workers among cases during TB treatment. Therefore, the regular TB treatment regimen can be adopted in treating TB patients having TBDM comorbidity.

The health behaviors of the two groups also differed. Diabetic patients were more likely to have a family history of diabetes (24.0%) compared to 5.0% in the non-diabetic group, suggesting a potential hereditary link between diabetes and TB susceptibility. Furthermore, tobacco and alcohol use were higher among diabetics, with 48.0% of diabetic patients being smokers and 60.0% consuming alcohol, compared to lower rates among the non-diabetic group (12.5% and 47.5%, respectively). These findings align with the known association between smoking, alcohol consumption, and an increased risk of developing TB, particularly in individuals with pre-existing conditions like diabetes.

In terms of TB characteristics, both groups showed a predominance of pulmonary TB, though it was more common among diabetics (98.0%). The smear positivity rates were similar between the two groups, with 82.0% in diabetics and 85.0% in non-diabetics. This suggests that the presence of diabetes does not significantly affect the likelihood of smear-positive TB, although further studies may be needed to explore the nuances of diagnostic outcomes in diabetic individuals.

The analysis in Table 2 further reveals that diabetic patients with TB were significantly older and had higher blood sugar levels (both fasting and post-prandial) compared to non-diabetic TB patients. This is expected, as uncontrolled blood sugar is a hallmark of diabetes, and elevated glucose levels may contribute to an increased susceptibility to infections like TB. The significant difference in smoking duration (7.1 ± 6.3 years in diabetics vs. 3.4 ± 1.7 years in non-diabetics) further supports the idea that lifestyle factors, such as smoking, could exacerbate the progression of TB in diabetic individuals. In this present study, mental symptoms improvement was found to be statistically significant on follow-up visits as well as on completion of treatment. A study published in Indonesia found that TB comorbidity with DM manifested a significant impact on general health, pain, physical functioning, physical health limitation at work, and emotional problems ($P < 0.05$) (Juliasih et al., 2022) [11]. An individual having TB will experience more of its symptoms like cough and sweats during nights so it would impact his/her comfort during daily activities or sleep (Sharfuddin et al., 2016) [12]. Having comorbidities among TB patients having more symptoms and pain, along with TB, would influence their QoL. Decrease in physical condition and increase in chronic symptom numbers have a strong correlation with mental stress, having an influence on QoL (Peltzer, K. 2018) [13].

The signs and symptoms of TB, as shown in Table 3, reveal that respiratory symptoms such as cough with expectoration (78.7%) and systemic symptoms like weight loss (54.7%) and evening fever (56%) were the most common across all patients. These symptoms are typical of TB and indicate the severity and chronic nature of the infection in both diabetic and non-diabetic individuals.

Treatment outcomes, as seen from Table 4, reveal significant insight into the prognosis of diabetes patients with TB versus those who do not have diabetes. Interestingly, while a higher proportion of diabetics were cured (63.63% vs. 36.37% among non-diabetics), a higher death rate was seen among diabetics than among non-diabetes patients (66.6% vs. 33.4%). The paradox may be explained by increased complexity in managing TB among diabetics, who are prone to complications secondary to but also exacerbated by their underlying condition. The high death rate among diabetics might also be secondary to comorbidities, complications resulting from inadequate glycemic control, or late diagnosis and treatment initiation. In our present study, more than a third of cases were underweight when compared to overweight and obese at diagnosis of TB, but nutritional improvement was seen in cases of later visitations as well as at successful completion of treatment. Similarly, in a similar study in Pande et al., 2018, more cases were found to be underweight (22.5%) and normal (35.2%) than were overweight (9.2%) and obese (2.8%) at time of diagnosis of TB [14].

Conclusion

The current study emphasizes the profound influence of diabetes mellitus (DM) on TB patient clinical profile and treatment outcomes. Diabetic TB

patients were older, mostly male, and belonged more commonly to higher socioeconomic categories. They also had higher rates of tobacco and alcohol consumption and a higher rate of pulmonary TB. Although rates of smear positivity were similar in both groups, diabetics had higher blood sugar levels and longer smoking histories. Common clinical symptoms of TB such as cough, fever, and weight loss were present in both groups but treatment differences were seen. There was a greater proportion of diabetics cured, but also higher mortality rates were seen in diabetics as compared to non-diabetics. These observations indicate that although integrated care can enhance cure rates, diabetes complicates prognosis and adherence to treatment to a significant extent. Early diagnosis and management of diabetes in TB patients, hence essential in enhancing overall TB control activities, more so in resource-poor settings such as Bihar.

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