Original Research Article

Impact of diabetes mellitus on tuberculosis treatment outcomes: a cohort study in Bengaluru, India

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ABSTRACT

Background: Tuberculosis (TB) remains a significant global health challenge, particularly in regions with a high prevalence of diabetes mellitus (DM). This study aims to evaluate the impact of DM on the treatment outcomes of TB patients in Bengaluru, India.
Methods: In this cohort study, we examined 592 patients with smear-positive pulmonary TB, half of whom had a comorbid diagnosis of DM. Conducted in the Bruhat Bengaluru Mahanagara Palike area, the study included patients registered under the national TB elimination programme (NTEP). Data were collected on demographic characteristics, treatment adherence, sputum positivity, and treatment outcomes over six months.
Results: The study revealed a high prevalence of DM among TB patients. Significant associations were observed between DM and various challenges, including higher rates of sputum positivity, poor adherence to anti-TB and anti-diabetic medications, increased adverse drug reactions (ADRs), and a higher default rate. TB patients with DM had a 1.5 times higher risk of unsuccessful treatment outcomes compared to non-diabetics. Furthermore, the risk of poor outcomes, particularly relapse, increased substantially in the TB-DM group during the six-month follow-up.
Conclusions: Our findings highlight the crucial need for integrated TB and DM management strategies. This includes routine DM screening for TB patients, personalized treatment regimens, and enhanced patient education and support. These measures are essential for improving treatment outcomes in TB patients with comorbid DM.

Keywords: TB, DM, Treatment outcomes, Comorbidity, Public health

INTRODUCTION

Tuberculosis (TB), caused by the bacterium *Mycobacterium tuberculosis*, has long been a major global health concern. Despite the discovery of its causative organism over a century ago, TB remains one of the world's deadliest communicable diseases, holding the infamous title of being the leading cause of death from a single infectious agent.[1] This persistent threat is especially pronounced in low- and middle-income countries (LMICs), where burden of TB continues to be substantial despite global efforts to combat the disease.[2]

India, in particular, bears a significant portion of this burden. As reported by the global TB report (2020), India accounts for approximately one-fifth of the global incidence of TB cases. This positions the country among the top high-burden countries contributing to an estimated 80% of the world's TB burden. Notably, nearly 40% of the Indian population is estimated to harbour latent TB bacilli, highlighting the pervasive nature of the disease within the country.[3]

In 2016, the global incidence of TB was estimated to be 10.4 million new cases, with a concerning proportion of these being multidrug-resistant TB (MDR-TB) cases.[4] Despite TB being a curable disease, the year also witnessed approximately 1.7 million TB-related deaths, underscoring the challenges in TB management and control.[5]

The END TB strategy, launched by the world health organization (WHO), aims to achieve a world free of TB. Its ambitious goal is to drive a rapid decline in TB burden, morbidity, and mortality, with the ultimate aim of eliminating TB by 2035 globally, and by 2025 in India (WHO, 2019). However, the journey towards this goal is fraught with challenges, particularly in high-burden countries like India, where concerted efforts are needed to address the multifaceted dimensions of the TB epidemic.[6]

Adding complexity to this scenario is the rising prevalence of diabetes mellitus (DM) globally. In 2017, there were an estimated 425 million people living with DM worldwide, a figure projected to rise to nearly 629 million by 2045.[7] Diabetes, characterized by elevated levels of blood glucose, poses its own set of health challenges and significantly contributes to global morbidity and mortality. Each year, around 10 million people develop new cases of DM, and up to 5 million deaths are attributed to DM-related complications.[8]

India is witnessing a rapid surge in the prevalence of DM, with an estimated 69 million people suffering from the condition. The prevalence of DM in the general population stands at about 7.8%, raising concerns about India potentially becoming the "diabetes capital of the world" by 2025. In 2016, DM was directly responsible for an estimated 1.6 million deaths, with nearly half of these occurring before the age of 70, primarily due to elevated blood glucose levels.[9]

The intersection of these two diseases, TB and DM, poses a unique challenge. Patients with impaired immunity, such as those with HIV/AIDS or DM, are at a higher risk of developing active TB. The dual epidemic of HIV/AIDS and DM, particularly in countries like India, complicates the TB landscape. The increasing prevalence of DM in high TB burden countries may adversely impact TB control efforts.[10]

This study aims to delve into the intricate relationship between TB and DM, focusing on South Indian context. Prevalence of TB in India, coupled with rising incidence of DM, underscores the need for a nuanced understanding of how these diseases interact and affect each other's management and outcomes. Through this research, we seek to shed light on impact of DM on TB treatment outcomes and explore potential strategies for integrated care for individuals grappling with this dual burden.

METHOD

Study setting

This research was conducted in the Bruhat Bengaluru Mahanagara Palike (BBMP) area of Bengaluru, India. Within this region, with a population of about 6.8 million, tuberculosis (TB) care is provided under the national tuberculosis elimination programme (NTEP). The BBMP area is serviced by 16 tuberculosis units (TUs), each

covering approximately 500,000 people, and 82 designated microscopy centers (DMC). These centers are situated in mix of BBMP hospitals, government hospitals, medical colleges, NGOs, and private sector hospitals. Each TU comprises 3-7 DMCs and 4 to 14 DOTS centers.

Study design

An ambispective cohort study was designed to investigate the impact of DM on the treatment outcomes of patients with pulmonary tuberculosis.

Study population

Study included patients with confirmed smear-positive pulmonary tuberculosis, who registered and receiving treatment under NTEP across all TUs in Bengaluru.

Inclusion criteria

Patients diagnosed with sputum smear-positive pulmonary tuberculosis, patients having fasting blood glucose level >126 mg/dl or postprandial blood glucose level >200 mg/dl, patients aged 18 years or older, patients willing to provide written informed consent and patients registered and able to be followed up in the respective TUs included in study.

Exclusion criteria

Patients diagnosed with TB through cartridge based nucleic acid amplification test (CBNAAT), pediatric TB cases, pregnant women and people living with HIV, patients on steroids, and immunosuppressants were excluded from the study.

Study period

The study spanned from November 2017 to May 2019.

Sampling method

Purposive sampling was used to select participants. During the six-month recruitment period, 592 patients meeting the inclusion criteria were registered across all TUs. An equal number of TB patients with and without DM were included to minimize selection bias.

Data collection

Data collection began after obtaining clearance from institutional ethics committee and permission from NTEP. Total of 6,663 new sputum-positive cases were diagnosed during the study period. From 1st January 2018 to 30th June 2018, patients aged 18 years and above screened for DM under NTEP. Of these, 738 cases identified as TB with DM. Ultimately, 296 TB with DM and 296 TB without DM patients consented to participate in study.

Data analysis

Data were entered into Microsoft excel 2010 and analyzed using SPSS version 20. The analysis encompassed bivariate and multivariate methods. Logistic regression was employed to investigate factors affecting TB treatment outcomes. A $p<0.05$ was considered significant for all statistical tests.

Outcome measures

Treatment outcomes were classified as 'cured' (negative sputum smears at the end of treatment) or 'completed treatment' (completion of the full course of anti-tubercular drugs with no symptoms at the end). Other outcomes included 'died', 'failure', 'lost to follow-up', 'transferred out', and 'switched to MDR-TB treatment'.

RESULTS

Participant characteristics

Out of 6,663 registered TB patients, 738 (11%) were diagnosed with comorbid DM. The sample consisted of 296 TB-DM and an equivalent number of TB non-DM patients. TB-DM group was predominantly male (71%), with a higher average age (50.33±12.31 years) compared to TB non-DM participants (44.22±13.65 years).

Socioeconomic and clinical profile

A majority of the study population belonged to the lower-middle socioeconomic class (57%). The TB-DM group reported higher alcohol consumption rates and more significant disruptions in sleep patterns (27%) compared to their non-DM counterparts. Poor adherence to anti-TB treatment was observed in 12.1% of TB-DM patients. Treatment interruptions and the prevalence of the additional comorbidities were notably higher in the TB-DM group.

Treatment outcomes

Sputum smear positivity at the end of the continuation phase of treatment was significantly higher in the TB-DM group. The odds of experiencing poor treatment outcomes were elevated in TB-DM patients (OR: 1.573; 95% CI: 1.146-1.892). Furthermore, the risk of relapse was substantially higher in this group after a 6-month follow-up period (adjusted OR: 2.23; 95% CI: 1.398-3.586).

Table 1: Demographic and socioeconomic characteristics of participants.

Characteristics	TB with DM, (n=296) N (%)	TB without DM, (n=296) N (%)	Total, (n=592) N (%)
Age group (in years)			
<35	3 (1.0)	37 (12.5)	40 (6.8)
35-44	29 (9.8)	34 (11.5)	63 (10.6)
45-54	65 (22)	52 (17.6)	117 (19.8)
55-64	150 (50.7)	100 (33.8)	250 (42.2)
>65	49 (16.5)	73 (24.7)	122 (20.6)
Gender			
Male	210 (70.9)	165 (55.7)	375 (63.3)
Female	86 (29.1)	131 (44.3)	217 (36.7)
Socioeconomic status			
Lower middle	187 (63.2)	152 (51.4)	339 (57.3)
Upper middle	29 (9.8)	10 (3.4)	39 (6.6)

Table 2: Clinical characteristics, comorbidities, and treatment adherence.

Clinical characteristic	TB with DM, (n=296) N (%)	TB without DM, (n=296) N (%)	Total, (n=592) N (%)
BMI category			
Undernutrition	102 (34.5)	115 (38.9)	217 (36.7)
Normal	104 (35.1)	102 (34.5)	206 (34.8)
Overweight	31 (10.5)	26 (8.8)	57 (9.6)
Obese	59 (19.9)	53 (17.9)	112 (18.9)
Comorbidities			
Hypertension	20 (6.8)	1 (0.3)	21 (3.5)
HIV	2 (0.7)	0 (0.0)	2 (0.3)
Adherence to ATT			
Poor (<90%)	36 (12.1)	16 (5.4)	52 (8.8)
Good (>90%)	260 (87.9)	280 (94.6)	540 (91.2s)

Table 3: Treatment outcomes and complications.

Outcome	TB with DM, (n=296) N (%)	TB without DM, (n=296) N (%)	Total, (n=592) N (%)
Treatment success			
Cured	242 (81.7)	270 (91.2)	512 (86.5)
Treatment completed	26 (8.8)	13 (4.4)	39 (6.6)
Treatment failure			
Lost to follow-up	7 (2.4)	9 (3.1)	16 (2.7)
Death	8 (2.7)	2 (0.7)	10 (1.7)
Increased incidence of ADRs (%)	20	12	16

Comparative analysis of outcomes

The TB-DM group exhibited a lower cure rate (81.7%) compared to TB non-DM patients (91.2%). Incidences of death, treatment failure, and multidrug-resistant TB cases were higher in TB-DM patients. Post-treatment follow-up revealed increased mortality and relapse rates among TB-DM participants.

Multivariate analysis findings

Diabetes was identified as a significant determinant, increasing the likelihood of unsuccessful treatment outcomes by 1.5 times. This association was more pronounced in the risk of relapse observed in TB-DM patients after 6 months.

DISCUSSION

Our Bengaluru-based study uncovers a notable 11% prevalence of DM among TB patients, significantly higher than Karnataka's general DM prevalence of 7.5%. This finding mirrors global trends in high TB burden regions, reinforcing the necessity for routine DM screening in TB patients (Jali et al).[11] The study also reveals distinct sociodemographic patterns, such as the predominance of TB among semi-skilled laborers, coupled with a 13% unemployment rate. These patterns align with similar socioeconomic trends observed in TB demographics across other LMICs, highlighting a socioeconomic disparity in TB prevalence (Stubbs et al).[12]

Our observation that 57% of TB-DM patients belong to the lower-middle class echoes studies indicating a higher TB burden in lower socioeconomic groups (Arnold et al).[13] Furthermore, our study identifies significant association between undernutrition and poorer TB outcomes, resonating with Bhargav et al research on the impact of nutritional status on TB prognosis (Bhargav et al).[14]

Correlation between moderate body weight and better TB outcomes also aligns with Brown et al emphasis on importance of nutrition in TB management (Brown et al).[15]

The complexities of managing TB in patients with DM are further highlighted by the variations in sputum conversion rates and glycemic control challenges. These issues are paralleled in global studies, including Wang et al, who explore the potential role of metformin in improving TB treatment outcomes in TB-DM comorbidity, Wang et al, and Karoli et al, who examine the significance of vitamin D deficiency in managing TB-DM comorbidity.[16,17]

Our findings of poorer outcomes and increased ADRs in TB-DM patients reflect the dual burden of these diseases, as underscored by Aweis et al and Babu et al.[18,19] The study underscores the urgent need for integrated TB and DM management approaches, advocating for tailored treatment regimens, comprehensive patient education, and the utilization of advanced technologies like artificial intelligence. The study also highlights the importance of strengthening follow-up strategies and enhancing healthcare provider training to improve patient care and the outcomes for those affected by the TB-DM comorbidity.

CONCLUSION

Our study underscores the significant prevalence of DM among TB patients in Bengaluru, India, and the implications it has for TB treatment outcomes. It advocates for routine DM screening, integrated management strategies, and a multifaceted approach encompassing patient education, nutritional support, and advanced technology use. The study's insights are crucial for policy makers and healthcare providers in high TB burden regions, emphasizing the need for revised clinical guidelines and enhanced public health strategies to effectively address the TB-DM nexus.

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