

Review Article

Diabetes Mellitus and Treatment Outcomes among Patients of Tuberculosis: A Review

Priyanka Hemrajani', Jugal Kishore²

¹Assistant Professor, Dermatology, ESIC-PGIMSR, Basaidarapur, New Delhi, India ²Director Professor, Community Medicine, VMMC & SJH, New Delhi, India **DOI:** https://doi.org/10.24321/2455.7048.202410

INFO

Corresponding Author:

Jugal Kishore, Community Medicine, VMMC & SJH, New Delhi, India **E-mail Id:** drjugalkishore@gmail.com **Orcid Id:** https://orcid.org/0000-0001-6246-5880 **How to cite this article:** Hemrajani P, Kishore J. Diabetes Mellitus and Treatment Outcomes among Patients of Tuberculosis: A Review. Epidem Int. 2024;9(3):18-

21. Date of Submission: 2024-06-15

Date of Acceptance: 2024-07-20

A B S T R A C T

The prevalence of diabetes mellitus (DM) is increasing in India which could be a threat to the National Tuberculosis Elimination Programme. This review aims to find the association of diabetes with treatment outcomes among patients with tuberculosis (TB). Scrutiny of various online search engines provided many research articles that were assessed in detail. Out of hundreds of articles, 9 studies indicated that the prevalence of DM varied from 5% to 66% and was associated with delay in recovery of patients suffering from TB and higher mortality. Early detection of DM among TB patients and TB among DM patients is a beneficial strategy.

Keywords: Diabetes Mellitus, Mycobacterium tuberculosis, DOTS

Introduction

The prevalence of Diabetes Mellitus (DM) is increasing rapidly throughout the world including India. DM increases the risk of tuberculosis (TB) 2–3 times, 2 times TB mortality, 4 times TB relapse, and 2 times development of multidrug resistance TB.^{1–3} TB is a fatal infectious disease caused by various strains of mycobacteria, the most common being *Mycobacterium tuberculosis*. It is spread through droplets from people with active TB infection via cough, sneeze, or respiratory fluids to healthy individuals. Symptoms of TB are chronic cough with or without blood-tinged sputum, fever, night sweats, and weight loss.⁴ Around one-third of the world's population shows infection with *M. tuberculosis*.⁵

TB patients accessing healthcare centres for directly observed treatment, and short course (DOTS) therapy for TB could also avail facilities for the management of diabetes at the same time. This would thus reduce the cost incurred by both the patients and the health system and prevent unnecessary duplication of delivery of services. Co-located DOTS centres and diabetic clinics at the primary health care level will be a big leap forward in the early detection and management of the two diseases. Collaborative efforts are required to end TB strategy in the United Nations (UN) high-level meeting on TB, where not only DM but also other co-morbidities such as HIV, undernutrition, mental illness, and non-communicable diseases should be addressed.⁶ Therefore, the World Health Organization 2011 recommended bi-directional screening for TB and DM.

This review aims to explore the research done in this field regarding the prevalence of DM and its effect on the treatment outcomes among TB patients.

Methodology

The review of the literature was undertaken in multiple ways. The majority of the research in this regard was

Epidemiology International (ISSN: 2455-7048) Copyright (c) 2024: Author(s). Published by Advanced Research Publications



done using the Internet. The major sites accessed for relevant literature were Google, PubMed, and Google Scholar. The keywords used were: tuberculosis, sputum smear, blood sugar levels, DM, and treatment outcome with Directly Observed Treatment Short course (DOTS) therapy. The searched articles were scrutinised for their contents and whether they matched the study's objectives. All observations are mentioned in Table 1. More than 100 articles were shortlisted but only 9 articles were recruited for detailed study.

Results

The results of the review showed that researchers were reporting higher deaths among TB patients who had co-morbidity. Subsequently, higher relapses and drug resistance to TB were reported among patients with DM as compared to patients without DM. Many factors were detected that are associated with the prevalence of DM in TB patients such as higher age, body mass index, tobacco smoking, and presence of other non-communicable diseases.

Table I.Prevalence of Diabetes Mellitus and Its Effect on Tre	eatment Outcomes among Tuberculosis Patients
---	--

S. No.	Name of Author	Year	Study Population	Result
1.	Oursler et al. ⁷	1994–1996	Adult TB patients	The strongest predictors of death in TB patients were DM, renal failure, chronic obstructive pulmonary disease, and HIV.
2.	Stevenson et al. ⁸	2000	Pulmonary TB patients	DM prevalence in urban areas is associated with 15.2% greater smear-positive TB incidence in urban and rural areas.
3.	Wang et al. ⁹	2003–2006	Culture-proven pulmonary TB patients	34% of culture-positive TB patients were associated with DM with a 12.2% mortality rate as compared to a non-diabetic mortality rate of 4.2%.
4.	Jeon and Murray ¹⁰	2008	TB patients	DM is associated with an increased risk of TB regardless of study design and population.
5.	Baker et al. ¹¹	2011	TB patients	DM is associated with an increased risk of failure and death during TB treatment.
6.	Viswanathan and Gawde ¹²	2011–2012	TB patients	Duration of sputum concersion was higher in DMTB as compared to non-DM and 14.7% vs 3.5% remained positive after the intensive phase of TB treatment.
7.	Viswanathan et al. ¹³	2012	TB patients	The frequency of DM in TB patients is more prevalent than expected for about 24% of DM patients who are associated with TB.
8.	Raghuraman et al. ¹⁴	2014	TB patients	29% prevalence of DM was observed in TB patients.
9.	Mave et al. ¹⁵	2021	TB patients with DM and without DM	The outcome was 20% for TB-DM as compared with 21% for TB-only participants, however, mortality was a little higher with DM (10% vs 7%), and early mortality was substantially higher among patients with DM.

Discussion

About 95% of TB patients and 70% of DM patients live in low and middle-income countries.^{16–19} DM affects the innate and adaptive immune responses necessary to control TB infection. While reduced ability to clear infection could conceivably lead to TB-related deaths among people with DM specifically. It is also possible that these patients face a greater likelihood of death during TB therapy because of DM-associated complications, such as heart disease, stroke, and renal failure.^{20–23}

The prevalence of DM in patients with TB varies from 5% to 66% in India. This variation is due to varied geographical and population characteristics. The incidence of DM is higher in South India due to the intake of food with a high glycaemic index. Most of the Indians who have higher body mass index have higher visceral fat or adipose tissues, decreased pancreatic beta-cell mass, reduced insulin secretion, and poor glycaemic control.²⁴ A study carried out by Raaja et al. determined that the prevalence of DM in TB patients was significantly associated with marital status and higher BMI (obesity and overweight).²⁵

We have observed that there is high mortality among TB patients who have diabetes. Similarly, Gautam et al. reported in their systematic review that TB patients with diabetes had an approximately two-fold higher risk of mortality as compared with non-diabetic TB patients.²⁶ A large proportion of people with DM as well as TB are not diagnosed or diagnosed too late. Early detection can help to improve care and control of both. It has been seen that these patients have delayed sputum conversions and high rates of recurrences and failures.²

Ten percent of TB cases are globally linked to DM and hence all people with TB should be screened for DM.²⁷

Early treatment would be beneficial as composite TB treatment outcomes are not increased significantly however, delay is linked with increased mortality and drug resistance to TB. The same findings are observed in a systematic review by Baker et al. that stated patients with DM receiving TB therapy were at risk for poor outcomes.¹¹

Conclusion

There is a paucity of research at the national level in India that elucidates the association of DM with sputum conversion and treatment outcomes of TB. However, from the available literature, it is seen that DM does not significantly increase the risk of adverse TB treatment outcomes but increases mortality and multidrug resistance TB. Early detection of TB among diabetes patients and screening of DM among TB patients would be beneficial strategies for stopping TB in India.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: None

Source of Funding: None

Conflict of Interest: None

References

- Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med. 2008;5(7):e152. [PubMed] [Google Scholar]
- Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Lönnroth K, Ottmani SE, Goonesekera SD, Murray MB. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. BMC Med. 2011;9:81. [PubMed] [Google Scholar]
- Liu Q, Li W, Xue M, Chen Y, Du X, Wang C, Han L, Tang Y, Feng Y, Tao C, He JQ. Diabetes mellitus and the risk of multidrug resistant tuberculosis: a meta-analysis. Sci Rep. 2017;7(1):1090. [PubMed] [Google Scholar]
- 4. Kumar V, Abbas AK, Fausto N, Mitchell R. Robbins basic pathology. 8th ed. Saunders Elsevier; 2007. p. 516-22.
- 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(4):574-9. [PubMed] [Google Scholar]
- United Nations General Assembly [Internet]. Resolution 73/3: Political declaration of the high-level meeting of the General Assembly on the fight against tuberculosis. New York: United Nations; 2018 [cited 2023 Oct 10]. Available from: https://www.un.org/en/ga/search/ view_doc.asp?symbol=A/RES/73/3
- Oursler KK, Moore RD, Bishai WR, Harrington SM, Pope DS, Chaisson RE. Survival of patients with pulmonary tuberculosis: clinical and molecular epidemiologic factors. Clin Infect Dis. 2002;34(6):752-9. [PubMed] [Google Scholar]
- Stevenson CR, Forouhi NG, Roglic G, Williams BG, Lauer JA, Dye C, Unwin N. Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence. BMC Public Health. 2007;7:234. [PubMed] [Google Scholar]
- Wang CS, Yang CJ, Chen HC, Chuang SH, Chong IW, Hwang JJ, Huang MS. Impact of type 2 diabetes on manifestations and treatment outcome of pulmonary tuberculosis. Epidemiol Infect. 2009;137(2):203-10. [PubMed] [Google Scholar]
- Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med. 2008;5(7):e152. [PubMed] [Google Scholar]
- 11. Baker MA, Harries AD, Jeon CY, Hart JE, Kapur

21

A, Lönnroth K, Ottmani SE, Goonesekera SD, Murray MB. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. BMC Med. 2011;9:81. [PubMed] [Google Scholar]

- 12. Viswanathan AA, Gawde NC. Effect of type II diabetes mellitus on treatment outcomes of tuberculosis. Lung India. 2014;31(3):244. [PubMed] [Google Scholar]
- Viswanathan V, Vigneswari A, Selvan K, Satyavani K, Rajeshwari R, Kapur A. Effect of diabetes on treatment outcome of smear-positive pulmonary tuberculosis – a report from South India. J Diabetes Complications. 2014 Mar-Apr;28(2):162-5. [PubMed] [Google Scholar]
- Alavi SM, Khoshkhoy MM. Pulmonary tuberculosis and diabetes mellitus: co-existence of both diseases in patients admitted in a teaching hospital in the southwest of Iran. Caspian J Intern Med. 2012;3(2):421-4. [PubMed] [Google Scholar]
- Raghuraman S, Vasudevan KP, Govindrajan S, Chinnakali P, Panigrahi KC. Prevalence of diabetes mellitus among tuberculosis patients in urban Puducherry. N Am J Med Sci. 2014;6(1):30-4. [PubMed] [Google Scholar]
- Mave V, Gaikwad S, Barthwal M, Chandanwale A, Lokhande R, Kadam D, Dharmshale S, Bhardwaj R, Kagal A, Pradhan N, Deshmukh S, Atre S, Sahasrabudhe T, Meshram S, Kakrani A, Kulkarni V, Raskar S, Suryavanshi N, Kornfeld H, Dooley KE, Chon S, Gupte A, Gupta A, Gupte N, Golub JE. Diabetes mellitus and tuberculosis treatment outcomes in Pune, India. Open Forum Infect Dis. 2021;8(4):ofab097. [PubMed] [Google Scholar]
- World Health Organization [Internet]. Global Tuberculosis Report 2020; [cited 2020 Oct 20]. Available from: http://www.who.int/tb/publications/ global_report/en/
- Djoussé L, Driver JA, Gaziano JM, Buring JE, Lee IM. Association between modifiable lifestyle factors and residual lifetime risk of diabetes. Nutr Metab Cardiovasc Dis. 2013;23(1):17-22. [PubMed] [Google Scholar]
- 19. International Diabetes Federation [Internet]. Diabetes Atlas. 10th ed; 2020 [cited 2023 Oct 23]. Available from: https://www.diabetesatlas.org/data/en/country/93/ in.html
- Cho NH, Shaw JE, Karuranga S, Huang Y, Fernandes JD, Ohlrogge AW, Malanda B. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271-81. [PubMed] [Google Scholar]
- 21. Sen T, Joshi SR, Udwadia ZF. Tuberculosis and diabetes mellitus: merging epidemics. J Assoc Physicians India. 2009;57:399-404. [PubMed] [Google Scholar]
- Martens GW, Arikan MC, Lee J, Ren F, Greiner D, Kornfeld H. Tuberculosis susceptibility of diabetic mice. Am J Respir Cell Mol Biol. 2007;37(5):518. [PubMed] [Google Scholar]

- Chang FY, Shaio MF. Decreased cell-mediated immunity in patients with non-insulin-dependent diabetes mellitus. Diabetes Res Clin Pract.1995;28(2):137. [PubMed] [Google Scholar]
- 24. Rhee EJ. Diabetes in Asians. Endocrinol Metab (Seoul). 2015;30(3):263-9. [PubMed] [Google Scholar]
- 25. Rajaa S, Krishnamoorthy Y, Knudsen S, Roy G, Ellner J, Horsburgh CR, Hochberg NS, Salgame P, Govindrajan S, Babu SP, Sarkar S. Prevalence and factors associated with diabetes mellitus among tuberculosis patients in South India—a cross-sectional analytical study. BMJ Open. 2021;11(10):e050542. [PubMed] [Google Scholar]
- 26. Gautam S, Shrestha N, Mahato S, Nguyen TP, Mishra SR, Berg-Beckhoff G. Diabetes among tuberculosis patients and its impact on tuberculosis treatment in South Asia: a systematic review and meta-analysis. Sci Rep. 2021 Jan 22;11(1):2113. [PubMed] [Google Scholar]
- 27. Rayfield EJ, Ault MJ, Keusch GT, Brothers MJ, Nechemias C, Smith H. Infection and diabetes: the case for glucose control. Am J Med. 1982;72(3):439. [PubMed] [Google Scholar]