



Type 2 Diabetes Mellitus and The Risk of Tuberculosis

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is a major comorbidity that increases the risk of tuberculosis (TB) through immune system impairment caused by chronic hyperglycemia, including macrophage dysfunction, reduced T-cell activity, oxidative stress, and cytokine imbalance. This literature review aims to analyze the relationship between T2DM and TB from the perspectives of pathophysiology, clinical impact, and healthcare system challenges. The method used is a descriptive narrative based on 10 scientific articles and case reports published between 2020 and 2025, selected through systematic searching. The results show that T2DM contributes to an increased risk of active TB, prolonged treatment duration, lower treatment success rates, and a higher risk of drug resistance. Behavioral factors such as poor glycemic control, smoking habits, and limited access to healthcare further

worsen the condition of patients with this comorbidity. On the other hand, bidirectional TB-DM screening efforts in Indonesia have not been optimal due to limitations in training, infrastructure, and inter-program coordination. In conclusion, T2DM increases susceptibility to TB and worsens its progression, highlighting the need for integrated healthcare services, strict blood glucose control, and systemic policy interventions to reduce the morbidity and mortality associated with this comorbidity.

Keywords: Type 2 Diabetes Mellitus, Risk, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is an infectious disease that remains a major challenge in global health, particularly in developing countries. According to data from the World Health Organization (WHO), Indonesia has one of the highest numbers of TB cases in the world. Tuberculosis is an infection of the lung tissue caused by *Mycobacterium tuberculosis*.¹

An estimated 10.8 million people (95% UI: 10.1–11.7 million) fell ill with tuberculosis (TB) worldwide in 2023, an increase from 10.7 million in 2022 (95% UI: 10.0–11.5 million), 10.4 million (95% UI: 9.7–11.1 million) in 2021, and 10.1 million (95% UI: 9.5–10.7 million) in 2020. This figure marks a continuation of the reversal of a long-term downward trend until 2020. In 2023, eight countries accounted for more than two-thirds of the total global tuberculosis (TB) cases: India (26%), Indonesia (10%), China (6.8%), the Philippines (6.8%), Pakistan (6.3%), Nigeria (4.6%), Bangladesh (3.5%), and the Democratic Republic of Congo (3.1%).²

The prevalence of TB varies across different geographical regions in Indonesia and can be influenced by the diagnostic approaches used. The prevalence of pulmonary TB in Indonesia with bacteriological confirmation is 759.0 per 100,000 population aged 15 and over, with a higher prevalence in urban areas, and the Sumatra region having the highest prevalence.³

Tuberculosis (TB) and diabetes mellitus (DM) are two global diseases with a large burden that exacerbate each other. Diabetes not only increases the risk of active TB but also adversely affects its treatment outcomes. According to the WHO (2021), diabetes is associated with a two to three-fold increased risk of active TB, a two-fold risk of death during therapy, a four-fold risk of TB recurrence after treatment completion, and a two-fold risk of developing drug-resistant TB (MDR-TB). The WHO also reported that in 2019, about 15% of TB patients worldwide also had diabetes, compared to 9.3% in the general adult population (20-79 years). This combination creates a double burden on the health system and requires comprehensive management. It is estimated that there are about 1.5 million people with TB and DM who need coordinated care and follow-up to optimize the

management of both diseases.⁴

Chronic hyperglycemia in diabetes mellitus increases the risk and severity of tuberculosis through macrophage immune impairment, including decreased phagocytosis due to dysfunction of receptors like CD11b, MARCO, and CD206, as well as an imbalanced cytokine response: increased IL-1 β and decreased IFN- γ and iNOS—all crucial for tuberculosis defense. Furthermore, hyperglycemia causes oxidative stress, the formation of advanced glycation end products (AGEs), and activation of the protein kinase C pathway as well as increased RAGE expression, which inhibits phagosome-lysosome fusion and weakens the elimination of *Mycobacterium tuberculosis*.^{5,6}

With this systematic literature review method, it is hoped that the research can provide a scientific contribution in the form of a comprehensive and up-to-date mapping of information on Type 2 Diabetes Mellitus and the risk of Tuberculosis, which can serve as a reference in clinical practice, further research, and health policy development.

METHODS

This research methodology, using a Literature Review with a Narrative Review design, involves examining the findings of the author's literature review related to the topic to be discussed. This review refers to various relevant scientific sources from publications in Indonesia within the last five years, from 2020 to 2025. The method used is descriptive qualitative, where the researcher explores, collects, and analyzes a number of journals and scientific articles that discuss the topic of T2DM and Tuberculosis in depth. Data sources were collected through systematic searches on several national and international journal databases, such as Google Scholar, NCBI, and ScienceDirect. In the search process, specific keywords such as "Type 2 Diabetes Mellitus", "Tuberculosis", "Risk", and "Risk Factor" were used to facilitate the identification of relevant articles. The credibility of each selected article was evaluated based on the quality of the journal in which the article was published, its SINTA accreditation, and the clarity and consistency of its scientific writing. In addition, the author performed a cross-validation process on the content of the

articles to ensure data consistency between sources, so that the information used in this review has high reliability.

RESULTS

Table 1. Literature Search Results

No.	Researcher	Research Title	Research Method	Results
1	Baez, Axhell A. (2021) ⁷	Association Between Diabetes Mellitus-Tuberculosis and the Generation of Drug Resistance	Review study	This journal found that Type 2 Diabetes Mellitus (T2DM) increases the risk of active tuberculosis (TB) up to threefold because chronic hyperglycemia causes immune dysfunction, particularly in macrophages, thereby facilitating <i>Mycobacterium tuberculosis</i> infection. Additionally, T2DM contributes to worsening TB treatment outcomes and increases the likelihood of drug resistance due to mechanisms such as the activation of efflux pumps

No.	Researcher	Research Title	Research Method	Results
				that reduce the effectiveness of anti-TB drugs. Therefore, optimal blood glucose control and an integrated therapeutic approach are crucial to improve TB treatment response in patients with T2DM.
2	Ssekamatte P, et al. (2023) ⁶	Immunologic, metabolic and genetic impact of diabetes on tuberculosis susceptibility	Matched Case-Control Study	This study shows that patients with T2DM have a higher risk of developing pulmonary tuberculosis, especially in patients with poor glycemic control. Other factors that contribute to increasing the risk of TB in T2DM patients are smoking habits, low frequency of diabetes check-ups, and a history of contact with TB

No.	Researcher	Research Title	Research Method	Results
				sufferers. Conversely, a higher body mass index (≥ 24) and higher education level are associated with a reduced risk of TB. These findings confirm the importance of good diabetes management and public health interventions to reduce the risk of TB in T2DM patients.
3	Obels, Ilja, et al. (2022) ⁸	Tuberculosis risk among people with diabetes mellitus in Sub-Saharan Africa: A systematic review	Systematic review and meta-analysis	This study identified nine studies that met the inclusion criteria, with a total of 110,905 participants from five countries. The results of this study's analysis show that individuals with DM have an odds ratio (OR) of 2.77 (95% CI: 1.90–4.05) for developing active TB,

No.	Researcher	Research Title	Research Method	Results
				indicating a strong association between DM and TB in the region.
4	Thong, P. M., et al. (2025) ⁹	Immune dysregulation of diabetes in tuberculosis	Narrative Review	This study shows that Type 2 Diabetes Mellitus significantly increases a person's risk of developing tuberculosis (TB). The main mechanism underlying this relationship is immune system impairment due to chronic hyperglycemia in DM patients. Hyperglycemia causes dysfunction of macrophages and T-cells, which play a crucial role in the body's defense against <i>Mycobacterium tuberculosis</i> . Furthermore, chronic inflammation and oxidative stress that occur

No.	Researcher	Research Title	Research Method	Results
				in DM weaken the immune response, allowing TB bacteria to multiply more easily and activate latent infection into active TB. This study emphasizes the importance of integrated management between blood sugar control and TB screening in DM patients to reduce morbidity and mortality due to this comorbidity.
5	Barry, S. E., Sawka, A., et al. (2025) ¹⁰	Macrophage Dysfunction in Tuberculosis–Diabetes Mellitus Comorbidity: A Scoping Review of Immune Dysregulation and Disease Progression	Systematic review with a thematic synthesis approach on relevant studies	This study shows that in patients with diabetes mellitus (DM), macrophage dysfunction is the main mechanism for the increased risk of tuberculosis (TB). This dysfunction includes a reduced ability of

No.	Researcher	Research Title	Research Method	Results
				macrophages to recognize and engulf <i>Mycobacterium tuberculosis</i> bacteria, an imbalance in macrophage phenotypes between pro-inflammatory (M1) and anti-inflammatory (M2), and impaired production of bacteria-killing molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS). Additionally, the antigen presentation ability of macrophages decreases, thereby inhibiting the activation of the adaptive immune response, while an increase in immunosuppressive mediators such as IL-10 and VEGF also weakens the body's immune defense. This condition creates a

No.	Researcher	Research Title	Research Method	Results
				chronic inflammatory environment that is ineffective in controlling TB infection, making patients with DM more susceptible to the development of tuberculosis. These findings confirm the importance of developing therapies that target the improvement of macrophage function as a strategy to prevent and treat TB in people with diabetes.
6	Nuraisyah, Fatma, et al. (2024) ¹¹	Risk Factors of Pulmonary Tuberculosis in Type 2 Diabetes Mellitus in Yogyakarta	Case-control study	This study shows that the risk factors of age and gender have a relationship with the incidence of TB in patients with T2DM based on multivariate analysis

No.	Researcher	Research Title	Research Method	Results
				with a p-value < 0.050, and gender was identified as the risk factor with the greatest influence on the incidence of TB in patients with T2DM. Meanwhile, the risk factors of BMI status and clinical symptoms on the incidence of TB in T2DM patients have a p-value > 0.050, so there is no significant relationship.
7	Batubara, F. A., & Alamsyah Lukito. (2024) ¹²	The Relationship Between Type II Diabetes Mellitus and the Increased Risk of Pulmonary Tuberculosis Incidents at Haji General Hospital Medan in 2022	Observational analytic with a cross-sectional approach	This study concludes that T2DM is a significant risk factor for the increased incidence of pulmonary TB. Therefore, it is important for health facilities to conduct TB screening on patients with T2DM for early detection

No.	Researcher	Research Title	Research Method	Results
				and more effective management. This preventive measure is expected to reduce the incidence of pulmonary TB in the population with T2DM.
8	Aditya Nugraha, I. B., Gotera, W., & Yustin, W. E. F. (2021) ¹³	Diabetes Mellitus as a Risk Factor for Tuberculosis	Narrative descriptive	This study discusses the relationship between diabetes mellitus (DM) and the increased risk of tuberculosis (TB). DM, especially type 2, can cause immune system disorders, thereby increasing susceptibility to infections, including TB. The decreased function of macrophages, immune cells that play an important role in the body's defense, is one of the mechanisms

No.	Researcher	Research Title	Research Method	Results
				explaining this relationship. In addition, hyperglycemia in DM can inhibit the immune response to TB infection, prolong the time for AFB sputum conversion, and increase the risk of developing drug-resistant tuberculosis (MDR-TB).
9	Ulfahimayati, Irvan Medison, Dessy Mizarti. (2020) ¹⁴	Type 2 Diabetes Mellitus as a Predisposing and Comorbid Factor for Primary Multi-Drug Resistant Tuberculosis	Case Report	This case report discusses a 58-year-old male patient with uncontrolled type 2 diabetes mellitus for 12 years who was diagnosed with primary multi-drug resistant tuberculosis (MDR-TB). The examination results showed resistance to rifampicin and radiological findings of infiltrates and cavities in

No.	Researcher	Research Title	Research Method	Results
				the lung apex. This study confirms that type 2 diabetes is a predisposing and comorbid factor that worsens the course of tuberculosis, making it important to conduct TB screening in diabetes patients and maintain strict blood sugar control during MDR-TB therapy.
10	Djody AF, Musdalifah M. (2024) ¹⁵	Bacteriologically Confirmed Pulmonary Tuberculosis with Extensive Lesions in a Patient with Type 2 Diabetes Mellitus: A Case Report	Case Report	This case report describes a patient with uncontrolled type 2 diabetes mellitus who developed pulmonary tuberculosis with extensive lesions. The patient complained of a productive cough for three months accompanied by fever, night sweats, and weight loss. Sputum examination

No.	Researcher	Research Title	Research Method	Results
				was positive for acid-fast bacilli and a chest X-ray showed infiltrates in the upper right lung. The uncontrolled diabetic condition is believed to have weakened the immune system, thereby increasing the risk of tuberculosis infection and aggravating the course of the disease. Management was carried out with standard anti-tuberculosis therapy and strict diabetes management. The author emphasizes the importance of tuberculosis screening in diabetic patients and blood sugar control to prevent complications and accelerate recovery.

DISCUSSION

The review of ten journals and case reports reveals a consistent pattern of findings regarding the significant association between type 2 diabetes mellitus (T2DM) and an increased risk of tuberculosis (TB). This relationship is multifactorial, involving immunological, metabolic, and genetic aspects, as well as social and behavioral factors.

Several studies, such as those by Baez (2021), Thong et al. (2025), and Barry et al. (2025), explicitly state that chronic hyperglycemia in T2DM patients leads to immune system dysfunction, particularly of macrophages and T-cells. This results in a decreased ability of the body to eliminate *Mycobacterium tuberculosis*. Barry et al. further explain that macrophages in individuals with DM experience impaired recognition and engulfment of bacteria, imbalanced production of ROS and RNS, and reduced antigen presentation capacity, all of which contribute to the immune system's inability to eradicate TB infection.

Additional support comes from epidemiological research by Ssekamatte et al. (2023) and Obels et al. (2022), which show an increased odds ratio (OR) for active TB in DM patients. In Sub-Saharan Africa, individuals with DM have an OR of 2.77 for developing active TB, indicating a strong and undeniable association. Additional factors such as smoking, poor glycemic control, and infrequent health check-ups exacerbate the risk, as mentioned by Ssekamatte et al.

Case reports by Ulfahimayati et al. (2020) and Djody & Musdalifah (2024) provide concrete clinical illustrations of the impact of T2DM on the course of TB, including an increased risk of drug-resistant TB (MDR-TB) and extensive lung lesions. This reinforces the findings of Baez (2021) and Nugraha et al. (2021), which link DM to reduced TB treatment effectiveness due to metabolic disturbances and the activation of efflux pumps affecting drug pharmacodynamics.

Several local studies by Nuraisyah et al. (2024) and Batubara & Lukito (2024) also emphasize the importance of TB screening in DM patients, especially at the primary healthcare facility level. Demographic factors like age and gender, as well as education level, are also mentioned to influence TB risk.

Overall, the reviewed literature indicates that:

- T2DM significantly increases the risk of active TB, especially in patients with poor glycemic control.
- Immunological mechanisms, particularly macrophage dysfunction and impaired T-cell response, are the primary biological basis for this association.
- Social and behavioral factors like smoking and access to healthcare services worsen this risk.
- TB drug resistance is more likely in DM patients, making case management more complex.
- The importance of an integrated approach, including blood sugar control, routine TB screening, and patient education, is key to reducing morbidity and mortality in the population with comorbid DM and TB.

Immunopathogenesis of Tuberculosis in Patients with Diabetes Mellitus

There is a theory that chronic hyperglycemia from DM causes damage to both innate and adaptive immunity, affecting cytokine responses and alveolar defenses. This condition also impairs neutrophil recruitment, monocyte movement, and the phagocytic action of alveolar macrophages, as well as reducing the antigen-specific release of interferon-gamma by T-helper cells. Impairments in pulmonary microvasculature and micronutrient deficiencies facilitate the invasion and progression of tuberculosis.¹⁶

In several studies, the radiological findings in TB patients with DM have been described as atypical, mostly involving the lower lung lobes with cavitary lesions. Park et al. found that there were differences in chest X-ray findings between DM and non-DM patients, where cavities were more common in DM patients diagnosed with TB.¹⁶

DM increases the risk of tuberculosis by impairing innate and adaptive immune responses. In turn, tuberculosis weakens islet cell function by causing islet amyloidosis, and anti-tuberculosis drugs disrupt blood glucose homeostasis by affecting liver and kidney function in tuberculosis patients, which increases the risk of developing DM in tuberculosis patients.¹⁷

The incidence of lung infections in DM patients is a result of the failure of the body's defense system; in this case, the lungs experience functional impairment of the respiratory epithelium and ciliary motility. Functional impairment of the pulmonary vascular capillary endothelium, rigidity of red blood cell corpuscles, and changes in the oxygen dissociation curve due to prolonged hyperglycemia are factors in the failure of the defense mechanism against infection.¹⁸

The Impact of Diabetes Mellitus on Tuberculosis Therapy

Type 2 Diabetes Mellitus (T2DM) has a significant impact on the effectiveness of tuberculosis (TB) therapy. Recent retrospective studies and meta-analyses show that TB-DM patients experience lower treatment success rates compared to TB patients without diabetes. Xu et al. (2023) reported that patients with Diabetes Mellitus have a greater chance of experiencing treatment failure in cases of drug-resistant tuberculosis (DR-TB), including Multi-Drug Resistant TB (MDR-TB). In addition to increasing the risk of treatment failure, DM also reduces the likelihood of MDR-TB patients achieving a full cure. These findings confirm that the presence of DM as a comorbidity worsens the prognosis of drug-resistant TB and requires special attention in its management.¹⁹

Type 2 Diabetes Mellitus (T2DM) significantly reduces the effectiveness of tuberculosis (TB) therapy through various clinical and pharmacological mechanisms. A meta-analysis by Zhao et al. (2024) involving 6,919 TB-DM patients showed that optimal glycemic control is associated with increased treatment success, accelerated sputum conversion, and reduction of cavitory lung lesions. Research by Khattak et al. (2024) also indicated that TB patients with DM comorbidity require a longer duration of therapy compared to TB patients without DM. This is due to impaired anti-tuberculosis drug metabolism and decreased immune function from chronic hyperglycemia, which can collectively hinder treatment success. These findings were obtained through a meta-analysis of 44 studies and strengthen the evidence that DM is a factor that complicates the clinical management of TB.^{20, 21}

Evidence from South Asia shows that TB-DM patients have a higher risk of treatment

failure and death compared to TB patients without DM. A study by Sri Iswahyuni et al. (2022) found a 1.57-fold increased risk of TB treatment failure in patients with DM comorbidity.²²

Overall, the presence of T2DM not only prolongs the duration and reduces the success of TB therapy but also increases the risk of resistance, relapse, and mortality. Therefore, the integration of strict glycemic management with HbA1c targets, regular sputum monitoring, and drug resistance screening is highly recommended to improve treatment outcomes in tuberculosis patients with diabetes comorbidity.

Implications for the Health System

Type 2 Diabetes Mellitus (T2DM) has been shown to increase the risk of Tuberculosis (TB) infection, thus requiring serious attention within the healthcare system. A study by Obels et al. (2022) indicates that individuals with DM have a much higher risk of developing TB, based on research from several studies in Sub-Saharan Africa. Furthermore, research by Menon et al. (2020) confirms a causal link between T2DM and an increased risk of pulmonary TB (PTB), which demands a coordinated global health response to tackle both epidemics simultaneously.⁸

The comorbidity between T2DM and TB requires the health system to undergo a significant transformation towards integrated services. The WHO and the Asia Pacific Observatory (2022) affirm that the need for bidirectional screening and integrated consultations is crucial for improving early detection and comprehensive management of TB-DM patients, but implementation at the field level is still limited. On the other hand, studies in India show that primary-level health workers are not fully prepared to handle this comorbidity due to a lack of training, clear operational guidelines, and supporting facilities. This has resulted in suboptimal screening for TB in DM patients and vice versa. A pilot study in rural India supports the effectiveness of training non-facility-based health workers in managing TB-DM. Although the training did not show significant improvement in glycemic parameters, it successfully increased awareness and cross-program collaboration. Additionally, an evaluation of a cluster-based training model in Tanzania proved that strengthening human resource capacity through direct training and the use of bidirectional screening algorithms

can improve clinical application in primary care facilities.^{23,24}

Furthermore, policy and financial support are crucial. A study in Asia noted that managing TB-DM comorbidity requires additional logistics and infrastructure such as glucometers, HbA1c testing, and strengthening inter-program referral systems, which demand specific budget support.

The implementation of the TB-DM bidirectional screening program in Indonesia has been underway since the issuance of national guidelines in 2017, realized through service integration in health centers (Puskesmas) and hospitals. Based on a study in Jakarta (2017–2019), 50.8% of TB patients aged >15 years had undergone a blood glucose test, increasing from 41.7% in 2017–2018 to 60.1% in 2019, with 20.8% of them diagnosed with DM. Over 90% of TB–DM patients received standard treatment, with 86.3% of them successfully cured or completing treatment.²⁵

The implementation of TB-DM co-management in Indonesia has shown progress but still faces various challenges in the primary health system. A cross-sectional study in Jakarta (2017–2019) showed an increase in DM screening coverage among TB patients from 41.7% to 60.1%, and that DM treatment was significantly associated with improved TB treatment success. However, an evaluation in Yogyakarta revealed low collaboration in bidirectional screening services, reaching only 16.5% despite existing national guidelines for integration, due to system fragmentation, lack of human resource capacity, and regulatory and financing issues at the primary level, such as in Puskesmas.^{26,27}

Meanwhile, the DIY Health Office (2023) promoted the use of chest X-rays to supplement symptoms in DM-TB screening, but its implementation is still hampered by the need for training and supporting infrastructure in private and local government facilities.²⁸

Thus, although the implementation of bidirectional TB-DM screening in Indonesia has started and shown positive results, various challenges related to human resource capacity, infrastructure, and policy and funding support still need to be seriously addressed for this integrated service to run optimally and provide maximum benefit for the control of both diseases.

CONCLUSION

Type 2 Diabetes Mellitus (T2DM) significantly increases the risk of active tuberculosis (TB) through multifactorial mechanisms, primarily immune system dysfunction such as impaired macrophage and T-cell function due to chronic hyperglycemia. This condition weakens the body's ability to fight *Mycobacterium tuberculosis* infection and worsens the prognosis of TB, including an increased risk of drug resistance and treatment failure. Epidemiological studies show an increased odds ratio for TB in DM patients, while poor glycemic control correlates with suboptimal treatment outcomes and longer treatment duration. The clinical and health system implications demand the integration of screening services and integrated TB-DM management, but implementation at the primary level still faces constraints such as limited human resources, training, and infrastructure. Therefore, enhancing human resource capacity, policy support, and funding are crucial to optimizing the management of comorbid TB and DM, thereby reducing morbidity and mortality in this vulnerable population.

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