

Association between tuberculosis, HIV infection, and diabetes mellitus: should we integrate screening and care? A systematic review

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Abstract

Tuberculosis (TB) and HIV/AIDS are among the leading infectious diseases worldwide, while diabetes mellitus (DM) is a major chronic endocrine and metabolic disorder. Together, these conditions contribute substantially to the global burden of disease and mortality and are increasingly recognized as interconnected comorbidities. The combination of these three diseases can worsen patients' health conditions, increase mortality risk, and complicate treatment, which is why this study aims to summarize the relationship between HIV, TB, and DM. To achieve this, a systematic literature search was conducted across four databases PubMed, Wiley, ScienceDirect, and Scopus focusing on English articles from the last 5 years, where researchers independently established eligibility criteria, conducted a comprehensive search, meticulously extracted data, and determined the risk of bias. The findings indicate a significant relationship between these conditions, as the six articles analyzed showed that the prevalence of DM in TB patients ranged from 7.6% to 22.6%, while the prevalence of HIV in TB patients reached up to 38.57%. Specifically, DM increases the risk of developing active TB and is associated with unfavorable treatment outcomes, whereas HIV progressively impairs cell-mediated immunity through CD4+ T-cell depletion, substantially increasing the risk of progression from latent TB infection to active disease. Ultimately, there is a complex relationship between HIV, TB, and DM that adversely affects patients' overall health, leading to the conclusion that integrated screening and management for these three diseases are essential to reduce mortality risk and improve treatment outcomes.

Keywords: Tuberculosis. HIV/AIDS. Diabetes mellitus. Comorbidity.

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Introduction

Tuberculosis (TB) and HIV/AIDS are among the leading infectious diseases worldwide,^{1,2} while diabetes mellitus (DM) is a major chronic endocrine and metabolic disorder.³ Together, these conditions contribute substantially to the global burden of disease and mortality and are increasingly recognized as interconnected comorbidities.⁴ TB and HIV/AIDS remain leading infectious diseases causing the highest mortality globally.⁵ According to the World Health Organization (WHO) data for 2022, approximately 10.6 million people fell ill due to TB, with 1.3 million deaths, including 167,000 individuals living with HIV.⁶

TB is the primary cause of death among people living with HIV, accounting for one-third of AIDS-related deaths worldwide.⁷ This is closely related to the immune system decline in HIV-infected individuals with TB.⁸ The compromised immune system makes it more difficult for HIV patients to fight infections, including TB. Consequently, they are at a higher risk of developing multidrug-resistant TB, a type of TB that is difficult to treat due to resistance to multiple drugs.⁹

Moreover, when the immune system weakens, latent TB can become active TB with a risk increase of up to 30 times.^{10,11} TB slows down the recovery of CD4+ T lymphocytes in individuals with HIV, enhances viral replication, and accelerates the progression of AIDS and mortality by 6-8 times.¹² The co-occurrence of HIV and TB presents a detrimental combination that worsens overall health, complicates treatment, and increases mortality risk.⁹

The incidence of TB is highest among patients with compromised immunity, such as those with HIV and DM, due to immunosuppression that hinders the body's ability to combat *Mycobacterium tuberculosis*.^{13,14} Abbas et al. noted that uncontrolled DM can damage various organs, including the immune system, making individuals more susceptible to infections, including TB.¹⁵ Conversely, research by Bisht et al. stated that the presence of TB makes individuals more likely to develop DM due to metabolic immune changes that can lead to insulin resistance.¹⁶

Several studies have also discussed the relationship between HIV and DM, indicating that individuals with DM are more susceptible to HIV infection compared to those without DM, due to a weakened immune system that cannot effectively combat the virus.^{17,18} Conversely, some studies suggest that HIV increases the risk of developing DM. This is linked to HIV treatments like antiretroviral therapy (ART), which can lead to weight

gain and affect glucose metabolism, increasing the risk of DM.¹⁹⁻²²

In addition to exploring the relationship between two diseases, several studies have examined the connections among all three diseases. Indicated that HIV occurs first, making the individual vulnerable to TB, and that HIV treatment can lead to insulin resistance, becoming a major risk factor for diabetes.²³ However, there is currently no review summarizing the relationships among HIV, TB, and DM to determine which disease occurs first and leads to the emergence of the others. Therefore, the researchers aim to summarize the connections between HIV, TB, and DM.

Methods

Research design

The methods in this study were conducted according to the PRISMA 2020 guidelines, an internationally recognized standard for systematic reviews and meta-analyses.²⁴

PECO and eligibility criteria

The PECO (Supplementary Table 1) presented in this study identifies key criteria in researching the relationship between TB, DM, and HIV. For the study design, included articles consist of cross-sectional and cohort studies, where cross-sectional studies provide prevalence data at a single point in time, while cohort studies offer longitudinal information related to disease progression. Regarding participants, only patients with comorbidities of HIV, TB, and DM are included, while patients with only one disease are excluded. In terms of exposure, this research considers the importance of having a positive diagnosis for HIV, TB, and DM, as well as co-infection among the three diseases. As a comparison, patients with co-infection will be compared to patients without any of the three diseases.

Selected outcomes must include articles that directly discuss these relationships, while irrelevant articles will be excluded from the analysis. Finally, only articles written in English will be included to maintain consistency and understanding in the research (Table 1).

The researcher assesses the eligibility of articles for inclusion using the Critical Appraisal Skills Programme³¹ and tools from the Centre for Evidence-Based Medicine.³²

Search and information sources

The databases used in this study include ScienceDirect, Wiley, PubMed, and Scopus, searched for publications

since 2019. The search terms focused on the three diseases: DM, HIV/AIDS, and TB. The initial search terms for the outcome variables were selected by one researcher (AIL), who reviewed previous systematic reviews that only summarized the relationships between two diseases.

Study selection

The study selection process involved directly searching various databases to identify relevant research. One researcher (AIL) was responsible for removing duplicate data. The remaining articles were then shared with two other researchers (MS and OFHP). These two researchers independently evaluated the titles and abstracts of each article based on the eligibility criteria (initial screening phase). Subsequently, they also independently reviewed the full text of the articles that passed the initial screening. Any disagreements were discussed until a consensus was reached among all authors. Reasons for excluding studies were recorded during the full-text review phase.

Data collection process and data items

Data were collected and extracted independently from the articles that met the criteria by six researchers (AIL, MS, OFHP, NHT, KS, PM). AIL integrated and formatted information regarding the year of publication, study design, country of origin, number of data and patients/participants, as well as exposure variables related to HIV, TB, and DM.

Risk of bias

To assess the quality of the included studies, the researchers used the Cochrane Risk of Bias Tool, as recommended by the Cochrane Handbook for Systematic Reviews. This tool includes six elements: random allocation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other potential sources of bias. Each element was rated with three categories: “yes (+),” “no (–),” or “unclear (?)” Based on the guidelines from the Cochrane Handbook and previous research, the quality of studies could be divided into three levels. Level A was assigned if the article fully met all six criteria. Level B was designated if one or more criteria were only partially met, indicating a low risk of bias. Conversely, if one or more criteria were not met, the article was categorized as Level C, indicating a high risk of bias.³³ The researchers (AIL, MS, OFHP,

NHT, KS, PM) independently evaluated the level of bias categorized as low, high, or unclear. Any differences in quality assessment among the researchers were resolved through discussion to reach a consensus among all authors.

Results

The literature search was conducted across four databases: ScienceDirect ($n = 339$), Wiley ($n = 199$), PubMed ($n = 14$), and Scopus ($n = 6$). A total of 558 articles were identified from these databases, which were then filtered to include only those from the last 5 years, open access, and published in English journals. After screening the 558 articles, 159 articles remained, and only 6 articles were included in the study as they met the inclusion criteria and aligned with the title of this research. The articles included in this literature review are those that (1) focus on DM, HIV/AIDS, and TB; (2) are written in English; and (3) were published in the last five years, specifically from 2019 to 2024 (Fig. 1).

Based on the 6 articles obtained through systematic searching, two types of research design methods were identified: cross-sectional study and cohort study. The cross-sectional studies were conducted in India ($n = 1$), Cameroon ($n = 1$), Africa ($n = 1$), Ethiopia ($n = 1$), and Tanzania ($n = 1$). The cohort study was conducted in India ($n = 1$). The collected articles were assessed for eligibility using critical assessment/critical appraisal.

Prevalence of cases of DM, HIV, and TB

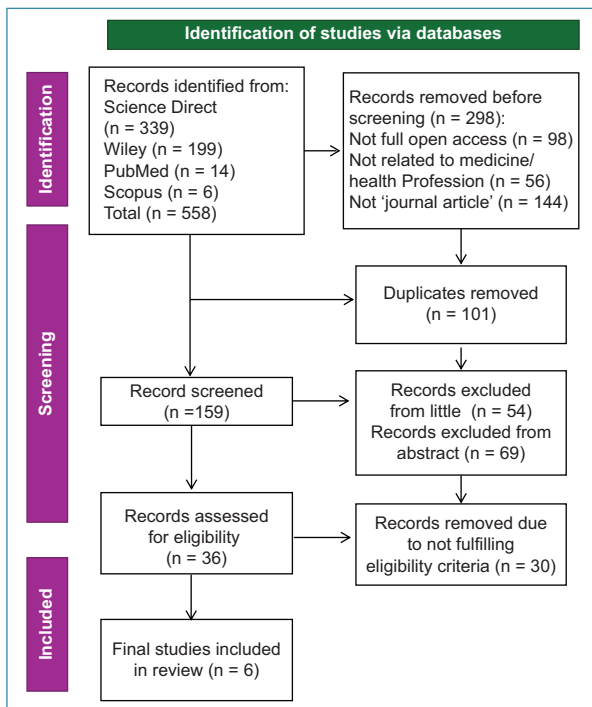
Based on table 1, six analyzed articles, five articles identified TB as the main sample criterion, while one article identified DM as the main sample criterion. The prevalence of comorbid diseases in patients can lead to an increased mortality rate among patients (Table 1).

The research conducted by Jacob et al. in India revealed that out of a total population of 16,527, the majority of patients were elderly, aged over 60 years (28.6%). The average age of TB patients observed was 46.83 ± 24.57 years, with a predominance of males (67.2%). The prevalence of DM among TB patients was found to be 22.6%, likely due to an increase in diabetes cases in India over the years. In contrast, the prevalence of HIV/AIDS among TB patients was only 1.2%, which is considered low, as data show that HIV prevalence in this research area has consistently been low. It was observed that diabetes is significantly associated with pulmonary TB, while HIV/AIDS is significantly associated with extrapulmonary TB.²⁵

Table 1. Prevalence of comorbid cases in TB and DM patients

No	Researcher	Number of samples	Case prevalence (TB comorbid)			Case prevalence (DM comorbid)		
			DM	HIV	DM + HIV	TB	HIV	TB + HIV
1.	Jacob et al. ²⁵	16.527	3.739 (22.6%)	195 (1.2%)	-	-	-	-
2.	Sama et al. ²⁶	1.115	135 (12.11%)	430 (38.57%)	65 (5.83%)	-	-	-
3.	Berkowitz et al. ²⁷	440	-	-	-	13 (3.0%)	48 (11.0%)	8 (1.8%)
4.	Giri et al. ²⁸	47.831	7.6%	1.2%	0.08%	-	-	-
5.	Tulu et al. ²⁹	269	31 (11.5%)	59 (21.9%)	-	-	-	-
6.	Munseri et al. ³⁰	660	64 (9.7%)	212 (32%)	11 (1.6%)	-	-	-

TB: tuberculosis; DM: diabetes mellitus.

**Figure 1.** PRISMA flow diagram study selection.

Research by Sama et al., in Cameroon indicated that among 1,115 TB respondents, the average age was 42.5 ± 15.28 years, with a majority being male. The prevalence of HIV among TB patients was high at 38.57%. The epidemiology of HIV has significantly impacted the epidemiology of TB, potentially due to the research location in the Northwest region, which has the second-highest prevalence of HIV after southern Cameroon.²⁶ The prevalence of DM among TB patients was 12.11%, aligning with estimated DM prevalence of 8.5-16.4% among TB patients in sub-Saharan Africa.^{26,34} The

combined prevalence of TB, HIV, and DM was 5.83%, reflecting the fact that HIV can lower the immune system and cause latent TB to become active.³⁵ In addition, initiation of ART can lead to rapid weight gain correlated with increased insulin resistance, contributing to DM.³⁶

Research by Berkowitz et al., in Africa involved 440 DM patients, with an average age of 54.6 years, 75% of whom were female. The prevalence of active TB among DM patients was 3%, with 54% of TB cases being asymptomatic. The active TB prevalence among DM patients was 4 times higher than the national prevalence, highlighting the need for active TB screening, especially in cases of hemoptysis. The prevalence of HIV among DM patients was 11%, and the prevalence of DM coexisting with TB and HIV was 1.8%. DM patients with TB were ten times more likely to contract HIV compared to those without TB.²⁷

Research by Giri et al., in India showed that out of 47,831 TB cases included in the study, 7.6% had both DM and TB, 1.2% had HIV and TB, while only 0.08% had DM, HIV, and TB. Individuals with TB who did not have DM had significantly better outcomes (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.5-1.8) compared to those with both TB and DM. Similarly, TB cases that were not HIV-infected had significantly better outcomes (OR 2.4, 95% CI 1.9-3.0) compared to those with TB and HIV.²⁸

Research by Tulu et al., in Ethiopia indicated that the prevalence of TB patients with DM was 11.5%, while the prevalence of TB with HIV was higher at 21.9%. This might be due to the high burden of HIV in the study area. In addition, HIV seropositivity was identified as a predictor of DM among TB patients in this study. The high prevalence of DM among TB/HIV cases may be linked to changes in quality of life and side effects of ART among HIV-positive patients. Routine screening and a collaborative framework are recommended to improve early

detection and management of DM and HIV among TB patients.²⁹

Research by Munseri et al., in Tanzania revealed that among 660 TB patients, the majority were male (63%) with an average age of 39.2 ± 14.3 years. Of these, 116 respondents (17.6%) had a family history of DM. The prevalence of TB patients with DM was found to be 9.7%, while the prevalence of TB with HIV was 32%, and TB patients with both DM and HIV was 1.6%. This study found that TB patients aged 44 and above had a fourfold higher risk of DM. Moreover, TB patients with a family history of DM had a threefold higher risk (Supplementary Table 2).³⁰

Is it necessary to integrate screening and treatment?

Overall, the available evidence indicates a consistent epidemiological relationship among TB, HIV infection, and DM, although the strength of the associations varies across populations and study settings (Supplementary Table 2). HIV infection was associated with the largest observed effect, increasing the odds of active TB among patients with diabetes by more than eleven-fold (OR 11.3; 95% CI 3.26-39.42).²⁷ Likewise, HIV/TB coinfection was associated with a five-fold increase in the odds of diabetes comorbidity (adjusted OR 5.11; 95% CI 2.01-12.98).²⁹ Across the included studies, the prevalence of TB-DM ranged from 7.6% to 27.6%, TB-HIV from 1.0% to 38.6%, and triple comorbidity from 0.08% to 5.85%. In addition, DM and HIV infection were consistently associated with poorer TB treatment outcomes compared with TB alone. These findings support integrated screening and collaborative management, particularly in high-burden settings, while emphasizing that implementation should be tailored to local epidemiological contexts.

Routine diabetes screening is recommended for TB patients over 44 years of age and/or those with a family history of diabetes. TB patients who are HIV seronegative are more likely to have DM compared to those who are HIV seropositive. Therefore, integrating diabetes screening into TB care can proactively manage the risks faced by patients and provide more targeted interventions. By conducting regular screenings, we can detect health issues earlier and perform necessary interventions to prevent complications. Further research is also needed to confirm these observations and understand the underlying factors, allowing for care strategies to be tailored more effectively to meet the specific needs of patients. This approach will

not only enhance individual health outcomes but also contribute to better public health management.

Discussion

This research has examined the prevalence of comorbidities in TB patients, specifically focusing on DM and HIV. The reviewed articles indicate that TB patients are likely to have comorbid conditions such as DM and HIV. The estimated burden of coexisting DM and TB primarily arises from studies assessing the prevalence of DM and glucose intolerance among patients diagnosed with TB at TB clinics. However, the community prevalence of these two disorders occurring together remains unclear. Many of these studies were conducted in hospitals where TB patients are treated, which may explain the higher percentage of patients with glucose intolerance and DM.³⁷ In a study involving five randomly selected TB care clinics in the southern state of Tamil Nadu, India, about 25% of TB patients had concurrent DM.³⁸ This aligns with the reviewed articles, which reported prevalence rates ranging from 7.6% to 22.6%, with the highest prevalence observed in studies conducted in India. According to the WHO, approximately 15% of TB cases worldwide are associated with DM, with India contributing over 40% of these cases.³⁹

The incidence of TB-DM appears unlikely to decrease in the near future, as DM weakens the immune system and increases the risk of developing active TB.⁴⁰ In most individuals exposed to the infection, the immune system typically fights it off, encasing the bacteria within granulomas or tubercles, which immunologically prevents the disease from becoming active. This represents a subclinical state known as latent TB infection (LTBI), which is asymptomatic and can persist for weeks or even decades. Latent infection is present in nearly one-third of the global population. Although not contagious, there is a risk (approximately 10%) of reactivation into active TB later (primary progressive TB).⁴¹ Reactivation occurs in individuals with compromised immunity, such as those with HIV infection or DM.⁴² Immunological data suggest that LTBI, in the presence of DM, leads to impaired production of protective cytokines and polyfunctional T cell responses, explaining the potential immunological mechanisms that may increase the risk of active TB. Various immune parameters change in patients infected with LTBI due to DM, affecting both innate immune responses and adaptive immune responses.⁴³

Similarly, TB causes "stress hyperglycemia" and this may make the management of DM more difficult. This

is concerning as poor glycemic control has been associated with poor outcomes in TB treatment.⁴ Metabolic and endocrine changes during TB disease theoretically contribute to stress hyperglycemia. Pro-inflammatory and anti-inflammatory cytokines released during active TB disease stimulate increased production of cortisol, adrenocorticotrophic hormone (ACTH), prolactin, and growth hormone which increase gluconeogenesis and glycolysis in the liver and kidney, increase insulin resistance, and decrease glucose uptake, resulting in increased blood sugar levels. Cytokines may also act on the hypothalamic-pituitary-gonadal axis, resulting in decreased dehydroepiandrosterone (DHEA) and testosterone levels, leading to increased insulin resistance followed by hyperglycemia. Cytokines, nitric oxide, and reactive oxygen species also increase insulin resistance and hyperglycemia.⁴⁴

DM and HIV/AIDS are comorbidities that significantly affect the diagnosis and management of patients with TB. Therefore, there is an urgent need to prevent the coexistence of these conditions through early diagnosis, appropriate management strategies, and the implementation of integrated and comprehensive care. This interaction can be explained by the syndemic theory, which emphasizes that coexisting diseases interact synergistically, thereby increasing disease burden and worsening health outcomes, particularly among vulnerable populations such as TB patients.⁴⁵

From a care-focused perspective, findings from various studies indicate that patients with TB require comprehensive management of comorbidities, particularly DM and HIV, to reduce complications and improve clinical outcomes. Screening and early detection of comorbid conditions in TB patients are essential components of integrated clinical management planning, consistent with the chronic care model, which emphasizes continuous care, coordinated service delivery, and active health system engagement in managing chronic diseases.⁴⁶ Several studies also highlight the importance of diabetes screening among TB patients, particularly in older age groups or individuals with specific risk factors, as part of an effective early detection strategy. In addition, collaborative approaches between TB, diabetes, and HIV services are recommended in accordance with the WHO collaborative framework, which emphasizes cross-program integration to improve screening coverage and ensure continuity of patient care.⁴⁷ Overall, the integration of screening and continuous comorbidity management is key to improving the quality of care for patients with TB.

Beyond integrating screening and treatment services, the implementation of TB-HIV-DM collaborative care

should also consider the epidemiological characteristics of each disease within individual countries and regions. The burden, distribution, and determinants of TB, HIV, and DM vary considerably across different epidemiological settings, indicating that a universal screening strategy may not be equally effective in all populations. Therefore, integrated screening programs should be designed according to local epidemiological profiles, healthcare system capacity, and population-specific risk factors to maximize their effectiveness and cost-efficiency.⁴⁸⁻⁵⁰

The epidemiological interplay among TB, HIV, and DM varies considerably across geographic and socioeconomic settings. In many low- and middle-income countries, including Indonesia, TB remains endemic, HIV continues to contribute substantially to the TB burden, and the rapidly increasing prevalence of DM has created a growing triple burden of disease.^{4,51-53} In contrast, in many high-income countries, TB is relatively uncommon and is concentrated among migrants from TB-endemic regions, whereas HIV epidemics are predominantly concentrated among key populations, particularly men who have sex with men, although epidemiological patterns vary across countries.^{50,54} Meanwhile, DM is highly prevalent in the general population and is largely driven by population ageing, obesity, and unhealthy lifestyles.⁵⁵ These epidemiological differences suggest that while integrated TB-HIV-DM screening may be particularly beneficial in high-TB-burden settings, screening strategies should be adapted to local disease epidemiology, healthcare infrastructure, and population risk profiles. Its integration will improve the quality of service.⁵⁶

Limitations

A notable limitation of this systematic review is the scarcity of primary articles that extensively delve into the intricate, multifactorial interrelationships among TB, HIV, and DM, thus restricting a more profound analysis of their synergistic impact and co-management implications.

Conclusion

The combination of these three diseases worsens the health condition of patients and increases the risk of death. The results of the analysis of the six reviewed articles revealed that patients with HIV are at higher risk of developing TB, while DM can worsen TB infection and increase complications. Therefore, it is important to integrate comprehensive screening and management for patients with one or more of these diseases to

improve overall health outcomes and reduce the burden of disease in vulnerable populations.

Authors' contributions

A. Insani Latif, O.F.H. Pabetting and M. Sari led the study conceptualization, data collection, statistical analysis, and manuscript drafting. P. Mandysova and N. Hijrah-Tiala contributed to data interpretation and critical revision of the manuscript. K. Suzuki, A. Harisa, and M. Abu provided methodological input and contributed to manuscript refinement. All authors approved the final version of the manuscript.

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Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Supplementary data

Supplementary data are available at DOI: 10.24875/AIDSRev.26000010. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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