



# Metformin and tuberculosis: extraordinary stories of ordinary co-prevalent patients

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Tuberculosis (TB) continues to be a major global health issue, causing millions of deaths annually [1]. The increasing prevalence of diabetes mellitus (DM) worldwide complicates the treatment of TB [2,3]. TB patients with diabetes mellitus (TBDM) are at increased risk for treatment failure and mortality [4]. In this context, host-directed therapy has emerged as a potential way to improve TB outcomes, with the common antidiabetic medication metformin being a focal point [5]. A recent study titled “Relationship between metformin use and mortality in tuberculosis patients with diabetes: a nationwide cohort study” explores the impact of metformin on mortality in patients with both TB and DM [6].

Together, TB and DM pose a significant threat to health, with DM significantly affecting TB prognosis [7,8]. Those with TBDM may be at higher risk for death compared to those with TB only [7,8]. Hence, the potential benefits of using metformin as additional therapy for TBDM patients have gained attention.

The aforementioned study [6] was a robust nationwide observational cohort investigation that used three national databases to create The Korean Tuberculosis and Post-Tuberculosis (TB-POST) cohort. Covering the period from 2011 to 2018, the cohort provides a comprehensive overview of TBDM patients undergoing treatment for drug-susceptible TB. The study’s exclusion criteria ensure the inclusion of patients with significant DM status, increasing the accuracy of the results. After propensity score matching, the group using metformin had a lower all-cause mortality rate during TB treatment compared to non-users. This result remained significant even after adjusting for demographic, clinical, and comorbidity factors following propensity score match-

ing. The positive effect of metformin was consistent across different subgroups based on sex.

Metformin, primarily prescribed for DM, appears to have a potential key role in managing TBDM. The study’s findings align with previous research demonstrating the ability of metformin to reduce TB risk in DM patients [9]. Metformin also influences the progression of pulmonary disease in individuals actively being treated for TB. Notably, patients receiving a combination of metformin and antituberculous medication had more favorable treatment outcomes, marked by a higher success rate and a greater proportion of culture conversions within the initial 2 months. These patients also experienced lower relapse rates within a 3-year period compared to those on antituberculous medication only [10]. Mechanistically, the impact of metformin goes beyond glycemic control, including antimycobacterial effects, the promotion of phagosome-lysosome fusion, and down-regulation of matrix metalloproteinases linked to TB-induced tissue damage [5,11].

The observed decrease in all-cause mortality, especially in non-TB-related deaths, suggests a need to reassess the role of metformin in comprehensive TB-DM care. However, the study acknowledges limitations, such as a lack of information on factors such as glucose control status, smoking, and body mass index. Further exploration through prospective investigations is essential to gain a clear understanding of the diverse effects of metformin on mortality.

This study presents a compelling narrative on the potential protective role of metformin in TBDM patients, encouraging clinicians and researchers to explore this promising therapeutic avenue further. The rigorous methodology and consistent findings across various analyses support the credibility of the results. As we aim for improved TB outcomes, metformin emerges as a hopeful intervention in the com-

plex interplay between TB and DM. Future research will be crucial for unlocking the full therapeutic potential of metformin in this high-risk population.

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