

Depression and Anxiety as Potential Risk Factors for Tuberculosis

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Tuberculosis (TB) is a chronic bacterial infection primarily caused by *Mycobacterium tuberculosis*. Despite a gradual decline in global TB incidence, the disease burden remains stable, with rising incidence and drug resistance in regions like sub-Saharan Africa. In 2022, 7.5 million individuals were affected by active TB, resulting in 1.6 million deaths. In Iran, TB incidence varies by province, with the highest rates in Sistan and Baluchestan. Mental health disorders, including depression and anxiety, may diminish cellular immunity, increasing the risk of progression from latent to active TB. Studies indicate that depressed individuals have a higher

risk of developing TB compared to their non-depressed counterparts. Given the high prevalence of mental disorders and their potential impact on TB incidence, further research is crucial, especially in Iran. This study could enhance understanding the complex interplay between mental health and infectious diseases and inform targeted public health strategies.

Dear Editor-in-Chief

Tuberculosis (TB) is a chronic bacterial infection primarily caused by *Mycobacterium tuberculosis* (1). Despite the gradual decline in global TB incidence, the global disease burden (GDB) remains stable. However, in certain regions, such as sub-Saharan Africa, both incidence and drug resistance are on the rise (2). Respiratory infections and tuberculosis were the fourth leading cause of death worldwide in 2019 (3). The World Health Organization reported that in 2022, 7.5 million individuals were affected by active TB, and 1.6 million (95% UI: 1.18–1.43 million) succumbed to the disease (4). In Iran, the incidence of TB per 100,000 population in 2022 was 37.63 in Sistan and Baluchestan, 24.84 in Golestan, 13.19 in Gilan provinces, and 8.5 nationwide (5).

Patients with pulmonary TB disseminate infectious particles through coughing, which are then inhaled by those nearby. These particles bypass the mucociliary defense in the terminal alveoli, settle, and multiply, potentially spreading throughout the body via the bloodstream. Delayed-type hypersensitivity and cellular immunity

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develop 4 to 8 weeks post-initial infection. The subsequent outcomes are twofold: 1- In 90-95% of cases, the immune response effectively halts bacillary multiplication. However, some bacilli may persist in a latent state. After several months to years, a weakened immune system can lead to the reactivation of dormant TB bacilli acquired during primary infection. Alternatively, re-exposure to TB bacilli can result in re-infection. TB resulting from reactivation or re-infection is termed post-primary TB, which predominantly manifests as active pulmonary TB and occasionally as extrapulmonary TB. 2- In 5-10% of cases, the immune response is insufficient to prevent bacillary multiplication, leading to the development of active pulmonary TB within a few months of initial infection (6-9).

Globally, approximately one-third of the population is infected with tuberculosis (TB) (1). The most significant predisposing factors that elevate the risk of latent TB infection progressing to active TB disease include 1- Compromised immune system, such as in cases of HIV, diabetes, malnutrition, chronic lung diseases, smoking, alcohol and drug use, and immunosuppressive medications; and 2- Re-exposure to TB bacilli through contact with patients with smear-positive pulmonary TB (7).

Mental health disorders, including depression and anxiety, can diminish the body's ability to combat physical illnesses by reducing cellular immunity (10). A case-control study comparing cellular immune markers in depressed and non-depressed patients revealed that CD8 and CD4 cell counts were significantly higher in the control group ($P = 0.001$). Furthermore, when comparing cellular immune markers in depressed patients before and after treatment, researchers found that Natural Killer cells, CD4, and CD8 cell counts increased significantly post-treatment ($P < 0.001$). These findings suggest that mental disorders may serve as risk factors for the progression and conversion of latent TB infection to active TB disease (11). A cohort study conducted in South Korea demonstrated that depressed individuals had a 2.63-fold higher risk of developing TB compared to their non-depressed counterparts, with a dose-response

relationship observed between the severity of depression and TB occurrence (12). Depression is generally seen in elderly people and causes insomnia, bad mood, and lack of appetite. Exposure to these complications for a long time leads to incomplete and non-comprehensive immunity to protect against microorganisms, including *Mycobacterium tuberculosis*. In addition, anorexia and depression lead to malnutrition and cachexia. Malnutrition affects cellular immunity. Cellular immunity is the primary host defense against tuberculosis in humans and laboratory animals. Similarly, a Taiwanese study found that patients with depression have a higher potential risk of developing pulmonary TB compared to non-depressed individuals (13).

Mental disorders, such as depression and anxiety, are highly prevalent worldwide and, while they may have low mortality rates, they are associated with substantial disability. In 2019, major depressive disorder was the fifth leading individual cause of Disability-Adjusted Life Years (DALYs) due to premature death and disability (14). If depression is indeed a risk factor for the development of TB, the burden of depression may pose a significant barrier to the global elimination of TB. Despite the potential implications, there is a paucity of research investigating the impact of mental disorders on the incidence of TB worldwide, and no such study has been conducted in Iran. Therefore, it is imperative to conduct an original investigation, preferably a prospective cohort study, to examine the relationship between depression, anxiety, and the risk of developing TB in the Iranian population. Such research could provide valuable insights into the complex interplay between mental health and infectious diseases, ultimately informing targeted interventions and public health strategies.

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Conflict of interests

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None

Authors' contributions

All authors made substantial contributions to the conception and design of the study.

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Tuberculosis, Depression, Anxiety, Iran, Risk factors

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