



Overview of COVID-19 and Pulmonary Tuberculosis Co-infection: Diagnostic and Therapeutic Challenges

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ABSTRACT

The co-infection of COVID-19 and pulmonary tuberculosis (TB) presents a significant public health concern, especially in regions with high TB prevalence. Both diseases primarily affect the respiratory system and share similar clinical manifestations, such as cough, fever, and shortness of breath, which complicates timely diagnosis and management. This review explores the current literature on the co-existence of SARS-CoV-2 and *Mycobacterium tuberculosis* infections, highlighting the diagnostic challenges due to overlapping radiological and laboratory findings. It also examines therapeutic complexities, including potential drug-drug interactions, treatment adherence issues, and immune system implications. Furthermore, the review discusses the impact of the COVID-19 pandemic on TB control programs, including disruptions in case detection, delayed treatment, and increased risk of TB transmission. By summarizing current evidence, this review aims to support clinicians and policymakers in improving the diagnosis, treatment, and management of patients affected by both diseases.

Keywords: COVID-19, Tuberculosis, Co-infection, Therapeutic Challenges

Introduction

The emergence of Coronavirus Disease 2019 (COVID-19), caused by the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has posed an unprecedented global health crisis since its identification in late 2019. Despite extensive public health measures and vaccination efforts, COVID-19 continues to exert a significant burden on healthcare systems worldwide (1,2).

Simultaneously, Pulmonary Tuberculosis (PTB), caused by *Mycobacterium tuberculosis*, remains one of the leading infectious causes of morbidity and mortality, particularly in low- and middle-income countries. The coexistence of these two respiratory infections presents a unique clinical and public health challenge (3).

Both COVID-19 and PTB primarily target the respiratory system, leading to overlapping clinical manifestations such as fever, cough, dyspnea, and weight loss. These similarities complicate timely diagnosis, especially in resource-limited settings where laboratory capacity and access to imaging are constrained (4). The radiological findings of both diseases such as infiltrates, consolidations, and cavitary lesion can appear remarkably similar, increasing the likelihood of misdiagnosis or delayed treatment initiation (5).

From a therapeutic standpoint, the management of COVID-19 and TB co-infection is complicated by potential drug-drug interactions, hepatotoxicity, and the need for prolonged treatment regimens. Moreover, the diversion of healthcare resources during the COVID-19 pandemic has disrupted TB control programs, leading to delayed diagnosis, treatment interruptions, and increased transmission rates (6,7).



Understanding the interaction between SARS-CoV-2 and *M. tuberculosis* is therefore critical for improving diagnostic strategies, optimizing treatment protocols, and guiding public health interventions. This review provides an overview of the epidemiology, pathophysiology, diagnostic challenges, and therapeutic considerations of COVID-19 and pulmonary tuberculosis co-infection (8,9).

Given these intertwined challenges, understanding the epidemiology, pathogenesis, and management of COVID-19–TB co-infection is essential for guiding clinical practice and public health policies (10).

This review aims to provide an overview of the current knowledge on the coexistence of COVID-19 and pulmonary tuberculosis, emphasizing the diagnostic difficulties and therapeutic complexities associated with their interaction.

Epidemiology & Risk Factors

Several systematic reviews/meta-analyses show that COVID-19/TB co-infection is less common than either disease alone but carries higher risk of adverse outcomes. For example: one meta-analysis found a pooled fatality rate of ~7.1% (95 % CI: 4.0-10.8 %) among co-infected patients; among in-hospital co-infected patients the mean fatality was ~11.4 %. Prevalence estimates vary widely by region (11).

The most common risk factors for COVID-19 and tuberculosis are presented in **Figure (1)**. In some high TB burden settings the co-infection rate was non-negligible: one study from Belarus found nearly 1 in 20 COVID-19 hospitalized patients with lung changes had active pulmonary TB. The global burden is influenced by underlying TB prevalence, health system disruption during the pandemic, and socio-economic determinants (12). Important risk factors include older age, malnutrition/low BMI, comorbidities (especially HIV, diabetes), poverty, and crowded living conditions (13).



Figure (1): The most common risk factors for COVID-19 and tuberculosis.

Pathophysiology & Immunological Interplay

Both TB and COVID-19 primarily affect the lungs and trigger complex immune responses; but the nature of immune dysregulation differs and may interact adversely. For TB, containment relies on a strong Th1 / IFN- γ / TNF- α response to form and maintain granulomas. For SARS-CoV-2,



severe disease is associated with lymphopenia, dysfunctional innate response, cytokine storm (e.g., IL-6, TNF- α) and immune exhaustion (14,15). One study found that COVID-19 infection or recovery leads to decreased Th17 levels in TB patients, and altered regulatory T-cell (Treg) dynamics, which may impair TB control or accelerate progression from latent to active TB (16).

The co-infection scenario may thus behave in two problematic directions: (17,18)

1. Pre-existing TB (active or latent) potentially worsens COVID-19 outcomes through compromised lung architecture and impaired immunity.
2. COVID-19 (or its treatment) may predispose to TB reactivation or progression by immune suppression, lung damage, or delayed TB diagnosis.
3. There is also modelling evidence showing that simultaneous dynamics of TB and COVID-19 (including vaccination levels, BCG status, etc) affect co-infection prevalence and control.

Clinical and Diagnostic Challenges

Both diseases share major symptoms: cough, fever, dyspnoea, fatigue. This overlap makes differential diagnosis difficult, especially in high TB-burden settings (19).

Radiological imaging may be misleading: TB often shows upper-lobe cavitation, fibronodular changes, pleural effusion; COVID-19 shows ground-glass opacities, bilateral lower-lung involvement yet co-infection may present mixed features. In one study, upper-lobe involvement and pleural effusion were significantly more common in TB-COVID-19 cases versus COVID-19 alone (20). Important laboratory features: Higher inflammatory markers (e.g., CRP, ferritin) appear in co-infected patients (21).

The pandemic disrupted TB services in many countries (screening, contact tracing, diagnostics), worsening delays in TB detection. Physicians may attribute symptoms to COVID-19 alone and miss concurrent or underlying TB, particularly latent TB reactivating. A case report from Egypt highlighted the need for vigilant screening (22).

TB diagnostics (sputum microscopy, Gene Xpert MTB/RIF, culture) may be delayed or unavailable in COVID-19 isolation settings. Ensuring infection control, avoiding aerosol spread, and concurrently testing for both infections require extra resources (23).

Co-infection may complicate interpretation of results: e.g., lung damage from TB may influence COVID-19 imaging presentation or residual lesions may persist post-COVID (24).

Therapeutic and Management Challenges

Drug-drug interactions: Anti-TB regimens (e.g., rifampicin, isoniazid, pyrazinamide, ethambutol) have significant interactions and toxicities; some treatments for severe COVID-19 (e.g., corticosteroids, immunomodulators) may increase TB reactivation risk or complicate TB therapy (25).

Both TB drugs and some COVID-19 treatments (and COVID-19 itself) may cause hepatic enzyme elevation, raising risk of hepatotoxicity. Use of steroids or biologicals for COVID-19 may suppress host immunity, increasing risk of TB activation in latent cases (26). Some data suggest co-infected patients have longer hospital stays, more severe lung damage, need for longer therapy and



monitoring. During COVID-19 surges, TB programs were disrupted (staff redeployment, lockdowns, decreased outpatient visits), affecting adherence to TB regimens, follow-up imaging, and contact tracing (27,28).

Public Health Implications

The dual burden of COVID-19 and TB is especially significant in low- and middle-income countries with high TB prevalence and constrained resources. The intersection magnifies vulnerabilities (poverty, malnutrition, crowded housing) (29). TB control programmes must adapt: integrate COVID-19 screening in TB services, ensure TB diagnostics continue under pandemic pressures, and use combined strategies when co-infection is suspected (30).

Preventive measures including vaccination (e.g., COVID-19 vaccines) plus TB prevention (BCG, latent TB screening) may reduce the dual risk. One modelling study showed that increasing vaccination coverage and reducing transmission lowered co-infection cases. Many studies call for more prospective data to understand the interaction fully (e.g., whether COVID-19 triggers TB reactivation) (31-33).

Life Quality and Shared Manifestations of COVID-19 and Tuberculosis

COVID-19 and Tuberculosis (TB) are infectious diseases that significantly affect patients' quality of life (QoL) through physical, psychological, and social consequences (Figure 2). Because both primarily target the lungs, they share many symptoms such as cough, breathlessness, fatigue, and chest pain and often lead to lasting respiratory impairment (34).

Physically, patients with either disease may experience long-term lung damage, reduced exercise capacity, and chronic fatigue. In TB, post-treatment lung disease (fibrosis, bronchiectasis) is common, while in COVID-19, many survivors suffer from "long COVID" symptoms such as persistent breathlessness and weakness (35).

Psychologically, both illnesses are linked to anxiety, depression, and stress. TB carries social stigma and isolation, whereas COVID-19 brings fear of death, quarantine-related stress, and uncertainty about full recovery. When co-infection occurs, these emotional burdens are even greater (36). Socially and economically, prolonged treatment, isolation, and reduced work ability lead to financial hardship and social exclusion, especially in low-income settings where TB is prevalent (37).

Overall, both COVID-19 and TB cause a significant decline in health-related quality of life, affecting physical, mental, and social domains. Recovery requires multidisciplinary care including medical management, pulmonary rehabilitation, psychological support, nutritional therapy, and social assistance to help patients regain function and well-being (34).

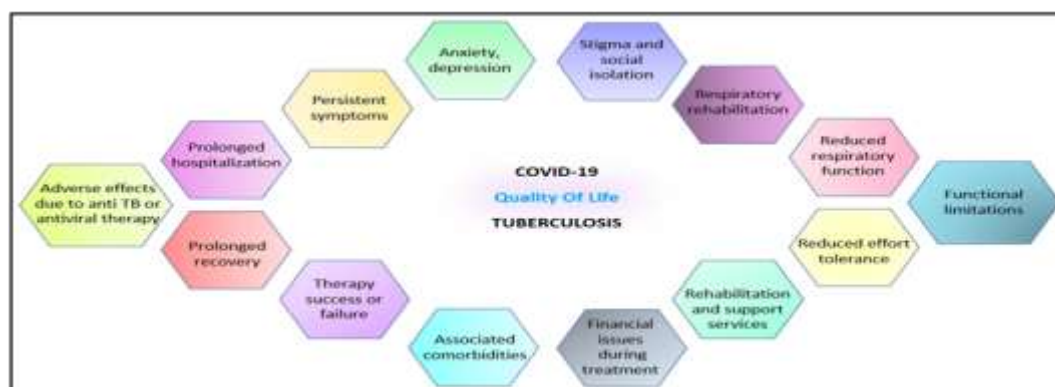


Figure (2): Life Quality and Shared Manifestations of COVID-19 and Tuberculosis

Recommendations

In terms of treatment, coordinated clinical management is vital. Standardized guidelines should be developed to address potential drug–drug interactions between anti-TB medications and COVID-19 therapies, such as rifampicin’s interaction with antivirals and corticosteroids. Close monitoring for hepatotoxicity and other adverse effects is necessary when administering combined treatment regimens. Ensuring the continuity of TB therapy during COVID-19 isolation is important; this can be achieved through community-based drug delivery systems, telemedicine, and digital adherence monitoring. Multidisciplinary healthcare teams including pulmonologists, infectious disease specialists, and pharmacists should collaborate to optimize treatment plans for co-infected patients.

Health system strengthening remains a key priority. The pandemic has disrupted TB control programs worldwide, leading to delays in diagnosis, treatment interruptions, and increased transmission. Restoring these services requires improving laboratory capacity, supply chains, and infection control measures. Training healthcare workers in dual disease management and infection prevention will enhance the resilience of health systems in handling both diseases concurrently.

Conclusion

COVID-19 and Pulmonary Tuberculosis co-infection presents complex diagnostic and therapeutic challenges due to overlapping clinical manifestations, potential drug interactions, and immune system interplay. A multidisciplinary approach, integrated diagnostics, and careful therapeutic management are vital for improving patient outcomes, particularly in TB-endemic settings.

Thus, effective management of COVID-19 and tuberculosis co-infection demands a multidisciplinary approach that combines clinical care, public health policy, and research innovation. Strengthening surveillance systems, expanding diagnostic capacity, and promoting collaboration between TB and COVID-19 programs are critical steps toward minimizing the dual burden of these respiratory diseases and improving patient outcomes worldwide.

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