Scientific Research Publishing

Advances in Infectious Diseases, 2025, 15(3), 401-412
https://www.scirp.org/journal/aid
ISSN Online: 2164-2656
ISSN Print: 2164-2648

Tuberculosis during the COVID-19 Pandemic: Retrospective Analysis in a Tertiary Hospital in Portugal

Emanuel F. Matias[1,2,3*#], Margarida Oliveira[1*], Filipa Ceia[1], Lurdes Santos[1]

[1]Department of Infectious Diseases, Local Health Unit of São João, Porto, Portugal
[2]Unit of Pharmacology and Therapeutics, Department of Faculty of Medicine, University of Porto, Porto, Portugal
[3]MedInUP—Center for Drug Discovery and Innovative Medicines, University of Porto, Porto, Portugal
Email: #ematias@med.up.pt

How to cite this paper: Matias, E.F., Oliveira, M., Ceia, F. and Santos, L. (2025) Tuberculosis during the COVID-19 Pandemic: Retrospective Analysis in a Tertiary Hospital in Portugal. *Advances in Infectious Diseases*, **15**, 401-412.
https://doi.org/10.4236/aid.2025.153032

Received: June 1, 2025
Accepted: July 15, 2025
Published: July 18, 2025

Abstract

Introduction: Tuberculosis (TB) remains a major public health challenge despite being a preventable and curable infectious disease. Early diagnosis and access to treatment are essential to tackle its transmission and mortality. The COVID-19 pandemic led to worldwide healthcare service disruptions and an underrecognized impact on the global fight against TB. **Objective:** To describe the clinical and epidemiological characteristics of TB patients diagnosed during the COVID-19 pandemic period. **Methods:** We conducted a retrospective observational study at a tertiary hospital center in Porto, Portugal, reviewing all patients admitted and diagnosed with TB between January 2020 and December 2022. Demographic data, clinical manifestations, immunosuppression status, microbiological and radiological findings, treatment and outcomes were analysed. **Results:** A total of 72 patients were diagnosed with TB during the study period. Most were male with a median age of 54 years. More than one-third were immunosuppressed. The median interval from symptom onset to diagnosis was 60 days. Pulmonary TB with sputum-smear positivity and cavitary lesions accounted for the majority of cases. Treatment was initiated in all but one patient. Overall, most patients (88.9%) achieved successful outcomes. **Conclusion:** During the COVID-19 pandemic, significant delays in TB diagnosis led to a substantial proportion of patients presenting with advanced pulmonary disease. These findings underscore the constraints felt during an unprecedented health crisis and the need for resilient TB programs capable of maintaining diagnostic and treatment services. Further research is warranted to quantify the long-term effects of the pandemic on TB control efforts.

*First authors.
#Corresponding author.

Keywords

Tuberculosis, COVID-19

1. Introduction

Tuberculosis (TB) is a preventable and mainly curable infectious disease, caused by the bacillus *Mycobacterium tuberculosis* [1]. Despite coexisting for at least 15000 years, the disease reached widespread proportions during the 18th and 19th centuries in rapidly urbanizing and industrializing Europe and North America [2] [3], and since then, it has persisted as a global epidemic with disproportionate effects on low-income populations [4]. Today, it is responsible for around 1,5 million deaths each year, more than any other infectious disease [5], and about a quarter of the global population is estimated to have been infected with the bacteria [6].

Following infection, the estimated lifetime risk for reactivation and progression to active disease is 5% - 10% [7], notably during the first two years and in immunocompromised patients, such as those co-infected with the human immunodeficiency virus (HIV), in which the risk is estimated to be 18 times higher [8]. Besides immune status, other determinants for infection acquisition and disease development include poverty, undernourishment, smoking and diabetes. About 90% of the patients are adults with more cases among men [9].

Tuberculosis typically affects the lungs (pulmonary TB) but can also involve other sites (extrapulmonary TB) [10]. Despite substantial improvement in testing, culture remains the reference standard for tuberculosis diagnosis, detection of drug resistance and monitoring the response to therapy [11]. Without treatment, the mortality of the disease is high, ranging from 70% in individuals with sputum smear-positive and 20% in people with sputum smear-negative pulmonary TB. Effective antibacterial drugs were first developed in the 1940s, and currently recommended regimens can achieve a cure in about 85% of the patients [12].

The World Health Organization's End TB Strategy was launched in 2015 as a joint commitment to ending the tuberculosis pandemic, targeting large reductions in its incidence rate, mortality and associated expenditures up to year 2035 [13]. Despite falling short of the milestones outlined, an encouraging decline in the global burden of the disease has since then been observed [14]. The COVID-19 pandemic inflicted profound health and social upheaval, significantly disrupting early TB diagnosis, screening, and access to treatment. As a result, the most immediate consequence was a sharp decline in new TB cases: global notifications dropped from 7.1 million in 2019 to 5.8 million in 2020, with only partial recovery in 2021 [15] [16]. This trend was mirrored in most high-income countries in Europe, North America, and Australia, where notifications declined while mortality increased [17]. Moreover, country-specific data, such as Armenia's 37.6% reduction in active TB case detection, primarily due to decreased testing and contact tracing, highlight the widespread operational breakdown in TB surveillance, diagnosis, and

control [18].

The present work aimed to characterize the experience of a Portuguese tertiary care center concerning the management of hospitalized patients with tuberculosis during COVID-19.

2. Methods

For the purpose of this study, a retrospective observational cohort analysis was conducted at the Department of Infectious Diseases of a tertiary care center in Porto, Portugal. The electronic hospital database (SClínico®) was systematically reviewed to identify all adult patients admitted for inpatient care between January 2020 and December 2022 who were subsequently diagnosed with tuberculosis during the course of hospitalization. All identified patients meeting these criteria were included in the study. Relevant clinical and demographic variables were extracted from medical records, and no missing information was identified.

Diagnostic criteria followed World Health Organization's consolidated guidelines on Tuberculosis [19]. Confirmed TB was defined by the identification of *Mycobacterium tuberculosis* complex (MTC) from clinical specimens through culture or molecular testing. Suspected TB included patients lacking microbiological confirmation but presenting compatible clinical, histological, or radiological features. Pulmonary TB involves infection of lung parenchyma, with smear-positive and smear-negative cases classified according to initial acid-fast sputum results. Extrapulmonary TB refers to disease affecting organs other than the lungs.

The descriptive analysis was conducted using SPSS® version 29.0.1.1. This study was conducted in accordance with the Declaration of Helsinki and approved by the institution's Ethics Committee, which waived the informed consent of the patients.

3. Results

A total of 72 patients were diagnosed with tuberculosis during the study period. Of these, 62 (86.1%) had pulmonary TB and 10 (13.9%) had extrapulmonary TB; disseminated TB was identified in 19 cases (26.4%). The cohort was predominantly male (72.2%) with a median age of 54 years (range 18 - 92). Eighteen patients (25.0%) reported current or past employment in high-risk occupations (e.g., construction, healthcare, industrial work, commercial sex work); three individuals (4.2%) were incarcerated at the time of diagnosis, and two (2.8%) were in precarious socioeconomic situations. Regarding lifestyle factors, 22 patients (30.6%) were active smokers, 12 (16.7%) had alcohol dependence, and 11 (15.3%) had a history of substance abuse. Identifiable immunosuppressive conditions were present in 28 patients (38.9%), including 15 (20.8%) with HIV infection. The median interval from symptom onset to diagnosis was 60 days (range 1 - 730), with immunocompetent patients experiencing a shorter diagnostic delay (median 45 vs 75 days). Detailed demographic and clinical characteristics are summarized in **Table 1** and **Table 2**.

Table 1. Sociodemographic and behavioral characteristics of the study population.

Characteristics of the population		
Sociodemographic Characteristics		N = 72 (%)
Gender	Female	20 (27.8%)
	Male	52 (72.2%)
Age	Median	54 years
	Minimum Value	18 years
	Maximum Value	92 years
	18 - 30 years	9 (12.5%)
	31 - 50 years	19 (26.38%)
	51 - 65 years	22 (30.56%)
	>65 years	22 (30.56%)
Occupation	Non-Risky Occupation	18 (25.0%)
	Retired from Non-Risky Occupation	14 (19.4%)
	Risky Occupation	10 (13.9%)
	Unknown	9 (12.5%)
	Retired from Risky Occupation	8 (11.1%)
	Unemployed	8 (11.1%)
	Inmate	2 (2.8%)
	Homeless	2 (2.8%)
	Former Inmate	1 (1.4%)
Habits of the Population		n (%)
Smoking	Yes	22 (30.6%)
	No	40 (55.6%)
	Ex-smoker	10 (13.8%)
Alcoholism	Yes	12 (16.7%)
	No	57 (79.1%)
	Ex-alcoholic	3 (4.2%)
Drug Consumption	No	58 (80.6%)
	Cocaine	1 (1.4%)
	Cocaine and Heroin	7 (9.7%)
	Narcotics	1 (1.4%)
	Cannabinoids	1 (1.4%)
	Ex-drug user	4 (5.5%)

Pulmonary TB predominated in both immunocompetent (35 cases, 79.5%) and immunosuppressed patients (27 cases, 96.4%). Common presenting symptoms included weight loss (77.4%), fatigue (74.2%), cough (71.0%), fever (46.8%), night sweats (30.6%), dyspnea (24.2%), hemoptysis (12.9%), and pleuritic chest pain (9.7%).

Among the 62 pulmonary TB cases, 35 (56.4%) had isolated pulmonary involvement, while 27 (43.6%) also exhibited extrapulmonary disease. As depicted in Table 3, diagnostic confirmation was achieved in 56 patients (90.3%): 52 by culture alone, 4 by molecular testing alone, and 38 by both methods. Sputum-smear microscopy was positive in 37 patients (59.7%), necessitating airborne isolation precautions. Radiological cavitation was observed in 33 cases (53.2%). Among MTC strains isolated by culture, 50 (96.2%) were drug-susceptible, one (1.9%) was polyresistant, and one (1.9%) was multidrug-resistant. Extrapulmonary sites among the 27 patients with concurrent involvement included: lymph nodes (9 cases, 33.3%); genitourinary tract (8 cases, 29.6%), osteoarticular system (7 cases, 25.9%); pleura or pericardium (7 cases, 25.9%), including 6 pleural cases and 1 pericardial effusion causing tamponade; gastrointestinal tract (4 cases, 14.8%); and central nervous system (3 cases, 11.1%).

Among the 10 patients with exclusively extrapulmonary TB, the affected sites were lymph nodes (4 cases), osteoarticular system (3 cases), pleura (3 cases), central nervous system (2 cases), gastrointestinal tract (1 case), and genitourinary system (1 case) (Table 4). Although disseminated TB was more common in the immunosuppressed cohort (35.7% vs. 20.5%), isolated extrapulmonary TB predominated among immunocompetent patients (20.5% vs. 3.6%).

Table 2. Comorbidities of the study population.

Comorbidities in the individuals of the sample		
Hypertension	19 (26.4%)	
Diabetes	14 (19.4%)	
Pulmonary and respiratory disease	Obstructive disease	11 (15.3%)
	Sequelae of TB	3 (4.2%)
	Pneumoconiosis	2 (2.8%)
	Obstructive Sleep Apnea Syndrome	1 (1.4%)
	Structural disease	1 (1.4%)
Hepatic disease	Non-Cirrhotic	9 (12.5%)
	Cirrhotic	4 (5.6%)
Chronic renal disease	6 (8.3%)	
Infection with HIV	15 (20.8%)	
	- CD4 count < 200	11 (73.3%)
	- CD4 count > 200	4 (26.7%)
Immunosuppression	27 (37.5%)	
	- By HIV	15 (55.6%)
	- By drugs	9 (33.3%)
	- By neoplasm	3 (11.1%)
Previous infection with Tuberculosis	11 (15.3%)	

During hospitalization, 14 patients (19.4%) were transferred to Intensive Care Unit (ICU), of whom 6 (8.3%) required mechanical ventilation. ICU admission and invasive ventilation were more frequent among patients without known immunosuppressive conditions than those with (27.3% vs. 7.1% and 11.4% vs. 3.6%, respectively). Antitubercular therapy was initiated in all but one patient, who died of respiratory failure before the diagnosis was confirmed. Following treatment initiation, 22 patients (30.6%) experienced adverse drug reactions, most commonly hepatic toxicity (18 cases), followed by cutaneous manifestations (4 cases) and neurological symptoms (3 cases).

Table 3. Clinical description of cases with pulmonary tuberculosis.

Pulmonary Tuberculosis	
Pulmonary disease only	35 (56.4%)
Pulmonary and extrapulmonary disease	27 (43.6%)
Type of diagnosis	
Confirmed	56 (90.3%)
Suspected	6 (9.7%)
Method of diagnosis	
Microbiological evidence	56 (90.3%)
Isolation in cultures	52 (92.8%)
STB	41 (73.2%)
BAL	5 (8.9%)
Both	4 (7.1%)
Identification using Polymerase Chain Reaction	4 (7.1%)
Both	38 (67.8%)
Clinical evidence or imaging results	6 (9.7%)
Disease characteristics	
Direct microscopy	37 (59.7%)
Lung cavitation	33 (53.2%)
Cultural TSA	
Sensitive	50 (96.2%)
Polyresistant	1 (1.9%)
Multi-drug resistant (MDR-TB)	1 (1.9%)
Extrapulmonary sites in Pulmonary Tuberculosis	
Lymph node disease	9 (33.3%)
Genitourinary disease	8 (29.6%)
Osteoarticular disease	7 (25.9%)
Pleuro-pericardial disease	7 (25.9%)
Gastrointestinal disease	4 (14.8%)
Central Nervous System disease	3 (11.1%)

Regarding outcomes, 64 patients (88.9%) were discharged with clinical improvement and referred for continued follow-up, 3 (4.2%) left against medical advice, and 5 (6.9%) died during hospitalization. Within six months, 13 patients (18.1%) were readmitted due to symptom exacerbation or treatment failure. In-hospital mortality was similar in patients with and without immunosuppressive conditions (7.4% vs. 6.8%), while readmission rates were slightly higher among the immunosuppressed cohort (21.4% vs. 15.9%).

Table 4. Clinical description of cases with extrapulmonary tuberculosis.

Extrapulmonary Tuberculosis Only	
No. Cases	10 patients
Type of Extrapulmonary Tuberculosis	
Lymph Node tuberculosis	4 (40%)
- with specific symptoms of lymph node involvement	0
Osteoarticular tuberculosis	3 (30%)
- with specific symptoms of osteoarticular involvement	2 (66.7%)
Pleuro-pericardial tuberculosis	3 (30%)
- with specific symptoms of cardiopulmonary involvement	2 (66.7%)
CNS tuberculosis	2 (20%)
- with specific symptoms of CNS involvement	2 (100%)
Genitourinary tuberculosis	1 (10%)
- with specific symptoms of genitourinary involvement	0
Gastrointestinal tuberculosis	1 (10%)
- with specific symptoms of gastrointestinal involvement	1 (100%)
Symptoms	
Fever	4 (40%)
Fatigue	7 (70%)
Loss of weight	5 (50%)
Excessive sweating	2 (20%)

4. Discussion

This retrospective analysis characterizes the demographic and clinical profile of 72 patients with tuberculosis admitted during the COVID-19 pandemic to an infectious diseases ward at a tertiary hospital in Porto, Portugal. Consistent with established epidemiological trends, the majority of patients were male and over 50 years of age—recognized risk factors for active TB. Notably, while over one-third of patients exhibited immunosuppressive conditions, most did not display the socioeconomic or clinical vulnerabilities commonly linked to increased risk, such as substance abuse, unstable housing, incarceration, or chronic comorbidities, despite these factors being significant predictors of TB incidence in Portugal.

[20]-[22].

Immunosuppression is a well-recognized risk factor for more severe and atypical manifestations of TB, including a higher likelihood of disseminated disease and poorer clinical outcomes [23]-[25]. In this cohort, disseminated TB was more frequent among immunosuppressed patients, consistent with existing evidence. Conversely, isolated extrapulmonary TB was more commonly observed in immunocompetent individuals, contrasting with patterns typically seen in HIV-associated TB, where extrapulmonary involvement is often multifocal. Mortality rates were similar across both groups, diverging from most published data, which may be explained by consistent inpatient care, timely diagnosis, or sample size limitations. Notably, six-month readmission rates were higher in immunosuppressed patients, suggesting greater vulnerability to treatment failure or complications. Overall, these findings align with the broader literature—highlighting increased rates of disseminated TB and adverse outcomes in immunosuppressed individuals, despite comparable short-term mortality.

A key finding of the study was a significant diagnostic delay, with a median time of 60 days—and in some cases, extending up to 730 days—from symptom onset to TB diagnosis, far exceeding typical pre-pandemic timelines [26]. Although not the central focus of this study, such latency has been well-documented in the literature and is likely attributable to a combination of patient- and system-level barriers exacerbated by the COVID-19 pandemic. For example, healthcare-seeking behaviors were often delayed due to fear of SARS-CoV-2 exposure, contributing to more advanced disease at the time of presentation. In addition, the symptomatic overlap between TB and COVID-19 frequently led to misdiagnosis or deferral of appropriate investigations [27]. Notably, many patients in this cohort did not present with traditional risk factors, which likely reduced clinical suspicion. In such cases, individuals with respiratory symptoms were often funneled into COVID-19 screening pathways, where mycobacterial testing was seldom pursued due to a low perceived likelihood of disease [28]. On a broad health system level, widespread service disruption—including lockdowns, reallocation of resources, and reduced access to services—contributed to sharp declines in TB case detection and treatment initiation, as reported globally [29]. These factors are consistent with the clinical severity observed in this cohort, as evidenced by a high prevalence of cavitary lesions and sputum-smear positivity in over half of patients, and the need for intensive care in nearly one-fifth of cases—figures that parallel international reports of tuberculosis during the COVID-19 pandemic [30]-[32].

This study is subject to several important limitations. First, as a single-center investigation based in a tertiary referral hospital, the cohort likely overrepresents severe or complex cases of TB and may not be generalizable to broader populations managed in primary or secondary care settings. Second, the absence of a pre-pandemic comparator group limits the ability to discern the specific impact of the COVID-19 pandemic on TB presentation, disease progression, and outcomes. Third, SARS-CoV-2 infection status—whether active, recent, or past—was not sys-

tematically documented at the time of TB diagnosis, limiting the capacity to assess possible interactions between the two infections. Although multiple international cohort studies and meta-analyses have shown that TB-COVID-19 co-infection is associated with more severe disease, including higher rates of respiratory failure, intensive care admission, and in-hospital mortality [33] [34], the present study cannot confirm such associations [33] [34]. These limitations highlight the need for well-designed, multicenter longitudinal studies with integrated microbiological surveillance to clarify the interaction and long-term impact of COVID-19 on TB epidemiology and outcomes.

Nevertheless, this retrospective analysis provides a noteworthy snapshot of TB management during an unprecedented global health emergency. The findings reveal not only the strain imposed by the COVID-19 pandemic on TB care, but also the adaptability and resilience of healthcare professionals in ensuring treatment initiation and continuity. These results should serve as a basis for strengthening TB services and infrastructures, reinforcing diagnostic capabilities, and safeguarding treatment adherence, particularly in anticipation of future health system disruptions.

Author's Contribution

E.F.M. and M.O. are first authors with equal contribution to the whole manuscript. Conceptualization: E.F.M., M.O. and L.S. Methodology: E.F.M. and M.O. Data collection: M.O. Investigation: E.F.M., M.O. and L.S. Writing—Original Draft: E.F.M. and M.O. Writing—Review & Editing: E.F.M., M.O., F.C. and L.S. Supervision: L.S.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Hershkovitz, I., Donoghue, H.D., Minnikin, D.E., May, H., Lee, O.Y.-C., Feldman, M., *et al.* (2015) Tuberculosis Origin: The Neolithic Scenario. *Tuberculosis*, **95**, S122-S126. https://doi.org/10.1016/j.tube.2015.02.021

[2] Nicklisch, N., Maixner, F., Ganslmeier, R., Friederich, S., Dresely, V., Meller, H., *et al.* (2012) Rib Lesions in Skeletons from Early Neolithic Sites in Central Germany: On the Trail of Tuberculosis at the Onset of Agriculture. *American Journal of Physical Anthropology*, **149**, 391-404. https://doi.org/10.1002/ajpa.22137

[3] Gutierrez, M.C., Brisse, S., Brosch, R., Fabre, M., Omaïs, B., Marmiesse, M., *et al.* (2005) Ancient Origin and Gene Mosaicism of the Progenitor of *Mycobacterium tuberculosis*. *PLOS Pathogens*, **1**, e5. https://doi.org/10.1371/journal.ppat.0010005

[4] Donoghue, H.D. (2009) Human Tuberculosis—An Ancient Disease, as Elucidated by Ancient Microbial Biomolecules. *Microbes and Infection*, **11**, 1156-1162. https://doi.org/10.1016/j.micinf.2009.08.008

[5] Raviglione, M. and Sulis, G. (2016) Tuberculosis 2015: Burden, Challenges and Strategy for Control and Elimination. *Infectious Disease Reports*, **8**, Article 6570. https://doi.org/10.4081/idr.2016.6570

[6] Houben, R.M.G.J. and Dodd, P.J. (2016) The Global Burden of Latent Tuberculosis Infection: A Re-Estimation Using Mathematical Modelling. *PLOS Medicine*, **13**, e1002152. https://doi.org/10.1371/journal.pmed.1002152

[7] Menzies, N.A., Wolf, E., Connors, D., Bellerose, M., Sbarra, A.N., Cohen, T., *et al.* (2018) Progression from Latent Infection to Active Disease in Dynamic Tuberculosis Transmission Models: A Systematic Review of the Validity of Modelling Assumptions. *The Lancet Infectious Diseases*, **18**, e228-e238. https://doi.org/10.1016/s1473-3099(18)30134-8

[8] Alsayed, S.S.R. and Gunosewoyo, H. (2023) Tuberculosis: Pathogenesis, Current Treatment Regimens and New Drug Targets. *International Journal of Molecular Sciences*, **24**, Article 5202. https://doi.org/10.3390/ijms24065202

[9] Bagcchi, S. (2023) Who's Global Tuberculosis Report 2022. *The Lancet Microbe*, **4**, E20. https://doi.org/10.1016/s2666-5247(22)00359-7

[10] Small, P.M. and Fujiwara, P.I. (2001) Management of Tuberculosis in the United States. *New England Journal of Medicine*, **345**, 189-200. https://doi.org/10.1056/nejm200107193450307

[11] Suárez, I., Fünger, S.M., Kröger, S., Rademacher, J., Fätkenheuer, G. and Rybniker, J. (2019) The Diagnosis and Treatment of Tuberculosis. *Deutsches Ärzteblatt international*, **116**, 729-735. https://doi.org/10.3238/arztebl.2019.0729

[12] Tiemersma, E.W., van der Werf, M.J., Borgdorff, M.W., Williams, B.G. and Nagelkerke, N.J.D. (2011) Natural History of Tuberculosis: Duration and Fatality of Untreated Pulmonary Tuberculosis in HIV Negative Patients: A Systematic Review. *PLOS ONE*, **6**, e17601. https://doi.org/10.1371/journal.pone.0017601

[13] Uplekar, M. and Raviglione, M. (2015) Who's End TB Strategy: From Stopping to Ending the Global TB Epidemic. *Indian Journal of Tuberculosis*, **62**, 196-199. https://doi.org/10.1016/j.ijtb.2015.11.001

[14] Dheda, K., Perumal, T., Moultrie, H., Perumal, R., Esmail, A., Scott, A.J., *et al.* (2022) The Intersecting Pandemics of Tuberculosis and COVID-19: Population-Level and Patient-Level Impact, Clinical Presentation, and Corrective Interventions. *The Lancet Respiratory Medicine*, **10**, 603-622. https://doi.org/10.1016/s2213-2600(22)00092-3

[15] Falzon, D., Zignol, M., Bastard, M., Floyd, K. and Kasaeva, T. (2023) The Impact of the COVID-19 Pandemic on the Global Tuberculosis Epidemic. *Frontiers in Immunology*, **14**, Article 1234785. https://doi.org/10.3389/fimmu.2023.1234785

[16] Ledesma, J.R., Basting, A., Church, H.T., Ma, J., Zhang, M., Vongpradith, A., *et al.* (2023) Global-, Regional-, and National-Level Impacts of the COVID-19 Pandemic on Tuberculosis Diagnoses 2020-2021. *Microorganisms*, 11, Article 2191. https://doi.org/10.3390/microorganisms11092191

[17] Nalunjogi, J., Mucching-Toscano, S., Sibomana, J.P., Centis, R., D'Ambrosio, L., Alffenaar, J., *et al.* (2023) Impact of COVID-19 on Diagnosis of Tuberculosis, Multidrug-Resistant Tuberculosis, and on Mortality in 11 Countries in Europe, Northern America, and Australia. a Global Tuberculosis Network Study. *International Journal of Infectious Diseases*, **130**, S25-S29. https://doi.org/10.1016/j.ijid.2023.02.025

[18] Khachatryan, N., Atshemyan, H., Manukyan, A., Khachatryan, A. and Poghosyan, K. (2022) The Impact of Covid-19 Pandemic on the Detection of Tuberculosis in Armenia. *Journal of Tuberculosis Research*, **10**, 199-204. https://doi.org/10.4236/jtr.2022.104015

[19] World Health Organization (2021) WHO Guidelines Approved by the Guidelines

Review Committee, in WHO Consolidated Guidelines on Tuberculosis: Module 3: Diagnosis-Rapid Diagnostics for Tuberculosis Detection.

[20] Imtiaz, S., Shield, K.D., Roerecke, M., Samokhvalov, A.V., Lönnroth, K. and Rehm, J. (2017) Alcohol Consumption as a Risk Factor for Tuberculosis: Meta-Analyses and Burden of Disease. *European Respiratory Journal*, **50**, Article 1700216. https://doi.org/10.1183/13993003.00216-2017

[21] Davies, P.D.O., Yew, W.W., Ganguly, D., Davidow, A.L., Reichman, L.B., Dheda, K., *et al.* (2006) Smoking and Tuberculosis: The Epidemiological Association and Immunopathogenesis. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **100**, 291-298. https://doi.org/10.1016/j.trstmh.2005.06.034

[22] Couceiro, L., Santana, P. and Nunes, C. (2011) Pulmonary Tuberculosis and Risk Factors in Portugal: A Spatial Analysis. *The International Journal of Tuberculosis and Lung Disease*, **15**, 1445-1455. https://doi.org/10.5588/ijtld.10.0302

[23] Lawn, S.D. and Zumla, A.I. (2011) Tuberculosis. *The Lancet*, **378**, 57-72. https://doi.org/10.1016/s0140-6736(10)62173-3

[24] de Perio, M.A., Kobayashi, M. and Wortham, J.M. (2020) Occupational Respiratory Infections. *Clinics in Chest Medicine*, **41**, 739-751. https://doi.org/10.1016/j.ccm.2020.08.003

[25] Kassaw, A., Kefale, D., Aytenew, T.M., Azmeraw, M., Agimas, M.C., Zeleke, S., *et al.* (2024) Burden of Mortality and Its Predictors among TB-HIV Co-Infected Patients in Ethiopia: Systematic Review and Meta-Analysis. *PLOS ONE*, **19**, e0312698. https://doi.org/10.1371/journal.pone.0312698

[26] Bhargava, A. and Shewade, H.D. (2020) The Potential Impact of the COVID-19 Response Related Lockdown on TB Incidence and Mortality in India. *Indian Journal of Tuberculosis*, **67**, S139-S146. https://doi.org/10.1016/j.ijtb.2020.07.004

[27] Narita, M., Hatt, G., Gardner Toren, K., Vuong, K., Pecha, M., Jereb, J.A., *et al.* (2021) Delayed Tuberculosis Diagnoses during the Coronavirus Disease 2019 (COVID-19) Pandemic in 2020—King County, Washington. *Clinical Infectious Diseases*, **73**, S74-S76. https://doi.org/10.1093/cid/ciab387

[28] Min, J., Ko, Y., Kim, H.W., Koo, H., Oh, J.Y., Jeong, Y., *et al.* (2022) Increased Healthcare Delays in Tuberculosis Patients during the First Wave of COVID-19 Pandemic in Korea: A Nationwide Cross-Sectional Study. *Journal of Korean Medical Science*, **37**, e20. https://doi.org/10.3346/jkms.2022.37.e20

[29] Williams, P.M., Pratt, R.H., Walker, W.L., Price, S.F., Stewart, R.J. and Feng, P.I. (2024) Tuberculosis—United States, 2023. *MMWR. Morbidity and Mortality Weekly Report*, **73**, 265-270. https://doi.org/10.15585/mmwr.mm7312a4

[30] Wang, Q., Cao, Y., Liu, X., Fu, Y., Zhang, J., Zhang, Y., *et al.* (2024) Systematic Review and Meta-Analysis of Tuberculosis and COVID-19 Co-Infection: Prevalence, Fatality, and Treatment Considerations. *PLOS Neglected Tropical Diseases*, **18**, e0012136. https://doi.org/10.1371/journal.pntd.0012136

[31] The TB/COVID-19 Global Study Group (2022) Tuberculosis and COVID-19 Co-Infection: Description of the Global Cohort. *European Respiratory Journal*, **59**, Article 2102538. https://doi.org/10.1183/13993003.02538-2021

[32] Di Bari, V., Cerva, C., Libertone, R., Carli, S.M., Musso, M., Goletti, D., *et al.* (2025) Impact of Severity of COVID-19 in TB Disease Patients: Experience from an Italian Infectious Disease Referral Hospital. *Infectious Disease Reports*, **17**, Article 11. https://doi.org/10.3390/idr17010011

[33] Gupta, N., Ish, P., Gupta, A., Malhotra, N., Caminero, J.A., Singla, R., *et al.* (2020) A

Profile of a Retrospective Cohort of 22 Patients with COVID-19 and Active/Treated Tuberculosis. *European Respiratory Journal*, **56**, Article 2003408. https://doi.org/10.1183/13993003.03408-2020

[34] Mihuta, C., Socaci, A., Hogea, P., Tudorache, E., Mihuta, M.S. and Oancea, C. (2025) Comparative Insights into COVID-19 and Tuberculosis: Clinical Manifestations, Inflammatory Markers, and Outcomes in Pulmonary versus Extrapulmonary Tuberculosis and *SARS-CoV-2* Co-Infection. *Journal of Clinical Medicine*, **14**, Article 2782. https://doi.org/10.3390/jcm14082782