

## Review Article



# Tuberculosis Patients During COVID-19 in India (2020–2023): A Brief State-of-the-art View

Jineetkumar Gawad<sup>1\*</sup> , Mayank Sharma<sup>2</sup>, Neelam Kamble<sup>1</sup>, Sanghadeep Gajbhiye<sup>1</sup> and Sunita Ogale<sup>1</sup>

<sup>1</sup>VIVA Institute of Pharmacy, Virar (East), Palghar, Maharashtra, India; <sup>2</sup>SVKM's NMIMS School of Pharmacy and Technology Management, Shirpur Campus, Shirpur, India

\*Correspondence to: Jineetkumar Gawad, VIVA Institute of Pharmacy, Virar (East), Palghar, Maharashtra 401 303, India. ORCID: <http://orcid.org/0000-0001-7196-2125>, Tel: +91-9860777446, E-mail: [gawadjinit@gmail.com](mailto:gawadjinit@gmail.com)

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## Abstract

Tuberculosis (TB) is an airborne life-threatening respiratory disease, and India endures the highest burden of TB cases worldwide. Moreover, the COVID-19 crisis has significantly disrupted essential health services in India, making TB control even more challenging. In a densely populated country such as India, the COVID-19 pandemic has further complicated TB regulation, as millions of Indians now carry latent TB infections (dormant stage of *Mycobacterium TB*) that could reactivate at any time. The purpose of the present review is therefore to highlight the scenario of TB patients during COVID-19 pandemic as COVID-19 and TB both severely affects patient's respiratory systems. The COVID-19 pandemic placed strain on many patients including those with TB and even in the 21st century, with today's advanced medical facilities and technologies, SARS-CoV-2 infection has created a mountain of challenges for mankind. Furthermore, the pandemic has redirected a portion of healthcare workers towards COVID-19 management activities, resulting in a limited workforce available to address TB management; thus, the threat to TB patients is expected to persist in the future. This short review therefore aims to enlighten young researchers about the possibilities and preparedness for future pandemic situations.

**Keywords:** Tuberculosis; COVID-19; Virus infection; Pandemic; Treatment; India.

## Introduction

World Health Organisation (WHO) estimates suggest that India accounts for almost 1/3 of all global Tuberculosis (TB) cases. TB remains a significant global cause of mortality, with India contributing to the majority of global TB cases.<sup>1</sup> Despite the brief decline in TB patients observed in 2020 and 2021, the National Tuberculosis Elimination Programme (NTEP) reported results beyond these numbers. 2022 was a milestone year for TB surveillance efforts in India, with a record number of approximately 2.5 million cases; an increase of 13% compared to 2021. Meanwhile, the total number of drug-resistance cases diagnosed in 2022 was 63,801. Sustaining the momentum of diagnosing previously undiagnosed TB patients by strengthening case-finding efforts (both passive and active) led to the above achievement under the program.<sup>2</sup>

Efforts to bridge the gap in TB case diagnoses in India showed promise before the COVID-19 pandemic, with a 60% rise in TB case detection from that of the previous decade. However, COVID-19 had a severe impact on TB patients, the diagnostic process, and ultimately on TB in India.<sup>3,4</sup>

Recent data suggests that from the pandemic's onset, the associated control and preventive measures taken may have affected various factors related to TB. A considerable

rise in TB-related deaths and setbacks in TB control were expected, but disturbingly, early data on TB case notification from India indicated a 70% decrease in case reporting time particularly from 15–20 weeks in 2020 as compared 2019.<sup>5–8</sup> The review aims to examine the different facets of TB and COVID-19, including how the processes of TB diagnosis were affected during the pandemic.

## TB before COVID-19

TB still represents a significant public health challenge worldwide, affecting nearly 30,000 individuals daily and causing 4,000 deaths worldwide each day, despite being preventable and curable. The standard treatment for drug-sensitive TB involves a six-month regimen combining four first-line anti-tubercular drugs.<sup>9–13</sup>

Drug-resistant TB (DR-TB) has emerged due to acquired and transmitted resistance among TB strains, leading to forms such as rifampicin-resistant TB (RR-TB), multi-DR-TB (MDR-TB), and extensively DR-TB (XDR-TB). MDR/RR-TB is becoming a potential hazard to TB control.<sup>14–16</sup>

Governments aiming for a 95% reduction in TB deaths and a 90% reduction in incidence by 2035, with interim mile-

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stones, must adhere to key principles in implementing the End TB Strategy. This includes government stewardship, strong coalitions with civil society, protection of human rights, and adaptation at the country level. Customizing the global strategy based on in-depth analyses of local TB epidemics is crucial alongside global collaboration, especially given rising travel, migration, and threats to health security. This approach aligns with ambitious targets and ensures effective TB control while respecting human rights and equity.<sup>17–20</sup>

Advancements in TB management have been achieved through the inclusion of new analogues such as Bedaquiline and Delamanid as well as repurposed drugs such as Linezolid and Clofazimine in combination regimens for DR-TB over the past couple of years.<sup>21</sup> The World Health Organisation is actively working to enhance treatment success rates and has introduced all-oral longer regimens with new drugs lasting 1.5–2 years for DR-TB patients. Furthermore, a concise year-long treatment therapy has been implemented, demonstrating promising advantages in minimizing drug burden, accelerating culture conversion time, reducing the risk of infection transmission, mitigating adverse drug events, and lowering overall costs. This approach contributes to enhanced treatment adherence.<sup>22–25</sup> Moreover, the provision of complimentary laboratory services for patients attending public health facilities and those referred from the private sector has been a longstanding practice since the program's inception, and over time, the initiative has established one of the most extensive TB diagnostic networks. Following the pandemic, the NTEP has displayed adaptability by incorporating global and Indian evidence into the treatment and care of individuals affected by TB. In recent years, India has made far-reaching progress in the management of TB including drug-resistant DR-TB and scaling up of shorter oral regimens across the country. Similarly, the program introduced a comprehensive package of differentiated care for TB patients to identify the patients requiring referral or hospitalization at the time of diagnosis to reduce preventable mortality among TB patients; various states/union territories have begun implementing the differentiated care approach adopting different modalities with collaborations. Also, addressing the various delays, thereby improving the quality of care provided to TB patients, has been one of the focus areas monitored periodically by the program. To offer last-mile service delivery for better access and quality care to TB patients, including DR-TB patients and their close contacts, the program has decentralized TB services to the Ayushman Bharat – Health and Wellness Centres.<sup>26</sup>

## Beginning of 2020

At the beginning of 2020, the WHO announced the infection of novel coronavirus globally, indicating that the highly infectious virus had spread beyond containment measures in many countries. The symptoms of COVID-19 were very common, such as flu or viral fever; initially, individuals may experience mild symptoms, often mistaking it for a common flu. Being a respiratory disease, the virus can spread through inhaling droplets in the air or by touching infected surfaces.<sup>27–32</sup>

India reported its first positive patient of COVID-19 on 30th January 2020 in Kerala, with the affected individual having a travel history from Wuhan, China. The Indian government issued an advisory for voluntary home quarantine

(self-isolation) to prevent early-stage virus spread. People at high risk for severe illness from COVID-19, such as the elderly, sick individuals, and children, were recommended to practice protective self-separation at home. In terms of drugs, Remdesivir and some other antivirals were used for the management of the virus.<sup>33–35</sup>

The pandemic significantly impacted TB patients and associated services, leading to a decline in the diagnosis of new active TB cases (possibly due to the testing and diagnosis process being affected). Challenges in outpatient settings, community TB management, monitoring, and the supply of anti-TB medications were observed. The pandemic restrictions also affected COVID-19 testing, with lockdown measures exacerbating these issues. Concerns regarding personal protective equipment, prevention of DR-TB, and the safety of healthcare workers were notable. Additionally, the pandemic had implications for TB immunization programs with economic consequences.<sup>36</sup> To attain the goal of ending TB by 2025, India has rebranded its program as the NTEP and is executing TB prevention and control initiatives with a mission-oriented approach. In March 2020, the impact of COVID-19 disrupted crucial strategic interventions, leading to a nearly 60% decrease in TB notifications during the lockdown. However, a rapid response plan has effectively restored and expanded TB services to levels surpassing those before COVID-19.<sup>37</sup> This program has revitalized the country's TB elimination efforts by incorporating innovative strategic interventions to accelerate the NTEP response (<https://tbcindia.gov.in/showfile.php?lid=3551>).

As of April 2023, the pandemic is considered to be in its end stage as suggested by the WHO. However, it is still essential to follow safety protocols to prevent further outbreaks. According to statistics from the Health Ministry, Government of India, there had been 21,179 active cases, 44,177,204 discharged cases, and 530,901 reported deaths due to COVID-19 in India by that time.<sup>38–41</sup> Despite 60 years of chemotherapy and 90 years of vaccination employing various strategies to prevent and control TB, it continues to be a significant global health challenge, ranking 13th in leading causes of mortality worldwide. In 2021, TB ascended to the second position, following COVID-19, as the leading cause of infectious fatalities, claiming the lives of approximately 1.6 million people (including 187,000 individuals infected with HIV). Notably, the COVID-19 era in 2020 witnessed a substantial global reduction in TB incidence, plummeting from 7.1 million cases in 2019 to 5.8 million in 2020. India, along with Indonesia and the Philippines, is prominently featured among the top three countries contributing to 67 percent of this global reduction in TB incidence. However, one study revealed an 80 percent reduction in TB notification rates in India during the lockdown period thus, despite India ranking fourth globally in COVID-19 infections and deaths, there is a potential scenario wherein a slowdown in COVID-19 could unveil hidden TB cases and fatalities, leading to an increase in TB counts in the future. Despite certain similarities in manifestation and differences in etiology, a comprehensive understanding of the epidemiological relationship between TB and COVID-19 is still lacking.<sup>42</sup>

## Diagnosis of TB during the pandemic

Despite some differences in their modes of transmission,

both TB and COVID-19 can spread through close physical contact between infected individuals.<sup>43</sup> Additionally, they share similar clinical features and presentations, which could have complicated diagnosis and management during the COVID-19 pandemic.

It is possible for a person to have concurrent infections of both SARS-CoV-2 (the virus causing COVID-19) and *Mycobacterium tuberculosis* (TB). In such cases, the damage caused by pre-existing TB infection may predispose the patient to develop COVID-19 or experience more severe COVID-19 symptoms. Therefore, it is important to be vigilant about the possibility of co-infection during the pandemic.<sup>44</sup> Globally, coinfection with TB and COVID-19 is prevalent, and individuals experiencing both infections face a higher risk of fatality compared to those with singular COVID-19 infections. Results shared significant differences between high-income countries and low- and middle-income countries.<sup>45</sup>

COVID-19-induced circumstances have significantly impacted TB services across various dimensions. Public and private health facility closures have resulted in reduced access to TB diagnosis and notifications. Fear of contracting COVID-19 has led to a decline in TB service uptake, exacerbated by the stigma of both diseases and challenges in supply chain management. NTEP officers and health workers engaged in COVID-19 activities have shifted focus, engendering diminished attention towards essential TB services such as active case finding and patient engagement. Lockdown-induced geographical restrictions have hampered TB adherence, while the non-availability of transport services complicates sample collection and dispatch. The use of NTEP labs for COVID-19 testing has diminished capacity for TB testing, diagnosis, and follow-up.<sup>46</sup> Lockdown-related mobility restrictions further impact the provision of additional TB program services, including those related to HIV, diabetes, and beneficiary transfer payments (<https://tbcindia.gov.in/showfile.php?lid=3551>).

Healthcare professionals should consider conducting simultaneous testing for both TB- and COVID-19-suspected patients who present with asymptomatic or unusual clinical symptoms. Maintaining a high index of suspicion for co-infection will help facilitate appropriate and timely management for affected individuals. Early detection and treatment of both diseases are crucial to ensure the best suitable/available outcomes for patients with concurrent TB and COVID-19 infections (<https://www.who.int/publications/digital/global-tuberculosis-report-2021/featured-topics/covid-19-tb-india>). Until 24th March 2020, India was on track to eliminate TB by 2025 but the national and state-specific COVID-19-induced lockdown affected all the key strategic interventions; however, the country is now better prepared to tackle TB than ever having advanced and effective interventions and technologies for the diagnosis, treatment, and care of TB cases. During the period Jan-June, 2020 almost half a million cases were not notified against the estimated target due to the COVID-19 and lockdown situation. Bi-directional screening was implemented to facilitate the screening of COVID-19 among individuals diagnosed with TB and vice versa. To enhance diagnostic capabilities, the number of machines for nucleic-acid amplification tests (NAATs) was doubled through the acquisition of 159 GeneXpert (CB-NAAT) machines and 1,512 Truenat machines. This resulted in an increased capacity for conducting an additional 9,200

COVID-19 tests and 4,600 TB tests per day. Consequently, the diagnostic capacity for TB, which had initially been redirected for COVID-19 testing, was not only restored but also augmented. Sputum smear microscopy testing for TB was replaced with NAATs for all individuals with presumptive TB. Moreover, laboratory services for TB and COVID-19 testing were decentralized and integrated to optimize their utilization, and referral linkages between TB and COVID-19 services were established.<sup>47–49</sup>

## Future recommendations for TB patients in India

India has set a determined goal to completely eradicate TB by the end of 2025; however, the COVID-19 pandemic has created a sufficient number of obstacles to achieving this goal. To mitigate the impact of the COVID-19 pandemic on TB infection control efforts, it is essential to adopt consistent practices that prioritize the ultimate goal.

Urgent action plans should be implemented to control TB infections as well as coinfection with TB and coronavirus respiratory disease, which has proven to be more fatal if not treated timely. Furthermore, availing of the advent of advanced medical technology and cell phones could facilitate quick and easy assessment and supervision for TB patients, contributing to improved management.<sup>50–52</sup>

Integrating TB and COVID-19 responses could enhance India's health outreach. Ensuring continuous drug and treaty supply for TB treatment through careful planning of local and regional distribution and transportation is crucial, especially for the vulnerable population at a higher risk of adverse TB outcomes.

Furthermore, the novel advanced diagnosis and treatment technologies developed to manage COVID-19 should be adapted or modified to effectively tackle TB as well. Despite the challenges posed by the pandemic, targeted health approaches, organized social policies, and special care for the mental health and health equity of infected TB patients and others must remain a priority.<sup>53,54</sup>

In conclusion, concerted efforts are needed to combat both TB and COVID-19, taking into account the specific challenges posed by the pandemic while ensuring equitable and effective healthcare for all.<sup>55,56</sup>

## Conclusions

The fact that India has the highest number of active TB cases worldwide underscores the importance of recognizing the burden of this disease, especially in the face of challenges presented by the COVID-19 pandemic. It is, therefore, crucial to adapt and re-evaluate prevention, testing, tracing, and management strategies for TB patients to effectively address their needs in the aftermath of the pandemic.

The experiences and lessons learned in battling COVID-19 can provide valuable insights for enhancing and improving existing TB programs and strategies. By leveraging the knowledge gained from managing COVID-19, India could identify areas for improvement and innovation to advance its efforts towards the ambitious goal of eliminating TB from the country by 2025.

Incorporating the insights gained from the COVID-19



response into TB control initiatives could lead to the development of more resilient and effective systems, better equipped to meet the requirements of TB patients and guarantee that they receive essential care and attention, even amid the pandemic. By giving equal priority to both diseases and adopting well-coordinated strategies, India could make substantial progress in tackling TB while simultaneously addressing the challenges posed by COVID-19.

Collectively, the effects of TB and COVID-19 response strategies could lead to a more comprehensive and effective healthcare approach, ultimately bringing India closer to achieving its goal of TB elimination by 2025.

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## Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Author contributions

Conceptualised the contents for manuscript and written the manuscript: JG; collected the relevant data: NK; proof read the manuscript: MS, SG, SO. All the authors mentioned here made significant contributions in preparation of this manuscript and have approved the manuscript.

## Abbreviations

TB, Tuberculosis; NTEP, National Tuberculosis Elimination Programme; RR-TB, Rifampicin-Resistant TB; MDR-TB, Multi-Drug Resistant TB.

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