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Impact of the COVID-19 Pandemic on tuberculosis management in India: A Brief Overview

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KEYWORDS

Tuberculosis

COVID-19

Emerging viral infections

Pandemics

ABSTRACT

Chronicles suggests that emerging and re-emerging viral infections disrupting the normal lifestyle of humankind, whether in the form of HIV, Ebola, Influenza, Nepah, or the current SARS-CoV-2 pandemic. Such viral infections disrupt the healthcare system along with the prevention and control of epidemics and pandemics, resulting in an increased burden of such diseases in the post-pandemic period. Tuberculosis (TB) routine services are interfered with by severe lockdowns due to the new COVID-19 virus. This article tried to measure the long-term epidemiological effects of such interruptions on TB prevalence in high-burden countries. The participating facilities performed a comprehensive review based on modifications to the care of TB patients during the COVID-19 pandemic. Retrospectively, clinical factors and household contact information were collected from a literature survey. Researchers looked at numerous strategies over the following five years to see whether they might lessen the effects on TB incidence and death. Present comprehensive literature was collected and analyzed using suitable keywords such as "COVID-19," "Pandemics," "Tuberculosis," and "India" during the current COVID-19 pandemic to investigate the influence of COVID-19 on tuberculosis management. The present article looks at the effects of the breaks in the delivery of TB care in hospital and primary care settings. Lockdown, social isolation, measures to prevent viral transmission, and public health guidelines impacted tuberculosis care. The present study revealed that the COVID-19 pandemic has adversely affected numerous TB prevention, monitoring, and treatment programs. Still, these adverse effects are diminished by the prompt restoration of TB services and the application of particular therapies as soon as restrictions are lifted.

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1 Introduction

COVID-19, a respiratory viral disease, was first reported in Wuhan, China, and later spread to almost every country with a slightly different infection rate (Wu and McGoogan 2020). The severity of infection ranges from a common cold to more severe illnesses such as pneumonia reported after the entry of the causative agent SARS-CoV-2 (Chen et al. 2020; Walaza et al. 2020; Budinger et al. 2021). Human-to-human transmission occurs when infectious droplets are inhaled or move into the body through contact with infected surfaces. Supportive care is the most common treatment option, while major illnesses may necessitate a ventilator (Ahn et al. 2020; Dhama et al. 2022).

Of 10 million globally reported tuberculosis (TB) instances, around 2.6 million were reported from India. Further, approximately 0.44 million people die yearly due to this disease. According to the World Health Organization (WHO), one-third of the world's multi-drug-resistant TB infections are found in India (Santosh and Pushp 2022). The worldwide risk of infectious illnesses, especially TB, has long been faced by public health agencies. The World Health Organization's (WHO) "real-life" analyses (surveys and national monitoring programs) provide the majority of information and projections related to global TB epidemiology (Golli et al. 2019). Although nowadays, TB incidence is decreasing, after this also, it remains a serious problem across the world (Crisan-Dabija et al. 2020), particularly in most middle-income and emerging nations, where it is the ninth worldwide leading cause of death. For Eastern European public health, TB has the highest incidence (4 times the average) in the European Union (EU), accounting for a quarter of the overall TB burden in the EU (Small et al. 2010). Various pandemic diseases also significantly affect several aspects of TB endemic. Like, in 1918 influenza pandemic accelerated the decreasing prevalence of tuberculosis in the USA (Noymer 2011). In India, the severity of the TB endemic has increased due to various factors, including a large number of severe forms (MDR or XDR-TB), HIV coinfection, and TB mortality in children. These factors have amplified the intensity of the country's tuberculosis epidemics (Dhamnetiya et al. 2021).

A worldwide health disaster, including TB, has occurred with the COVID-19 pandemic. But national tuberculosis programs, while preserving TB services, actively work to provide an efficient and prompt response to COVID-19 (Tadolini et al. 2020). Although the transmission routes differ, tuberculosis and COVID-19 are transmitted by close personal contact. Because tuberculosis is a prominent transmissible infection in India, public health should continue to focus on surveillance, clinical evaluation, testing, contact tracing, and diagnostic confirmation with supervised/inspected treatment regimes during the COVID-19 pandemic (Lancet 2020). Therefore, the present article looks at the effect of the COVID-19 pandemic on various TB management services (Figure 1).

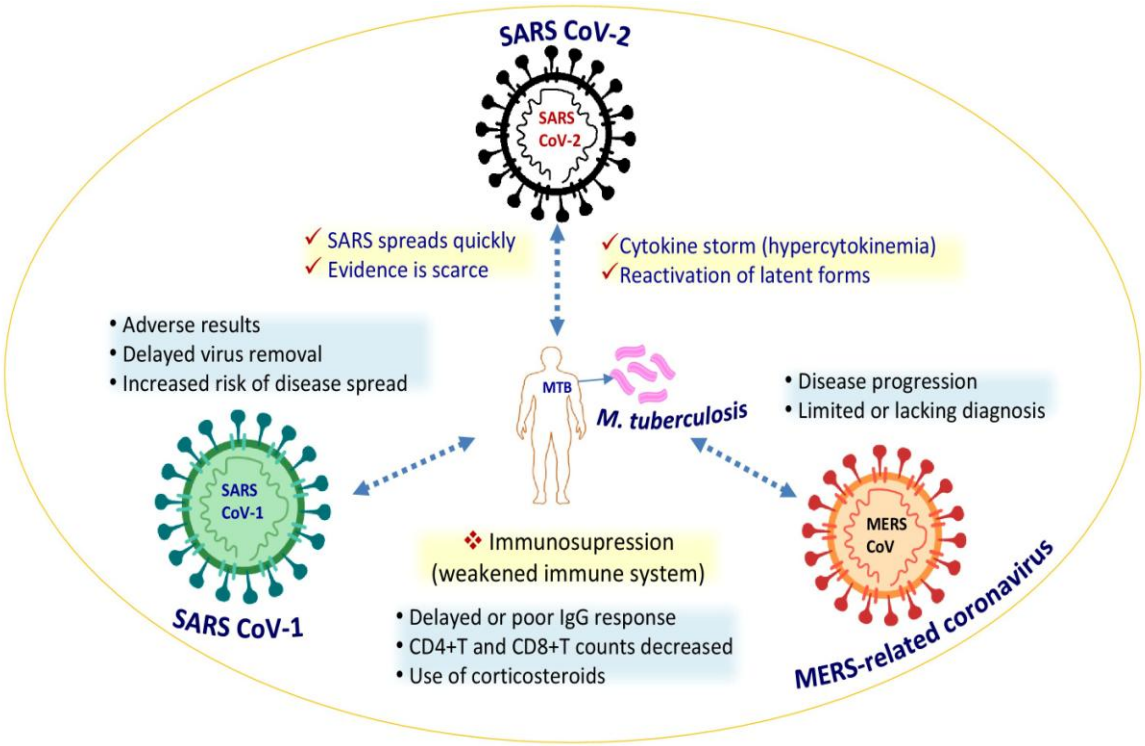

Figure 1 Coronaviruses and MTB: recognized and possible interaction

2 Impact of lockdown

Information regarding the possible connections between COVID-19 and TB in the wake of COVID-19 announcements as an International Public Health Emergency is in scanty, and all the available data were based on assumptions and modelling, then scientific verification (Tadolini et al. 2020; Motta et al. 2020; Migliori et al. 2020; Buonsenso et al. 2021). The novel SARS-CoV-2 virus has resulted in global illness, mortality, and societal consequences. Many countries have used population-wise lockdowns to halt the virus spread and allow their health services to manage it without drug treatments (Anderson et al. 2020). These lockouts significantly impact the transmission of SARS-CoV-2 (Walker et al. 2015; Flaxman et al. 2020; Prem et al. 2020). However, with such comprehensive actions, unexpected repercussions are unavoidable. After the dislocation, under pressure, the negative interruptions in health services (e.g., the spread of infectious illnesses) might endure long in poor and middle-income nations' health systems (Parpia et al. 2016; Arinaminpathy and Dye 2010).

TB incidence and death have substantially declined in recent decades due to continuous advancements in diagnosis, therapy, and prevention. However, COVID-related lockdowns in March 2020 brought the stop TB program to serious attention in several countries (Garg et al. 2022). For example, in India, an 80% reduction in the daily TB notifications was reported after the first weeks of the national lockdown on March 24, 2020 (Zignol et al. 2012). In other nations, such as South Africa, a decline of nearly half in the number of persons tested for tuberculosis was reported during the lockdown (Coker 2004). Such falls may also be attributable in the other part of the world; this might be due to the delay in reporting or decreases in access to diagnosis and treatment; whatever the factors are responsible for this decline but all these have a sustainable effect on the national monitoring and controlling program of TB disease. Missing diagnoses would increase the incidence of transmission while deteriorating treatment outcomes would raise the chance of TB mortality during the lockdown period.

3 Impact of the COVID-19 pandemic on Mycobacterial infection

COVID-19 and tuberculosis (TB) need public awareness and cooperation to effectively prevent, diagnose, and treat. Both diseases have airborne transmission and can be quickly detected (Dheda et al. 2022). Although surveillance on TB and viral infections should be separate because the data related to COVID-19 is still insufficient in the majority of countries, and the specific crucial clinical and immunological data which can be associated the TB with COVID-19 are not yet available (Visca et al. 2021). The primary distinction between these two is that tuberculosis is treatable, but there is no conclusive evidence of effective antiviral treatments for COVID-19. Although Remdesivir, lopinavir, hydroxychloroquine, lopinavir, and interferon repurposed, antiviral drugs had little to no impact on hospitalized patients with Covid-19 as evidenced by overall mortality and length of hospital stay (WHO Solidarity Trial Consortium 2021). For both diseases, research on novel and efficient vaccine candidates is ongoing, and for tuberculosis, various potential candidates are being evaluated to replace the traditional BCG vaccine (Cantini et al. 2020). Currently, mRNA vaccines, RNA-based replicating vector vaccines, and inactivated virus vaccines are in the clinical trial stage for SARS-CoV2 variants and candidates for DNA vaccines are in the pre-clinical trials stage (Narayanan et al., 2022). Proper and regular treatment is the primary method of disease control in the absence of an adult-specific tuberculosis vaccine. Increased tuberculosis transmission is anticipated because so many cases were missed or away from regular treatment during the past two years due to the pandemic effect (Pai et al. 2022).

Detrimental synergism between respiratory viruses (RSV, influenza viruses, and SARS-CoV-2) and bacterial infections elevates the risk of relatable mortality due to chronic lung sickness and immune suppression (Oliva and Terrier 2021). Especially patients with PTB may have a greater risk of these severe infections when compared to non-TB persons. Further, epidemiologic data also imply that patients with TB have a higher risk of viral diseases and are severely associated with pandemics or epidemics (Redford et al. 2014; Prem et al. 2020).

4 Diagnostic Tests

To determine the most appropriate diagnostic tests in most scenarios that apply to Mycobacterium TB and SARS-CoV-2, the WHO has established assured criteria like user-friendly, robust, sensitive, specific, and deliverable to end users. However, regardless of the pathogen, a fundamental shortcoming of all present assays is the difficulty in swiftly determining the pathogen if it is alive and contagious (Mina et al. 2020). The viability of *M. tuberculosis* requires a minimum of six weeks of culture results. Even in these days of cutting-edge technology, information regarding the COVID-19 individuals compared to 'no COVID-19' individuals, the IFN-response to the SARS-CoV-2-unrelated antigens Staphylococcal Enterotoxin B (SEB) and cytomegalovirus (CMV) was compared in whole blood using an innovative experimental method by Petrone et al. (2021), which claims that the SARS-CoV2-specific response may be measured in whole blood and can be seen in both acute and convalescent patients (Murugesan et al. 2021). Both nucleic acid detection and antigens-based tests are available for both diseases, but *M. tuberculosis* is diagnosed using culture-based and smear methods, and SARS-CoV-2 is diagnosed using serology.

Recently, testing people with COVID-19 for TB and vice versa has been the subject of significant debate. The common clinical

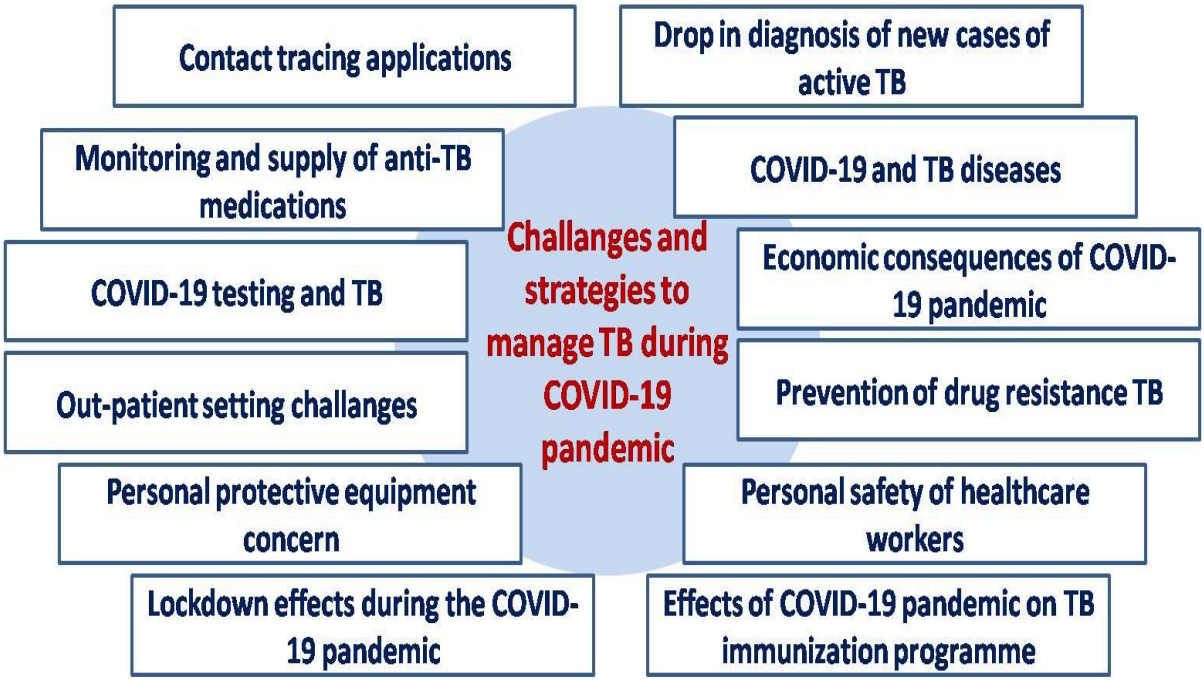

Figure 2 TB management, challenges and strategies during the COVID-19 pandemic

characteristics and manifestations of COVID-19 and TB are fever, breathing deficiency, and coughing. The disease development processes have clear distinctions, and COVID-19 infection develops less quickly than tuberculosis (Visca et al. 2021). Concurrent TB does not exclude the possibility of COVID-19 infection, especially in a TB-endemic country like India (Jain et al. 2020). The European Laboratory Initiative recommended the utilization of the GeneXpert equipment for COVID-19 testing without diminishing its TB usefulness (Simoes et al. 2022). Further, the Truenat™ Beta CoV Test on the Truelab™ workstation has recently been approved for use as a test for COVID-19 by the ICMR (Figure 2).

4.1 Challenges in Diagnose new cases of active tuberculosis

The need to find supplementary strategies to support patients with tuberculosis has been rising with the constraints of confinement and face-to-face reduction. Telemedicine can assist in the management of TB in communities. Admitted Social Health Activist (ASHA), one of the primary members of India's NRHM, would have to visit a TB patient's house to see whether the patient is following treatment (Xu et al. 2017). The continuing lockdown during the COVID-19 epidemic has seriously affected the treatment of TB sufferers, that's why, according to the Nikshay Government of India Central TB Portal (Suárez et al. 2019), the diagnosis of new TB patients has dropped dramatically during the lockdown. The factors associated with this dropdown are the closing of outpatient departments (OPD), lack of access to treatment, and the denial of government or private injection.

5 Anti-TB medication supervision and distribution

The Minister of Health and Family Welfare (MOHFW), Government of India, is attempting to arrange guaranteed diagnosis and treatment of TB patients in a one-month approach, but during the lockdown, many difficulties have been raised in this (Suarez et al. 2019). Monitoring the sickness process of TB patients was a big challenge for health workers to serve TB patients in the era of social alienation and self-isolation due to the lack of medications and restocking the medication at the patient's home. The various countries ' local governments have devised many strategies for establishing outreach services to contact TB patients and send TB medications via mail (Xu et al. 2017). In the case of multidrug-resistant TB, the World Health Organization (WHO) recommends reducing the TB preventive regimen to 1 month per day for persons who have close contact with active TB patients who are treated with rifapentine and isoniazid (https://tbcindia.gov.in). Recently, the government of India advised patients in the ambulatory setting of TB drugs that they should be supplied for one month with TB drugs, as well as a 2-month supply for exceptional conditions, to lessen the patients' requirement to attend clinics and consequently, the danger of disease transmission (https://tbcindia.gov.in).

5.1 Applications for contact tracking

The main factors for the management of both tuberculosis and COVID-19 in society are contact tracing and monitoring. The unexpected increase in the requirement for COVID-19 patient

tracking, the government of India's establishment of the ArogyaSetu 'COVID Health Bridge' app for mobile tracking, raises worries about the diversion of the contact monitoring services given for COVID-19 and tuberculosis (Sharma et al. 2020). The Uttar Pradesh Government Ayush Kavach app was also found helpful in tracking COVID-19 individuals. The impact of the COVID-19 pandemic on the inconvenience of essential contact tracking for TB patients should be ignored. The knowledge gained through the TB contact apps should be used to improve the COVID-19 app's functionality. After the completion of the lockdown, an incidence of TB cases may arise, and to avoid this, the effective use of Ni-Kshay Aushadhi, a web-based application that allows the monitoring of all TB patients, including MDR cases, is required (Jain et al. 2020).

5.2 COVID-19 Effect on the TB Vaccine Program

TB protection is provided by the Bacille Calmette-Guerin (BCG) vaccination. Suspension vaccination programs have documented vaccine-preventable deaths connected with diseases and an increased strain on health systems due to the COVID-19 pandemic lockdown (Lobo et al. 2021). In countries with high TB incidence, such as India, South Korea, Indonesia, China and Turkey, the WHO recently suggested extending the newborn neonatal TB BBG vaccine. Evidence indicates that BCG also protects against many viral and non-mycobacterial infections. The idea that BCG vaccination could be used for protection against the adverse effects of coronavirus disease stems from the non-specific effects of BCG, which happen through the induction of trained immunity (Curtis et al. 2020). Phase IV trials are now underway to assess the role of these non-specific vaccines in SARS-CoV-2 infection protection (Lobo et al. 2021).

6 Discussion

The awareness of tuberculosis patients is still the cornerstone of tuberculosis prevention and treatment, which will help diagnose and cure TB patients. Further remote teleconsultation would be helpful in monitoring and treatment of TB patients. The continuation of vital care for TB patients throughout the COVID-19 epidemic should not be ruptured till the demolishing of COVID-19. To avoid the transmission of SARS-CoV-2 in tuberculosis patients a proper hospital care for patients with tuberculosis should be confined to severe cases, as learned from past outbreaks (Visca et al. 2021; Dheda et al. 2022). Since the first discovery of coronavirus in 1960, three human coronaviruses have been known to cause deadly respiratory illnesses. The newest emerging coronavirus (SARS-CoV-2) has resulted in an increasing number of worldwide reported deaths and thousands of new cases confirmed every day, and epidemic diseases like TB also contributed to this pandemic. COVID-19 causes a wide spectrum of host immune responses in asymptomatic patients, from mild cytokine storms to deadly cytokine storms (Dhama et al. 2020). Immunosuppression which has been used to treat COVID-19 can potentially reactivate TB. The gold standard diagnostic testing for COVID-19 includes culture and PCR-based techniques for TB; however, a definitive point-of-care test that can immediately detect if someone is currently infected with TB. New SARS-CoV-2 variants (like omicron) are emerging due to vaccine equity issues, and they are particularly harmful to nations with low vaccination, high poverty, and high tuberculosis rates. More research is required to completely understand COVID-19's abilities to stimulate the reactivation of an existing TB infection. Because COVID-19 and TB have similar signs and symptoms, getting imaging services (chest radiography or computed tomography) may be simpler to uncover evidence of pre-existing TB. There is insufficient information to establish the probable impact of COVID-19 on TB patients' treatment because most of these patients are still receiving treatments in existing series. New SARS-CoV-2 variants like omicron are emerging due to vaccine equity issues, and they are particularly harmful to nations with low vaccination, high poverty, and high tuberculosis rates (Dhama et al. 2022).

Moreover, Crisan-Dabija et al. (2020) suggested that influenza pandemics, seasonal outbreaks, coronavirus epidemics, and other pandemics negatively influence individuals with tuberculosis. A global patient research project is underway to improve the description of communication between the two illnesses (WHO) conducted by the Global Tuberculosis Network and funded by WHO on TB and COVID. These studies mainly describe the features of COVID-19 patients, including diagnostic trials and recommended treatments, and TB patients (current or former). The secondary goal of these types of projects is to (i) evaluate the logistical and organizational viability of a global repository for COVID-19 and TB patients and (ii) explain the clinical outcomes (COVID-19 disease outcomes and TB patients' intermediate and final treatment results). With this global study and others, the GTN has recommended several priority research issues, which included (i) how COVID-19 would affect TB services in the next few years, considering the growing impacts of its third wave?, (ii) is COVID-19 associated with an increased risk of TB illness in those with TB?, (iii) does the BCG vaccine offer COVID-19 protection?, (iv) What additional factors influence mortality in patients with TB and COVID-19?, (v) Is there a difference in treatment for TB & COVID-19 co-infected patients? (Or, to put it another way, what additional services do these patients require?), and (vi) what effect does COVID-19 have on TB mortality?

Compared to COVID-19, tuberculosis care and management have been neglected, while the high infection rates, the emergence of new variants, and the absence of the SARS-CoV-2 vaccine in tuberculosis-endemic countries will continue to feed

the global pandemic. The simultaneous epidemics of tuberculosis and COVID-19 exacerbate the vicious cycle of poverty and mortality (Dheda et al. 2022). Disruptions to HIV diagnosis and treatment programs may also contribute to the tuberculosis pandemic in some circumstances (Hogan et al. 2020). Maintaining the most important HIV and tuberculosis prevention programs and medical services could significantly lessen the overall effect of the COVID-19 pandemic (Hogan et al. 2020). Therefore, it is essential to support and refocus HIV and tuberculosis programs.

Conclusion and Future Prospects

The outbreak of COVID-19 and the limitations of lockdowns significantly impact the national and worldwide implementation and monitoring of TB surveillance initiatives. Delays in treating people with TB would aggravate their condition and require more comprehensive management. Individuals with TB may also acquire antibiotic resistance; these patients are susceptible to coronavirus superinfection. It is suggested that an effective and timely response, including monitoring and therapy, should be given to COVID-19 and TB patients. Despite the rapidly rising number of cases, there is still a long way to go before we know to evaluate how the COVID-19 pandemic will affect patients with latent TB and TB sequelae and suggest management in this situation. COVID-19 can strike at any time during a patient's TB journey, with the worst outcomes occurring in individuals with active pulmonary TB disease. According to the research available, death because of TB is significantly affected by various other important factors like malnutrition, diabetes, poverty, HIV coinfection and COVID-19. We need higher-quality prospective studies to address the research's most pressing concerns. Meanwhile, anyone with or without active TB, particularly those with HIV coinfection, must do all possible to prevent the growth of COVID-19 and, when possible, should be vaccinated appropriately.

Competing interest

The authors have no potential conflict of interest to declare.

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