

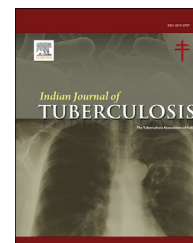


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Editorial

Challenges in TB control and the anticipated COVID-19 third wave: Way forward

Keywords:

Covid-19

Pulmonary TB

Lockdown

At the time of writing this, Coronavirus disease 2019 (COVID-19) continues to remain a major global issue. The second wave of COVID-19 between April 2021–June 2021 has severely affected the Indian subcontinent. As countries succeed in overcoming the COVID-19 second wave to an extent with vaccines and drugs, the fear of an impending third wave looms large. In nations like Africa, Brazil, India and Southeast Asia, the COVID-19 crisis may converge with another common infectious disease: tuberculosis (TB).^{1,2} TB and COVID-19 are currently the two main causes of death due to infectious diseases. The convergence between these two diseases raises concerns among health authorities, especially in TB endemic countries - Is COVID-19 flaring up TB? What will be the impact of the impending third wave on TB control? Can it be minimized?

1. Effect of COVID-19 on TB management

Worldwide this viral pandemic has caused a setback to the gains achieved in TB control by impairing TB diagnosis, delaying treatment initiation, aggravating TB deaths which in turn will adversely impact the TB Elimination targets of 2030. Since both TB and COVID-19 primarily affect the lungs, they share common symptoms which include cough, fever and breathing difficulty. Persistent respiratory symptoms in post-COVID-19 recovered patients can be mistaken as COVID-19 sequelae or secondary infection and delay the diagnosis of TB. When patients with such symptoms are hospitalized, in the background of the pandemic, the patches or opacities seen on chest x-ray and CT scan are assumed to be due to COVID-19, and the diagnosis of TB is missed which flares up later during post-COVID recovery. The delay in diagnosis of TB can

result in increased severity of the disease at presentation as well as the risk of TB transmission in the community. Also, during this period the GeneXpert machines were diverted for COVID-19 testing instead of testing for TB. Further, those hospitalized for COVID-19 were administered high doses of corticosteroids whether or not clinically indicated. From an immunological point of view, the TB and COVID-19 share dysregulation of immune responses and have the potential to converge in a “perfect storm”. Such irrational use of steroids can lead to immunosuppression, especially among diabetics, malnourished, those on dialysis or immunosuppressants, resulting in reactivation of dormant or latent TB infection (LTBI) especially among those recovering from COVID-19.

Once initiated on TB treatment, adherence and continuation of treatment were also impacted by the pandemic. Supply and supervision of TB drug administration were severely affected due to the mobilization of TB program staff to tackle the COVID-19 pandemic. Transportation of drugs and medical supplies, as well as restricted mobility of patients and healthcare staff due to multiple lockdowns, resulted in a delay in TB diagnosis, treatment initiation and follow-up leading to missed doses and treatment failure. Even BCG vaccination of children was severely reduced during this pandemic.³ Another important aspect is that both TB and COVID-19 share similar social determinants, including overcrowding, poverty, and air pollution.⁴ Extended lockdown periods resulted in lack of jobs affecting the family economy severely. Hence with the lifting of lockdown, people are more eager to return to jobs and livelihood rather than seek health care thus further delaying the diagnosis.

Increasing COVID-19 cases took a heavy toll on the health care system. Many staff in other national programs including the TB Elimination program were diverted to work in COVID

care centres. Redeployment of TB services staff and reallocation of finances to COVID-related activities has impacted all activities of the TB elimination program from diagnosis to treatment and prevention. Supply chains were disrupted in many parts of the country. TB notification decreased between January 2020–June 2020.⁵ All this will adversely affect our progress made towards TB elimination targets. Global TB report 2020 has recognized this threat of COVID-19 and has called for action to accelerate progress towards global TB targets.⁵

2. Preparing for the “next”

India has faced two waves of COVID-19 so far - first in November–December 2020 and the second in March–April 2021. Given the emergence of new viral variants with higher transmissibility, lifting of lockdown, waning of protective immunity against the virus amongst the vaccines, there is a probability of a third wave of COVID-19 – maybe of a milder nature.⁶ Also, the intervening period between the COVID-19 waves is when we have to be cautious. Surveillance for both TB and COVID-19 needs to be meticulously followed as there is every likelihood that respiratory symptoms may be mistaken for one or the other. Also, an increase in TB cases may be expected in the post-COVID phase. This could be due to the combination of relaxation of lockdown with the availability of better transportation facilities, return of TB staff on CoV2 duty to their respective diagnostic centres leading to more TB cases being diagnosed. Activation of latent TB during the post-COVID phase can further worsen the situation. Hence, these individuals may need close monitoring for an extended period of time.

With the emergence of newer CoV2 variants like delta-plus and lambda, their effect on TB disease and latent TB infection have to be closely monitored. Continuous surveillance of both diseases is the need of the hour. There is not sufficient evidence available to suggest that the COVID-19 third wave will largely affect children. Research so far has indicated that healthy children have milder disease, better prognosis and low mortality in comparison to adults. Hence, when we commence vaccination in children, and scale-up for other age groups, those with a higher risk must get vaccinated first followed by the group at lesser risk.

What can we do differently? Modelling studies have shown that between 2020 and 2025 COVID-19 may cause an additional 6.3 million cases of TB globally and an extra 1.4 million death.⁷ To contain and mitigate the devastation caused by the dual infection, encourage the private sector to work with the public sector. Civil-society organizations (CSOs) and the media can raise awareness of COVID-19 and TB among the public. Majority of the infection control practices for SARS CoV2 are applicable for TB also. The wearing of masks, social distancing and avoiding large gatherings have to be re-emphasized on every occasion to reduce transmission of both diseases. The media can highlight stories on the realities of people affected by COVID-19 and TB and help spreading message on prevention and vaccination. Increasing the awareness about TB, availability of free diagnostic and treatment services including newer and patient-friendly regimens

in the Government sector should be publicized very widely using all forms of media like television, WhatsApp, Instagram etc. Famous and popular personalities, media-friendly “faces” should be made TB ambassadors in every state and they should be fully and more frequently used to publicize messages about TB.

Identify groups particularly at risk of both the disease, like pregnancy, diabetes, HIV, drug resistance TB and offer them extra support and care including priority in COVID vaccination. TB program should ensure uninterrupted diagnostic and management services during the coming days. Bidirectional testing of symptomatic patients should be practiced diligently. During the pandemic, telehealth services should be offered to all patients on TB treatment to answer queries and alleviate their fears about drug reactions and symptom management. Mobile digital x-ray vans and drug delivery at the patient's doorstep should be encouraged thus avoiding exposure of vulnerable patients to other infectious diseases. In addition, the use of artificial intelligence tools for a timely interpretation of a large number of chest x-rays taken in the field camps has to be considered.

Genomic surveillance have to be conducted across the country periodically to monitor for the emergence of further drug resistance to both COVID-19 and TB in the wake of any further pandemic or “third” wave. Government should invest and support more scientific and operational research to align and address COVID and TB research. For example, taking the corollary of HIV where immunosuppression can result in the progression of LTBI to active TB, immunomodulation secondary to COVID may also have a similar effect.

3. Going forward

COVID-19 pandemic has been a great eye-opener in the realm of medical research and development. The pandemic saw the convergence of industry, academicians, regulators and civil society organisations like never before. Good governance, Political commitment and international collaboration reached new heights during this period. Never before have we witnessed such an accelerated rate of adaptation of research findings for the clinical management of patients. New drugs and vaccines were made available for use even before phase 3 trials were completed. Fast-tracking of regulatory approvals, public-private as well as industry-academic partnership reached their peak during this pandemic. This forms a good role model which should be adopted in the TB field.

To achieve the SDG goal of TB elimination, fast-tracking of new drugs, regimens, vaccines, and most importantly, faster implementation of research findings in patient management should be the new norm. Extended monitoring and safety data collection can be done in the field as done for COVID-19 vaccines. Symptomatic COVID patients were quarantined. This along with lockdown definitely paved the way for reducing transmission and thus decreases new infection. This can be adopted for symptomatic pulmonary TB patients at least till they become sputum smear-negative and less transmissible. Is it time to bring back sanatorium care for symptomatic Pulmonary TB? In addition, financial security for TB patients could alleviate the economic burden caused by the disease.

Currently, available COVID-19 vaccines have definitely reduced the severity of the disease, hospitalization and death. As we scale up COVID-19 testing and vaccination drive, learning from the unprecedented speed of developing these vaccines, emphasis must be placed on fast-tracking the development of TB preventive vaccines on a mission mode.^{8,9} Only such a strategy can help achieve India's TB elimination targets, five years ahead of the rest of the world. Sharing of research results through pre-prints among international researchers, updated real-time guidance documents as and when new shreds of evidences are available should be adopted for TB elimination also. Pandemic has paved way for on-line interactions and better connectivity. Capacity building of TB program staff through online training sessions paves way for an empowered and educated workforce for TB.

TB research programs are affected in countries as the resources and manpower are diverted to COVID research. CSOs and the media should actively highlight the disruptions to TB health services and research and emphasize the needs of people with TB, and press for political commitment and continued funding for research while tackling other emergencies. Going forward TB research should not be a casualty of COVID-19. In fact, accelerated development of COVID-19 vaccines has developed the capacity of many clinical trial sites and laboratories across the globe.¹⁰ Real-time COVID-19 data for wider visibility and dissemination lead to flattening the curve with appropriate interventions. Likewise, periodic availability of TB burden related data and transparency for appropriate action could pave way for bending the curve to achieve TB elimination targets.

To summarize, this pandemic revealed that newer diagnostics, treatment, and vaccines can be rapidly developed, fast-tracked for regulatory approvals and made available for patient management when they are fully supported politically and financially with public-private and industry-academic partnerships.

4. Conclusion

To conclude, the COVID-19 pandemic has changed the global society. This pandemic has shown that accelerated research and faster adoption of research findings, rapid information sharing with enhanced global collaboration can result in improved clinical care. With continued access to TB services, good public-private partnership along increased coverage of COVID-19 vaccinations and selective lock-down we can better face the challenges in TB control during future COVID waves. As we learn to live with the CoV2 virus and embrace the new "normal", if lessons learnt from COVID-19 can be applied to the oldest pandemic, then TB elimination is not an impossible goal to achieve.

Conflicts 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.

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19 July 2021

Available online 28 July 2021

<https://doi.org/10.1016/j.ijtb.2021.07.014>

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