

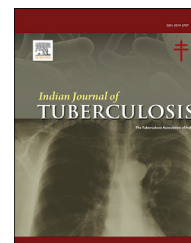


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## Viewpoint

## TB control in India in the COVID era

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## ABSTRACT

COVID-19 pandemic has disturbed the delivery of health care in almost all countries of the world. This has affected mostly the public health control programs. Because of lock downs, restrictions in movement, psychological fear of contacting the disease in health care facilities, diversion of health care workers for containment and management of COVID-19, utilization of diagnostic facilities like CBNAAT machines for COVID work, conversion of hospitals for care of these patients, financial diversion etc has created issues in the NTEP to focuss on TB control in India. Case notification and other areas of the program to achieve End TB by 2025 have suffered. Various ways of overcoming these difficulties have been discussed.

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The COVID-19 pandemic caused by the novel corona virus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has upset the major public health care system throughout the world. Globally, by 3rd July 2020, there have been 10,719,946 confirmed cases of COVID-19, including 517,337 deaths, reported to WHO. In India, from Jan 30th to 3rd July 2020, there have been 625,544 confirmed cases of COVID-19 with 18,213 deaths.<sup>1</sup> The COVID 19 pandemic has placed unprecedented demands and pressure on the health system. Health facilities and workforce are diverted and assigned a wide variety of activities related to controlling the outbreak. In doing so, other essential health services would be severely compromised. It is likely that seeking health care may be deferred because of social/physical distancing requirements or community reluctance owing to perceptions that health facilities may be infected. Continuing to provide essential services, while focusing on COVID 19 related activities, is

important not only to maintain people's trust in the health care delivery system,<sup>2</sup> but also to minimize an increase in morbidity and mortality from other health conditions. During the Ebola outbreak in 2014–15, increased number of deaths was caused by measles, malaria, HIV/AIDS and tuberculosis (TB) because of failure in the health system and that exceeded deaths from Ebola itself.<sup>3,4</sup> Prevention and treatment services for non-communicable diseases (NCDs) are affected severely since the pandemic began. A WHO survey completed by 155 countries during a 3-week period in May 2020, confirmed that the impact is global, but low-income countries are the most affected.<sup>5</sup> More than half (53%) of the countries surveyed have partially or completely disrupted services for hypertension treatment; 49% for treatment for diabetes and diabetes-related complications; 42% for cancer treatment, and 31% for cardiovascular emergencies. Rehabilitation services have been disrupted in almost two-thirds (63%) of the countries,

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even though rehabilitation is key to a healthy recovery following severe illness from COVID-19. In almost all (94%) health staff working in the area of NCDs are reassigned and diverted to support COVID-19. The postponement of public screening programmes (cancer) was also widespread, in more than 50% of countries. Most common reasons for discontinuing or reducing services were cancellations of planned treatments, a decrease in public transport available and a lack of staff because health workers had been reassigned to support COVID-19 services. One of the main reasons for discontinuing services was a shortage of medicines, diagnostics and other technologies in about 20% of countries. Many countries had devised alternative strategies for continuing care which may or may not be the ideal.<sup>6</sup> Many countries implemented lockdowns and quarantines to curtail the spread of the virus, and a large number of global populations are still under these restrictions. These restrictive measures, like physical distancing, gatherings, travel, etc has led to many adverse impact on societies, economies, and health care delivery systems. All countries of the world are struggling to maintain their health care systems to cope under such extraordinary conditions. In addition to affecting medical care of various diseases, whether therapeutic or preventive, COVID-19 has bad prognosis if associated with certain disease conditions like cardiovascular disease, chronic respiratory diseases (COPD and bronchial asthma), diabetes mellitus, hypertension, chronic kidney diseases, and cancer etc.

However, the medical and social consequences of association of TB and COVID-19 are not clearly understood and experience on COVID-19 in TB patients and vice versa are limited. There are certain similarities and differences between the two diseases. Limited and preliminary observations suggest that TB infection is likely to increase susceptibility to SARS-CoV-2 with increased COVID-19 severity.<sup>7</sup> If it is so it will have a major impact in India as one third of its population is infected with TB. There are striking similarities between the two. Both cause major infection-related morbidity and mortality. While COVID-19 had caused over 0.5 million deaths so far over a period of 6 months, TB was the leading cause of mortality from an infectious disease worldwide in 2018, causing 1.2 million deaths out of the nearly 10 million new cases reported that year.<sup>8</sup> COVID-19 cases have already crossed that figure within 6 months of its origin. In India COVID-19 mortality is above 18,000 over a period of 3 months out of the over 5 lakh infections during this time. On the other hand, in India in 2019, 2.41 million new TB cases were reported and there was a mortality of nearly 79,000 in that year.<sup>9</sup> The global Case Fatality Rate (CFR) for TB is about 3.5% among patients who were HIV– and 18.8% for HIV+ of all ages.<sup>10</sup> However, a recent review has found the an overall case fatality ratio among Indian patients with TB during treatment of 5.16% (95% CI 4.20%–6.34%).<sup>11</sup> On the otherhand, the CFR for COVID-19 for the world is 4.8% and for India it is 2.92% only.<sup>12</sup> While the Basic reproduction number ( $R_0$ ) is 2.2 for COVID-19; the same for TB is ( $R_0$ ) higher like it was 4.3 in China (2012); and 3.55 in Southern India (2004–2006).<sup>13</sup>

Both COVID-19 and TB present with respiratory symptoms with small differences. During the COVID-19 pandemic, diagnosis and treatment of TB, or TB and COVID-19 co-infection, are likely to be compromised. Elderly and associated co-

morbidities are increased risk factors for severe disease and cause adverse outcomes in both conditions. Considerable social impact like stigma, discrimination, and isolation are associated with both diseases in addition to the economic impact because of loss of productivity and catastrophic costs to individuals and households. There are some important differences between the two also. TB has been labelled as a pandemic many times over the past three centuries, whereas this is the first COVID-19 pandemic. Children are often less severely affected by COVID-19, whereas 1.1 million children had TB disease in 2018, of whom 200,000 died and in India about 3,42,000 incident cases of paediatric TB are estimated to occur every year accounting for 31% of the global burden and 13% of the overall TB burden in the country as per the 2019 India TB Report. The association between poverty and COVID-19 is unclear. TB will be associated with the poverty, in which poorer people have a higher likelihood of infection, disease, and adverse outcomes. Moreover, unemployed populations including contract workers will experience increases risk of TB. While most of the cases and deaths from TB occur in low- and middle-income countries, COVID-19 occurred more in the developed countries following China and most deaths occurred in USA.<sup>1</sup> COVID-19 has mobilised more global and human resources in a few months than TB has in decades. However, the number of COVID-19 cases and mortality might increase in future as now India is the fourth highest number.

The exact relationship is still unclear despite many similarities and dissimilarities. The clinical and epidemiological interactions of COVID-19 with TB (with or without HIV) seem to be highly complex. Transmission of TB might rise because of increased respiratory symptoms associated with COVID-19, or it may even decline due to COVID-19-related self-isolation, use of masks and quarantine and no social gatherings and mass travel. Millions of people treated for TB that have residual, long-term lung damage are likely to be at a higher risk of severe disease and death from COVID-19. Because of extreme pressures on health systems, exacerbated by COVID-19, people with TB are likely to face decreased access to diagnostic and treatment services, which might also result in adverse outcomes.<sup>14</sup>

Both TB and COVID-19 spread by close contact between people, although the exact mode of transmission differs, explaining some differences in infection control measures to mitigate the two conditions. Hospital procedures that generate aerosols predispose to infection of both conditions and should only be conducted within recommended safeguards.

Although clinical course and outcome of COVID-19 is well reported from different parts of the world, including commentaries, perspectives and reviews, information is scanty about the clinical course of co-infections with TB. Global and national experience with concomitant TB and COVID-19 is extremely limited. In an analysis of 1217 consecutive respiratory specimens collected from COVID-19 patients, TB bacillus was not detected.<sup>15</sup> Because of its immunological effects, COVID-19 pandemic is likely to affect TB in many ways in many countries. A Global Tuberculosis Network (GTN) study of 49 cases of TB and COVID-19 from 8 countries and 3 continents<sup>16</sup> revealed that most patients had prior TB with one-third having first COVID-19; 18.3% had both diseases

diagnosed within the same week. Most patients had active TB and 7 (14.3%) had post-TB sequel. The impact on the healthcare system (e.g., days of admission, intensive care unit beds, etc.) was relevant in this study. The information on BCG (*Bacillus Calmette-Guérin*) vaccination was modest. Another study data from 69 consecutive cases in 8 countries and 20 hospitalised patients with TB and COVID-19 showed that 8 out of 69 (11.6%) patients died. Most of them were young migrants. It was noted that mortality was more in elderly patients with co-morbidities; TB was not a major determinant of mortality and migrants had lower mortality due to younger age and lower number of co-morbidities. However, the authors postulated that in settings where advanced forms of TB frequently occur and are caused by drug-resistant strains higher mortality rates can be expected even in young individuals.<sup>17</sup> In another small series of 20 TB patients<sup>18</sup> diagnosed with COVID-19 co-infection from North Italy, most were males and the median age was 39 with a range of 27–47 years. 50% of patients had a BMI < 18.5 Kg m<sup>-2</sup> at admission and eight had co-morbidities but none had HIV co-infection. Three patients reported having been vaccinated with *Bacillus Calmette-Guérin* (BCG).

Even if there is scarcity of data about the interaction and coexistence of both the diseases, one can draw conclusions or may expect similar outcomes from experience gained from other viral diseases occurring in the past and their impact on TB. Crisan-Dabija et al<sup>19</sup> examined the issue of the effect of the three human coronaviruses known to cause fatal respiratory diseases: the SARSCoV-1 that led to a global epidemic in 2002; the Middle-East respiratory syndrome coronavirus discovered in 2012 and still affects people from 27 countries; and most recently, the novel coronavirus (SARS-CoV-2) and the influenza pandemic of 1918–19. The authors noted that these epidemics have a negative impact on TB patients; transmission prevention was crucial for containing the epidemics and in order to decrease the opportunity of SARS-CoV-2 spreading amongst TB cases, hospital treatment for TB patients should be limited to severe cases. Immunopathogenesis of these viral illnesses also will affect course of TB<sup>19</sup> and diagnostic confusions. Similar observations are also made by a consensus by the World Association for Infectious Diseases and Immunological Disorders (WAIDID), GTN and members of ESCMID Study Group for Mycobacterial Infections (ESGMYC).<sup>20</sup> Similarly, Ebola virus disease (EVD) in 2013–15 in Liberia, West Africa had major negative effects in the form of significant decreases in diagnoses of smear-positive pulmonary TB, the declines in HIV testing and antiretroviral therapy uptake and poor treatment success.<sup>21</sup> The devastating EVD outbreak of 2014–2015 in West Africa impacted significantly on all sectors of the healthcare systems in these countries, including the TB prevention and control programmes. The outbreak had an adverse impact on the healthcare workforce and healthcare service delivery. At the height of the EVD outbreak, numerous staff members in these countries contracted EBV at the Ebola treatment units and died. Many healthcare workers were also infected in healthcare facilities that were not Ebola treatment units but were national hospitals and peripheral health units that were unprepared for receiving patients with EVD. In all these countries, the disruption to TB services due to the EVD epidemic would have increased *Mycobacterium tuberculosis*

transmission, TB morbidity and mortality, and decreased patient adherence to TB treatment, and the likely impact will not be known for several years to come. Many other aspects of the dual disease have been described by different authors.<sup>22–29</sup>

The COVID-19 pandemic will impact existing and well-performing public health programs including the TB control programs.<sup>30</sup> There is likely to be grave consequences for the existing and yet to be diagnosed TB patients, more so in low and middle income countries where TB is endemic and health services are not well equipped. TB control programmes will be under severe strain due to diversion of resources, loss of focus with increased attention of COVID-19 care, constraints due to overutilization of laboratories meant for TB work, issues related to availability of TB care workers, restriction of movements of patients and contacts etc with DR-TB centres being diverted for COVID related work because of change in the priorities of health care delivery. This is going to lead to a reduction in quality of TB care and poor outcomes. The Government of India has already made these arrangements of diverting the man power and use of CBNAAT machines for COVID work. This is an enormous challenge for the Governments and societies for ensuring that the pandemic has the least possible impact on key health programs that will need continued close monitoring. There is a significant decline in the claims made under the Ayush Bharat- Pradhan Mantri Jan Arogya Yojana during the lockdown period in India. There was a steep decline of 64% (as compared to two weeks earlier) in the claims made under the health scheme in the first week since the lockdown was announced. The report confirms the concerns about reduced access to healthcare due to the sudden imposition of the nationwide lockdown to contain the COVID-19 pandemic.<sup>31</sup>

Under the Revised National Tuberculosis Control Program (RNTCP), India has an ambitious goal of Ending TB by 2025, 5 years ahead of the Global target. The strategy aimed to end the TB epidemic, with targets to reduce TB deaths by 95% and to cut new cases by 90% compared to that was in 2015; and to ensure that no family is burdened with catastrophic expenses due to TB. To achieve these goals, the RNTCP, India developed the National Strategic Plan (NSP) 2017–2025. Due to various challenges and issues for achieving these goals, and to put thrust on the strategies, in January 2020 the RNTCP, was renamed as the National Tuberculosis Elimination Program (NTEP). A revised draft NSP 2020–2025 is under preparation to enhance these strategies. The COVID-19 pandemic will disturb the balance jeopardizing various TB control activities working in full swing and despite political commitments at the highest level – the Prime Minister.

TB case notification through Nikshay, an online case notification system through the e-platform, is a key to the NTEP. Case detection, treatment and compliance are the key factors in the End TB strategy. COVID-19 pandemic in India has adversely affected the TB case notification. Table 1 depicts the decline in case detection and notification.

Thus, there is a large gap in the case detection although the case notification was steadily increasing. This happened as a result of repeated lockdowns. Between March, 20th and 3rd July of every year the number was increasing, but for this year of COVID-19, the case notification has drastically reduced to less than a half.

**Table 1 – Nikshay Dash-board showing TB notification.**

| Year            | Public Sector    | Private Sector | Total reported | Between 20th March till 3rd July | Target (Both sectors) | Percentage reported |
|-----------------|------------------|----------------|----------------|----------------------------------|-----------------------|---------------------|
| 2017            | 14,10,579 (99%)  | 3,24,386 (36%) | 17,35,262      | 5,62,161                         | 23,25,312             | 75%                 |
| 2018            | 15,98,105 (110%) | 5,02,823 (35%) | 21,00,928      | 6,79,222                         | 21,00,928             | 73%                 |
| 2019            | 17,26,656 (92%)  | 6,82,068 (69%) | 24,08,724      | 7,53,087                         | 28,71,755             | 84%                 |
| 2020 (3rd July) | 6,55,633 (34%)   | 2,37,520 (22%) | 8,93,153       | 3,62,604                         | 29,99,030             | 30%                 |

Weekly reports were diminished by 75% in the three weeks following 22 March (average 11,367 weekly cases), compared to an average of 45,875 weekly cases during the previous weeks of 2020, when a strict nation-wide lockdown was imposed. This drop was attributable to a combination of factors including delays in entering the data onto the real-time national online TB surveillance system Nikshay, reduced attendance to health services, reassignment of health personnel and a reduction in TB testing and detection. Similar reduction by 20% was noticed for February 2020 in comparison with the number of cases detected in February 2019. According to estimates the global TB case detection were decreased by an average of 25% over a period of 3 months (as compared to the level of detection before the pandemic). This will lead to a predicted additional 190,000 (56,000–406,000) TB deaths (a 13% increase), bringing the total to 1.66 (1.3–2.1) million TB deaths in 2020, near the global level of TB mortality of the year 2015.<sup>32</sup>

Modelling analysis by Collaboration between Stop TB Partnership and Imperial College, Avenir Health, Johns Hopkins University and USAID project to examine the potential impact of the Covid-19 response on tuberculosis in High-burden countries that included India, Kenya and Ukraine predicted that if there is a 2-month lockdown with 2 months recovery, then for India, an excess of 5,14,370 cases will be detected between 2020 and 25 (3.55% increase and an excess of TB related deaths of 1,51,120 during this period of 5 years which is an excess of 5.70%. With a three-month lockdown and a protracted 10-month restoration of services, an additional 6.3 million cases of TB will develop between 2020 and 2025 with an additional 1.4 million TB deaths during the same period. India will have an additional burden of 1,788,100 new cases (increase of 12.32%) and 511,930 excess deaths (19.31%) during this period. The modeling also found that the global response to the COVID-19 pandemic is having unintended yet drastic consequences on TB services, with lockdowns and limitations on diagnosis, treatment and prevention services expected to increase the annual number of TB cases and deaths over the next five years leading to loss of gains obtained during the past years.<sup>33</sup>

Operational research on tuberculosis is an important focus of the End TB strategy. Because of the above mentioned factors and difficulty in getting TB patients, close down of facilities has slowed down the operational research areas. TB Research Consortium of the Indian Council of Medical Research had undertaken many priority areas like vaccine trial, newer therapeutics, active case finding in vulnerable groups and prevalence survey in the country are either

stopped for the time being or recruitment had slowed down drastically.

Urgent measures need to be taken to minimize the impact of the COVID-19 pandemic on TB, and to save lives of TB patients and to get the country back on track in achieving the targets. Steps should be taken to ensure continuity of TB diagnostic services, notification, treatment and prevention services during the lockdown period and to undertake a massive catch-up effort to actively diagnose, trace, treat and prevent. Stop TB Partnership and partners has called upon the leadership of all countries—particularly those with high TB burdens—to ensure the continuity of the TB response in the time of COVID-19, to take proactive measures that include those who are most vulnerable and to provide protection against economic hardship, isolation, stigma and discrimination. Further, the NTEP need to secure the human and financial resources needed for seamless continuation of TB services amid the COVID-19 response. Recognizing that this is an unprecedented situation, the Stop TB Partnership and the WHO are continuing support for national TB Programmes and partners through their multiple technical, innovative and people-centered platforms. The Union also is providing technical help in form of guidance during this time.

Infection control practices for vulnerable populations and lessons to care for the sick should be the goal. This will benefit both the diseases. Protection of health care workers is an important issue and by all means they should be protected to continue providing TB care as front-line warriors. One important positive effects of COVID-19 is about the awareness of infection control practices, including use of face masks, cough etiquettes, and social distancing which are to be and practised after the COVID-19 pandemic that will help TB control also. TB treatment should not be stopped. TB preventive treatment, treatment for drug-susceptible or drug-resistant TB and TB-HIV need special attention. Support for uninterrupted TB preventive treatment and treatment of TB disease should be ensured alongside the COVID-19 response. TB services are not to be disrupted during the COVID19 response. The Stop TB Strategy, the Union and WHO, as well as our NTEP has published guidelines for the programs how to work during the COVID-19 pandemic.<sup>34</sup> People with TB should make far fewer visits to TB clinics and healthcare facilities, and should be provided with enough medication so that they can complete their treatment at home. Staff at healthcare facilities must receive urgent training on the importance of universal safety precautions, appropriate use of personal protective equipment (PPE) and criteria for self-isolation to reduce the spread of COVID-19 in TB clinics. All people with TB should receive and wear a surgical mask while attending a TB

clinic and be screened for COVID-19 through an appropriate triage system. Telephonic conversations/consultations will be the order of the day and TB patients be provided with the number to contact whenever necessary. All-oral regimens for drug-resistant TB (DR-TB) need to be administered. People with TB - HIV and who are not on antiretroviral therapy (ART) should be started on ART on the same day as TB treatment, with ART and TB prescriptions aligned. The program needs to ensure TB patients to receive necessary psycho-social, nutritional, and economic support. TB care providers are to be well briefed and must use essential personal protection equipment. The program should ensure systems that are in place for remotely monitoring side effects and minimizing hospital visits. It is of vital importance to maintain uninterrupted TB drugs supply by planning early procurement and careful planning of local distribution and transportation in lock down situations. The National and sub-national governments should support special vulnerable population group because these populations are at greater risk of TB, because of living conditions, working environment or because of other socio-economic factors that result in barriers to accessing health services. Despite the emergency nature of the COVID-19 pandemic, health approaches, as well as social policies, should consider rights and gender equity. Social, legal and economic protections are to be ensured to maintain good mental health and to act against stigma and discrimination.

Although India aims to End TB by 2025, the present COVID-19 crisis and its consequential direct and indirect effects on TB have derailed the efforts and therefore, there may be a need in a shift in priority. However, if the programs continue to focus on remedial measures to reverse this trend the situation could be saved and if the NTEP does not take remedial measures, the country may have to revise its End TB target of 2025.

### Declaration of competing interest

The author has none to declare.

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