

Tuberculosis and COVID-19 in India: Challenges and opportunities

The 2019 novel coronavirus or recently renamed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization (WHO) was first notified from Wuhan City of Hubei Province of China in December 2019 in the form of unexplained pneumonia.^[1] Disease associated with SARS-CoV-2 also termed as coronavirus disease 2019 or COVID-19 has now become a potential threat to global health within a short span of time by spreading across 210 countries and territories.^[1,2] The WHO has declared COVID-19 as a pandemic on March 11, 2020. Since then (as on June 11, 2020), almost 7,514,815 confirmed cases and 420,316 deaths have been reported worldwide.^[2] India confirmed its first case on January 30, 2020. Since then (as on June 11, 2020), 297,001 confirmed cases with 8321 deaths have been reported.^[3]

Tuberculosis (TB) is already existing as unprecedented pandemic worldwide over several years. It was already declared a global health emergency by the WHO in 1993.^[4] The estimated global burden of TB is 10 million, with nearly half of them having drug resistance in 2018.^[5] Of 10 million cases, 3 million (30%) remain undiagnosed. TB remains the deadliest infectious killer as compared to the novel COVID-19. The estimated mortality was 1.2 million among HIV-negative people in 2018 and an additional 0.25 million among HIV-positive people. Around 4000 people die and 30,000 people fall ill every day despite this disease is preventable and curable. Approximately 3 of 10 TB patients (27%) in the world belong to India. Around 1400 people die and 7500 people fall ill every day due to TB even in India.

Although COVID 19 and TB share many similarities, there are striking differences too. The causative agent responsible for COVID-19 is novel virus SARS-CoV-2, whereas for TB, it is bacteria *Mycobacterium tuberculosis*. Both can manifest with similar respiratory symptoms such as fever, cough, breathlessness, and weakness with varying severity with chronicity of symptoms in TB as compared to acute or rapid progression in case of COVID 19. Both are transmitted mainly through close contacts. However, the incubation period from exposure to disease in TB is usually longer with a slow onset, whereas symptoms may appear 2–14 days after exposure in COVID-19 with a median incubation period of 5 days. TB can exist in active or latent form depending on the immune status, whereas the latent period is not defined for COVID-19. The mode of transmission in TB is primarily through droplet nuclei of aerosols generated by an infected person with TB, who may be

infectious for usually longer duration before initiation of effective treatment.^[6] SARS-CoV-2 can transmit mainly through droplets and fomites but can be through aerosols based on recent evidence.^[7] A person once infected with SARS-CoV-2 can transmit the infection to additional 2–3 persons, but a person infected with TB can infect additional 1–4 persons. Both share common risk factors such as advanced age, diabetes, smoking, chronic kidney disease, chronic respiratory disorders, and immunocompromised state. Evidence is lacking whether active or previously treated TB and HIV can enhance the severity and complications of COVID-19 or not. The case fatality rate (CFR) remains higher for TB and estimated to be 15% worldwide^[5] as compared to COVID-19 which is approximately 1.4%–3.4%. In India, CFR for TB is 17% in 2018,^[5] whereas projected CFR for COVID-19 is 2%–4% considering the worst scenario. Exact CFRs are unreliable to calculate at this point of time with spreading novel SARS-CoV-2 infection, as there is significant heterogeneity among different countries regarding the demographic profile and extent of testing. However, we do have well-defined options like multiple treatment regimens for TB including complicated drug-resistant forms, chemoprophylaxis, and availability of Bacille Calmette–Guérin (BCG) vaccine, but there is no specific evidence-based treatment and vaccines for SARS-CoV-2 currently. Active surveillance is well defined for TB, but for SARS-CoV-2, it is evolving and changing depending on the level of transmission.^[8,9] Diagnosis for pulmonary TB can be established rapidly which usually includes sputum or bronchoalveolar lavage (BAL) with automated cartridge-based nucleic acid amplification test (CBNAAT). COVID-19 can also be detected rapidly with reverse transcription–polymerase chain reaction or CBNAAT either from a nasal and oral pharyngeal swab or a sputum/BAL test if required.^[10] Antibody testing from blood to detect COVID-19 can also be performed preferentially in hotspot areas to detect community transmission. Both diseases require contact tracing and infection control measures that include handwashing, cough etiquette, social distancing, regular cleaning of surfaces, isolation, prolonged quarantine, and respiratory protection by using barriers like masks and gloves. There is no doubt that these measures have been prioritized to prevent COVID-19 but still remain underutilized for TB. Definitive treatment and vaccines are available for TB, whereas limited treatment options are available for novel COVID-19 disease. Further research is ongoing for treatment and vaccines for COVID-19. Both the diseases are associated with social stigma and have created huge

economic impact worldwide, but the burden of disease is acute for COVID-19 in contrast to chronic for TB.

Social distancing is one of the important preventive measures for COVID-19. The Government of India has imposed nationwide lockdown with effect from March 25, 2020,^[11] and has extended further till May 3, 2020. It becomes quite challenging for most of the countries to ensure smooth functioning of programmatic services leading to disruption of routine TB care. There is anticipation that people with TB and COVID-19, particularly in case of coinfection, may exhibit unfavorable treatment outcomes with transmission of infection in community, especially if TB treatment is interrupted. The situation will be alarming for high-burden countries like India. Various issues that need to be encountered are reallocation of staffs already working under National TB Elimination Program (NTEP) to combat COVID-19 creating overburden, priority to diagnose COVID-19 rather than TB by laboratories leading to diagnostic delay, use of established TB hospitals and sanatoriums for admitting patients with COVID-19, depletion of drug stocks due to decreased manufacturing capacity and disruption of transportation facilities, interruption of Directly observed treatment, short course (DOTS) treatment due to restricted mobility, and lack of streamline health policy. India is already engaged in accomplishing the herculean task of ending TB by 2025^[12] and has also started preparing for management of COVID-19 patients. Reallocation of resources might be difficult in this situation due to existence of several hurdles such as limited health infrastructure (hospital beds, ventilators, and respiratory barriers), significant burden of undiagnosed TB patients, coinfection with HIV, priority to treat DR-TB patients with regimens containing newer drugs, and low health expenditure. Diverting resources for COVID-19 may create an acute shortage for needy TB patients. Estimation of TB and COVID-19 coinfection is not possible at this moment but could not be underestimated in India. Malnutrition, social diversity, poverty, and overcrowding in unauthorized colonies, especially slums, are also rampant in our densely populated country (1.34 billion) and this can create a significant hindrance to containment plan. All these factors will be responsible for delay in diagnosis and treatment of both TB and COVID-19, which may lead to a spike in both diseases and increased transmission of infection in community. The impact of lockdown can be perceived as only 34,566 TB patients were notified nationwide during the past 3 weeks in comparison to 1,14,460 patients in early March 2020 (pre-lockdown phase).^[13] Therefore, it becomes essential that our national TB program should remain operational and that people have easy access to diagnostic services, treatments, and support services for TB during this era of COVID-19 pandemic. There should be an intact procurement and supply management systems to ensure adequate supplies of TB medications and timely ordering of new drugs to avoid stock-outs. TB programs must have a system in place to continue to support patients on DOTS treatment by ensuring adherence, monitoring of side effects

from the medications, health education, and providing psychosocial support. The Government of India has provided directives under NTEP to continue uninterrupted services across all states and union territories. All public and private laboratory service providers continue sputum collection for diagnosis under universal safety precautions and also follow infection prevention and control measures. Self-administered therapy as an alternative to daily observed therapy has been adopted by provision of drugs for 1 month in advance preferably from the nearest DOTS center or can be provided even at home.^[14,15] Other measures have also been adopted like avoidance of routine outpatient department (OPD) visits and admission of only critically ill patients, task-shifting of health care workers, concurrent screening for both diseases and diversion of funds for TB in addition to COVID-19 with aid of donor support having public-private partnership (Global Fund, UNITAID and others). Optimal distribution of drug stocks, personal protective equipments, and respirators for health-care workers must be ensured. A more number of accredited private laboratories need to be involved for testing. Promotion of virtual events in place of conferences is required for information, education and communication in order to create health awareness among community as well as health care workers. Digital platforms such as virtual OPD or video-observed therapy, smart pill boxes, and other mobile phone-supported adherence strategies in the form of teleconsult like 99DOTS must be utilized. DR-TB centers need to follow all infection control measures strictly to prevent nosocomial transmission. The frontline health-care workers need to be well prepared to care for their patients. Community volunteers may be appointed for awareness raising, prevention, and early notification for both TB and COVID-19. All these measures emphasize on patient-centric care that may favor better outcome even in these adverse conditions.

BCG is the only vaccine available for TB that prevents dissemination, whereas for COVID-19, vaccines are still under development. Data from few epidemiological studies reported reduced morbidity and mortality for COVID-19 in Asian and African countries where BCG vaccination policy is adopted universally in contrast to Europe and the USA with low vaccination coverage.^[16-18] This may offer a ray of new hope for developing countries like India. BCG revaccination practices, particularly in the elderly age group, may provide additional protection against severe COVID-19. However, findings need to be validated with robust evidence.

Focusing solely on COVID-19 can lead to damage of fragile gains that have been achieved for the elimination of TB under END TB strategy by the WHO. Strategies adopted for curbing epidemics of both TB and COVID-19 can complement each other leading to overall decrease in mortality. We need to reframe our health policy at this point of time. This will require a coordinated approach from our government and public as well as private health sector. What we have built recently for COVID-19 pandemic like

effective notification, promotion of active surveillance, contact tracing, and effective infection control measures may provide opportunity in future to end TB. If these opportunities can be utilized in TB elimination program, India will also get benefit in fulfilling the dream of ending TB by 2025. There is utmost requirement for further investment and research on newer vaccines as well as drugs for both the diseases with an aim to achieve better outcomes. There is no doubt that India is putting every effort to stop ongoing novel COVID-19 pandemic, but old silent killer TB which is preventable and treatable, should not be forgotten. If we show even half of this effort for the elimination of TB, morbidity and mortality can be reduced remarkably in the near future and may help in achieving goals of eliminating the TB from India.

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