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Review Article

CHALLENGES DURING COVID- 19 PANDEMIC ON THE MANAGEMENT OF TUBERCULOSIS (TB) IN INDIA

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A B S T R A C T

Background and aims: Tuberculosis (TB) remains a significant cause of morbidity and mortality worldwide including in India and needs surveillance, clinical assessment, testing, contact tracing, confirmation of diagnosis with supervised or in-supervised treatment regimens for effective eradication. The novel coronavirus-19 (nCoV-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new coronavirus that was only recently discovered in 2019. The virus causes coronavirus disease 2019 (COVID-19). We reviewed the challenges due to the COVID- 19 pandemic on the management of Tuberculosis and current strategies adopted to mitigate them.

Methods: We carried out a comprehensive review of the literature using suitable keywords such as 'COVID-19', 'Pandemics', 'Tuberculosis' 'Challenges', and' management', on the search engines of PubMed, Scopus, Google Scholar and Research Gate in March 2021 during the current COVID-19 pandemic to assess the impact of COVID-19 on the management of Tuberculosis.

Results: We found considerable challanges in Tuberculosis service provisions both in the primary care and hospital settings. Lockdown, social distancing, isolation strategies and public health guidelines to prevent viral transmission impacted the delivery of all aspects of Tuberculosis care.

Conclusions: COVID-19 pandemic has had a significant impact on the delivery of various tuberculosis diagnostic, treatment, surveillance and prevention programmes. Lockdown and public health guidelines have resulted in tough challenges in the traditional management of tuberculosis and have required reconfiguration of methods to support patients including wide ruse of remote consultations.

INTRODUCTION

The novel coronavirus-19 (nCoV-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new coronavirus that was only recently discovered in 2019. The virus causes coronavirus disease 2019 (COVID-19). The COVID-19 pandemic due to novel corona virus SARS-CoV-2 is predominantly are spiratory illness and ranges from a common cold to a more severe disease including pneumonia. The mode of human to human transmission is via drop let infections which are either in haled or enter the body by touching infected surfaces. Currently, the main treatment modality is supportive therapy, whilst serious illness may require ventilator assistance and efforts are in progress to produce an effective vaccine[1].

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, a bacterium known since 1882 when it was discovered by Dr Robert Koch, but there is historical evidence of TB in humans for thousands of years.

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Tuberculosis (TB) and COVID-19 are both infectious diseases that attack primarily the lungs. Both diseases have similar symptoms such as cough, fever and difficulty breathing. TB, however, has a longer incubation period with slower onset of disease.(WHO-2020)[2].

India accounts for more than one-fourth of the world's Tuberculosis (TB) cases. This amounts to about 2.6 million cases out of 10 million cases worldwide. The disease has been the reason for the death of nearly 0.44 million people in India. One-third of the global drug-resistant TB cases are in India, while experience on COVID-19 infection in TB patients remains limited, it is anticipated that people ill with both TB and COVID-19 may have poorer treatment outcomes, especially if TB treatment is interrupted. TB patients should take precautions as advised by health authorities to be protected from COVID-19 and continue their TB treatment as prescribed. (WHO-2020) [2]. Though the mode of transmission differs slightly, both TB and COVID-19 spread by close contact between people. As TB remains a significant

communicable disease in India, surveillance, clinical assessment, testing, contact tracing, confirmation of diagnosis with supervised and un-supervised treatment regimens should remain a public health priority in presence of COVID-19 pandemic. COVID-19 pandemic has made significant restrictions on 'face to face assessments and movement of people due to national lockdown and infection control strategies [3]. We reviewed the impact of COVID- 19 on TB management including surveillance and monitoring and current strategies adopted to mitigate them.

Essential TB services during the COVID-19 pandemic

Health services, including national programmes to combat TB, need to be actively engaged in ensuring an effective and rapid response to COVID-19 while ensuring that TB services are maintained. WHO Global TB Programme, along with WHO regional and country offices, has developed an information note to assist health authorities.

Diagnosis: Accurate diagnostic tests are essential for both TB and COVID-19. TB laboratory networks have been established in countries with the support of WHO and international partners. These networks as well as specimen transportation mechanisms could also be used for COVID 19 diagnosis and surveillance.

Treatment and care: TB programme staff with their experience and capacity, including inactive case finding and contact tracing, are well placed to share knowledge, expertise, and to provide technical and logistical support. The use of digital health technologies should be intensified to support patients and programmes through improved communication, counselling, care, and information management, among other benefits.

Prevention: Measures must be put in place to limit transmission of TB and COVID-19 in congregate settings and health care facilities, as per WHO guidelines.

Vaccination: One of the most effective ways to prevent diseases caused by pathogens, like bacteria or viruses, proved to be vaccination.

Human resources: Respiratory physicians, pulmonology staff of all grades, TB specialists and health workers at the primary health care level may be points of reference for patients with pulmonary complications of COVID-19. (WHO-2020)[2].

As the world comes together to tackle the novel coronavirus (COVID-19) pandemic, it is important to ensure that tuberculosis (TB) prevention and care approaches are adapting appropriately to offer uninterrupted, safe and high-quality TB services. Considering the similarity of TB and COVID-19 illnesses in disease presentation and transmission, as well as synergies in the response (e.g., prevention, infection control, adherence support, etc), the pandemic presents many questions for the TB field that require learning through research and innovation. To keep all relevant stakeholders up to date on this important issue, WHO Global TB Programme has developed open-access databases for research publications, clinical trials and ongoing research projects at the interface of TB and COVID-19.

COVID-19 and tuberculosis epidemiology

Tuberculosis has long been the world's leading infectious killer. until on April 1st 2020 COVID-19 overtook tuberculosis as the infectious disease killing the most people per day. It is no coincidence that the areas of the world predicted to be most affected by the social and economic consequences of COVID-19 are also the areas with the highest tuberculosis burden[4]. This is because tuberculosis is a social as well as an infectious disease – poorer, undernourished people living in densely populated areas are at higher risk of tuberculosis, and tuberculosis entrenches poverty by increasing costs, reducing income, and causing stigma and discrimination[5-7]. Indeed, poverty is the key driver of the tuberculosis pandemic, with several studies demonstrating how tuberculosis incidence rates rise and fall in association with measures of socioeconomic development and social protection [8-10]. In contrast, measures of biomedical care have had no detectable impact on tuberculosis incidence, despite helping to save millions of lives [10-11]. If the estimates of impoverishment described above are tragically borne out, history warns us to soon expect a dramatic rise in tuberculosis incidence.

COVID-19 and tuberculosis diagnosis: The COVID-19 pandemic is also likely to have a significant impact on the provision of biomedical care for tuberculosis-affected households. Access to diagnostic testing is likely to be reduced, partly because of limited human and material resources, but also because of the social stigma of having a cough or being unwell. This stigma has always been important for tuberculosis and has been exacerbated by the COVID-19 pandemic, potentially driving people with tuberculosis to hide their illness from others and delay accessing healthcare until disease and infectiousness are advanced [12]. The COVID-19 pandemic might be expected to increase the number of these "missing" people, who are a major source of ongoing transmission and have a high risk of tuberculosis-related morbidity and mortality. [13-14].

COVID-19 and tuberculosis treatment and prevention: Though the mode of transmission differs slightly, both TB and COVID-19 spread by close contact between people. As TB remains a significant communicable disease in India, surveillance, clinical assessment, testing, contact tracing, confirmation of diagnosis with supervised and un-supervised treatment regimens should remain a public health priority in presence of the COVID-19 pandemic. COVID-19 pandemic has made significant restrictions on 'face to face assessments and movement of people due to national lockdown and infection control strategies [15].

Provision of appropriate treatment for people who are diagnosed with tuberculosis might also be affected, particularly for people with drug-resistant tuberculosis, due to disruptions in the production and transportation of medicines and supplies, reduced nutritional and mental health support, limited access to healthcare facilities, and reduced clinical care to manage adverse drug reactions and comorbidities, such as HIV, diabetes, and cancer. Furthermore, impaired management of these comorbidities is also likely to significantly increase the risk of progression from latent tuberculosis infection to active disease in the general population. Relatedly, tuberculosis preventive treatment for household members is likely to be severely weakened, as strained health systems focus their limited resources on diagnosis and treatment, and visits to health facilities for non-emergencies are minimised. This is particularly alarming because transmission of tuberculosis to household members is likely to be increased by COVID-19, mediated by delayed tuberculosis diagnosis and

heavier household tuberculosis exposure during household quarantine. Unfortunately, isolation and quarantine of unwell individuals within households is unfeasible for much of the world's population living in crowded housing in the densely populated urban areas where most of the world's tuberculosis occurs. This increased tuberculosis transmission is likely to be worsened by COVID-19- associated economic challenges such as undernutrition, increasing tuberculosis susceptibility [16-17].

Preventing COVID-19 from worsening tuberculosis Taken together, the social, economic, and biomedical consequences of the COVID-19 pandemic are likely to combine to create a perfect storm concerning tuberculosis. What can be done to address this evolving crisis? Many of us wish that we had done more, sooner to address the current COVID-19 pandemic; what lessons can be learned to prevent COVID-19 from causing a secondary tuberculosis emergency? Already, the WHO has issued an information note urging the continuity of essential services for people with tuberculosis during the pandemic[18].However, if much of the progress gained in tuberculosis care and prevention is not to be rapidly undone, further steps must be urgently taken to mitigate some of the broader impacts discussed above.

Challenges and strategies to manage TB during the COVID-19 pandemic

1. Drop in the diagnosis of new cases of active TB
2. Out-patient setting challenges
3. Community TB challenges
4. Contact tracing applications
5. Monitoring and supply of Anti-TB medications
6. COVID-19 testing and TB
7. COVID-19 and TB disease
8. Lockdown effects during the COVID-19 pandemic
9. Personal Protective Equipment concerns
10. Prevention of drug resistance TB
11. Concerns of the safety of healthcare workers / Personal safety of health care workers
12. Effect of COVID-19 pandemic on TB immunization program
13. Economic consequences of COVID-19 pandemic

Drop-in diagnosis of new cases of active TB

TB patients have been badly hit by uncompleted lockdown due to the COVID-19 pandemic. The diagnosis of new TB cases has seen dramatic drop since the lockdown according to the Central TB Nikshay portal of the Government of India. The estimated number of the diagnosis of the number of new cases of tuberculosis detected as of April 27, 2020, in government healthcare centres saw a significant fall to 34,342 compared to 1,56,000 cases in April month of 2019, a 78 % decrease [19]. Ministry of Health and Family Welfare (MOHFW), Government of India (GOI) are trying to ensure uninterrupted diagnosis and treatment for TB patients.

Out-patient setting challenges

The need to avoid face to face consultations during the COVID -19 pandemic to reduce the risk of viral transmission has undoubtedly had an impact on the management of patients with TB, particularly in the outpatient setting. A provision to keep the clinics open so people with tuberculosis symptoms do not avoid health facilities or delay their assessment due to the COVID-19 pandemic must be balanced with health care risk .Multi-month dispensing will limit the hospital visits and minimize the risk of unnecessary exposure to COVID-19 infection. To reduce the pressure on facility-based healthcare systems, virtual communication platforms such as e-Sanjeevani, a Government of India, integrated telemedicine solution will help assist patients [20]. Telemedicine is already playing an emerging role in the remote management of chronic illness such as diabetes mellitus [21,22]. In line with World Health Organization (WHO) recommendations, technologies like electronic medication monitors and video-supported therapy can help patients complete their TB treatment[23].

Community TB challenges

With the lockdown restrictions and reduction in face-to-face appointments, there has been increasing the necessity of finding complementary ways of assisting patients with TB. Telemedicine can help in the community management of TB. Case management of patients with TB can take place via video link or teleconferencing. Should patients require assistance with medications or there be a risk of compliance with medications, patients are enrolled in to a DOTS programme [24], which entails a daily face-to-face consultation via video link to ensure these patients, are appropriately managed in the community. In extreme cases where neither video nor teleconferencing is appropriate for managing patients, these patients can be followed up with home visits ensuring that the appropriate personal protective equipment is worn by the health- care workers involved. An outreach worker ASHA (Accredited Social Health Activist), one of the key members of National Rural Health Mission, India will have to make a home visit to a TB patient to check if the patient is adhering to the treatment[25].

Diabetes is estimated to be the cause of 15% of active TB cases, due to impaired host defences caused by diabetes. TB Patients with concurrent diabetes have the severe cavitating disease, adverse treatment outcomes, a higher rate of recurrence following Anti-tubercular treatment, and a higher risk of mortality from TB than patients with TB alone [26]. Remote management and monitoring of both diabetes mellitus and TB possible with telemedicine will address both diseases[21].

Contact tracing applications

Contact tracing and tracking form key elements of managing both TB and COVID-19 in the community. The sudden surge in demand for care of COVID-19 patients including the introduction of Aarogya Setu (lit. 'Health Bridge') the Government of India COVID-19 tracking mobile application has raised concerns about the distraction of contact tracing services provided for TB programmes [27].The response to the COVID-19 pandemic should not affect the continuity of essential contact tracing applications (apps) used for people affected by tuberculosis. Lessons learnt from TB contact apps should be used to make the COVID-19 app work better.

Monitoring and supply of anti-TB medications

Monitoring of the disease process in patients' remains an issue in the era of social distancing and self-isolation. Provision of medications for TB patients in these times could prove difficult, due to the short supply of the medications as well as re-stocking medications to patients at home. Several strategies have been put in place, including the utilization of

out reach services to reach patient with TB and the postal delivery of TB medications[25]. Morecrecently, the Government of India has issued advice regarding the provision of TB medications to patients in the out patient setting, stating that these patients should be provided with TB medications to last one month, and in exceptional circumstances, 2-month supplies, to reduce the need for patients to attend clinics and therefore reduce the risk of transmitting the disease[24].

COVID-19 testing and TB

The testing of patients with TB for COVID-19 and vice versa has been a topic of much discussion in recent times. It is known that COVID-19 and TB have similar clinical features and presentations, namely a fever, shortness of breath and coughing. There exist subtle differences between the two disease processes but COVID-19 infection tends to develop pover a shorter period than TB.

European Laboratory Initiative has recommended the use of Gene X pertmachines for COVID-19 testing without compromising their use for TB[28]. Recently Indian Council of Medical Research (ICMR) also has approved the use of the' Truenat TMbeta CoVteston Truelab TM workstation' which were used for testing drug-resistant tuberculosisasa screening test for COVID-19[29].

COVID-19 and TB disease

COVID-19 and TB relationship: As the knowledge and studies about COVID-19 and TB is emerging, early evidence suggests patients with latent TB and established disease have an increased risk of the SARS-CoV-2 infection and predisposition towards developing severe COVID-19 pneumonia [30,31]. Mathematical model-based forecasting studies from New Delhi, India emphasize the importance of primary prevention measures especially in TB patients and the need for TB centres to prepare for concurrent infections [32].

Table Similarities and Difference between COVID19 and tuberculosis (TB)

	COVID 19	**Tuberculosis**
	Differences	
Onset	Acute	Chronic
Transmission	Droplet-transmitted, by touching – (from person to person through droplet particles and contaminated surfaces).	Airborne transmission; by inhalation – (from person to person through droplet nuclei).
Infectiousness	Currently an average of 2.2 people infected per one person with COVID-19.	Range from less than 1 to up to 4 people infected per one person with TB.
Pathogen	Viral disease Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).	Bacterial disease Mycobacterium tuberculosis
The incubation period (exposure to disease)	Short (5-14 days)	Longer
Symptoms	• Fever, cough (usually dry), sore throat and shortness of breath. Loss of smell and taste. • During the 2nd week of illness (sometimes): difficulty in breathing (severe acute respiratory distress). • Clinical presentation classified: • Asymptomatic/mild disease (80% of people with COVID-19) • Moderate disease (15%) • Severe disease (5%)	• Systemic/generalised symptoms include fever, weight loss and night sweats. • Lung specific symptoms can include cough, shortness of breath, chest pain and coughing up blood.
Testing specimen	Nasopharyngeal or oropharyngeal swab	Sputum tests for those with cough. Other samples depending on symptoms.
Diagnostic tests	RT-PCR; rapid test antibody kit, Chest CT scan	Chest radiograph, Mycobacterium culture or molecular techniques, demonstration of acid-fast bacilli (AFB), serological assays.
Pathology	Endothelial damage and coagulopathy small vessels	Caseation necrosis and granuloma formation
Treatment	Supportive; HCQS? antiviral Remdesivir Symptomatic and supportive treatments currently. Antibiotics if the secondary bacterial infection is suspected. Concentrated oxygen. Ventilator. Many drug trials underway.	Anti-tuberculosis treatment Drug-sensitive TB 4 antibiotics for 2 months and 2-3 antibiotics for 4 months. For drug-resistant TB treatment, antibiotics for 9-24 months.
National policy adoption	Fast	Slow
Prevention	Self- distancing, hand washing, PPE strategy. Social distancing, cover your cough (cough etiquette) and frequent handwashing with soap for at least 20 seconds. Wearing a mask, particularly if experiencing symptoms or taking care of someone with symptoms. Personal protective equipment (PPE) for health care professions.	Prevention measures include TB preventive therapy for close contacts of people with TB and other risk populations, such as people living with HIV, appropriate TB treatment of people with TB and good airborne infection control and prevention measures.
Vaccine	Covaxin and Covishield- Vaccine research and development underway.	BCG vaccination is partially efficacious at protecting infants and young children against severe forms of TB,
	Similarities	
Organ affected	Lung	Lung
Genetic and non-genetic factors-lack of knowledge for individual susceptibility	Yes	Yes
Spread	Close contact	Close contact
Rapid diagnosis	Required	Required
Action strategy	Find, Track, Trace, Test, Isolate and Prevent strategy	Find Test, Treat, Monitor and Prevent strategy. DOTS and Monitoring of treatment
Health system	Burden	Burden
Public awareness	Required	Required
Data sharing platform at national and international level	lacking	lacking
Mortality	High	High
Risk factors	Elderly, Diabetes, HIV immunosuppression, chronic obstructive pulmonary disease	Elderly, Diabetes, HIV immunosuppression, chronic obstructive pulmonary disease
Personal protection measures	basic infection prevention and control, cough etiquette, patient triage, hand washing	basic infection prevention and control, cough etiquette, patient triage
Role of digital health technologies	Yes	Yes

Abbreviations:RT-PCR-RealTimePolymeraseChainReaction;HIV-HumanImmunodeficiencyVirus;HCQS-hydroxychloroquinesulphate.

Implications of concurrent infection of SARS-CoV-2 and TB: Concurrent infection of SARS-CoV-2 and mycobacterium tuberculosis (TB) can occur during the current COVID-19 pandemic is possible [33]. Damage caused by the TB infection can predispose a patient to COVID-19. Patients who concurrently develop COVID -19 tend to show a worse prognosis, probably due to pre-existing lung damage from the TB infection. Therefore patients should be tested for either disease if there is clinical deterioration, even if the clinical picture is atypical [34]. The testing of TB patients for COVID -19 applies to both patients at home as well as patients who are inpatients, including those who are deemed high risk i.e. HIV positive patients [35]. Nigeria Ministry of Health has identified TB as one of the risk factors for severe COVID-19 infection and death [36]. Nigeria has a similar profile of endemic presence of TB to India.

***Impact of COVID-19 on TB disease care*:** There are concerning reports suggesting that COVID-19 may slow down the recent gains in TB control [37]. Adewole. O, points out the significant impact of the COVID-19 pandemic on TB treatment. He has highlighted a marked reduction in the number of presumptive and confirmed TB case detection in 2020 during the current pandemic compared to the same time in 2019 in Nigeria. COVID-19 prevention and lockdown strategies have restricted diagnosis, access to test and treatment centres in Nigeria. The similar dramatic drop since the lockdown according to the Central TB Nikshay portal of the Government of India [10]. As the population in some regions are latently infected, it is anticipated that SARS-CoV-2 infection might initiate the development of active TB in the coming months [38].

Course and complications of concomitant COVID-19 and TB infection: Tandolini *et al*. [39] report Anti-TB treatment does not provide immunity against COVID-19. Hence it is vital patients are rapidly tested for both COVID-19 and TB or vice-versa if a patient demonstrates atypical symptoms which do not fit classical clinical features of either disease. Motta *et al*. [40] highlight the importance of awareness of the possibility of concomitant COVID-19 and TB infection with a serious course and fatality associated with such combined infection. The case-fatality rate reported in their 2 cohort studies on migrants with concomitant TB and COVID-19 infection was high (overall 10.8%) especially in elderly patients with co-morbidities. Interestingly these patients are suspected to have developed a nosocomial infection in the early phases of the COVID-19 pandemic. They emphasize the importance of strict infection control measures for all hospital patients especially those with higher risk e.g. elderly patients with co-morbidities.

Lockdown effects and interruption of the supply chain in health care during COVID-19: pandemic Non-COVID-19 health services like TB surveillance has been hampered with a focus on the emergency planning for the pandemic including improving rates of COVID-19 testing and organising quarantine facilities. There is a concern that there may be a surge in the number of patients with TB once the lockdown is lifted. Effective Utilization of Nikshay Aushadhi; a web-enabled application, which facilitates monitoring of universal access to all TB patients including Multi-Drug Resistant cases is required during the COVID-19 pandemic [41].

Personal protective equipment (PPE): There has been worldwide concern about the availability of PPE and paucity of protective materials such as hand sanitisers, mask, and gowns. PPEs shortage in health centres make it impossible for health care workers to provide safe regular health-care services for a patient with tuberculosis [42]. This affects the sampling of patients with active TB and their transport to central government laboratory since health workers are reluctant to take samples due to lack of appropriate PPE.

Prevention of drug resistance TB*:* Provision of anti-tuberculosis treatment, in line with the latest WHO guidelines, must be ensured for all TB patients, including those in COVID-19 quarantine and those with confirmed COVID-19 disease. People-centred outpatient and community-based care should be strongly preferred over hospital treatment for TB patients as this will not only prevent the patient from an in-hospital visit but also allow monitoring of uptake of anti-TB drugs. This will reduce the chances of drug-resistant TB. TB patients were likely to be at increased risk of COVID-19 infection so TB patients should continue treatment and take precautions like social distancing, mask, and hand hygiene to protect themselves from COVID-19. A recent study showed there are cases of multidrug-resistant TB cases not put on treatment after being diagnosed due to COVID-19 [43].

Concerns of the safety of healthcare workers / Personalsafety of health care workers: India's response to the COVID-19 pandemic has been hampered by the difficulties health care workers face in carrying out COVID-19 duties during lockdown impacting on the non -COVID-19 health services like that of TB and Malaria. In these extraordinary times, the health care providers must adapt and be flexible. Health Care Workers (HCWs) continue to safeguard themselves, their colleagues, their families, and their patients in this crisis. They need to be protected and supported. However, there are reports of rising violence against the health care workers undertaking testing and contact tracing of patients [44].

Effect of COVID-19 on TB immunization program: Bacille Calmette-Guerin vaccine (BCG) has a protective effect against tuberculosis. Due to the COVID-19 pandemic lockdown, suspension of immunization services has been observed, this may result in vaccine-preventable disease-related deaths and an increased burden on health systems. Recently WHO recommends mandatory neonatal BCG vaccination in countries or settings with a high incidence of tuberculosis like India, China, Turkey, South Korea, Indonesia, etc. to be continued during the COVID-19 pandemic [45]. There has been rising debate about the role of BCG in reducing the impact of COVID-19 [46].

Economic consequences of COVID-19: pandemic Together the social, economic, and biomedical consequences of the COVID-19 pandemic have created a perfect storm concerning tuberculosis disease management [47]. A recent study from the United Nations advocate that the long-lasting social and economic impacts of the COVID-19 pandemic could threaten public health programmes and disproportionately affect poorer people in poorer countries like Africa, South-East Asia, and Central and South America which are also the areas with the high tuberculosis burden. An increase in tuberculosis transmission and new cases is expected to be worsened by COVID-19-associated economic challenges. Impact on health due to undernutrition and constraints on funding of public

welfare programmes is likely to increase susceptibility to tuberculosis and other communicable diseases [48].

Management of COVID 19 and TB

- Ensure effective infection prevention and control measures, to protect the health and safety of health workers, staff, and patients. Personal protective equipment should be provided for all health staff involved in care delivery for both TB and COVID-19.
- Stand against stigma and discrimination and promote the human rights of the most vulnerable. Stigma and fear around communicable diseases like TB and COVID-19 hamper the public health response. Governments, citizens, media and communities have an important role to play in preventing and stopping stigma.
- Scale-up simultaneous testing for TB and COVID-19, taking into consideration similarity of symptoms (cough, fever and difficulty breathing), and based on exposure or presence of risk factors. As countries prepare to share existing molecular platforms for COVID-19 testing, it will be essential to maintain current molecular diagnostic services for TBpatients.
- Promote access to people- cantered prevention and care services. Home-based and community-based prevention and care should be strongly preferred over hospital treatment for TB patients (unless serious conditions require hospitalization) to reduce opportunities for transmission. This includes WHO recommended, all-oral TB treatments for multidrug-resistant TB and extensively drug-resistant TB. Digital adherence technologies can help bridge the communication gap. TB preventive treatment should be ensured for household contacts, especially given the increased risk of exposure.
- Build and strengthen community, youth and civil society engagement to close gaps in care. Community health workers, youth volunteers and civil society can be engaged in reaching those at risk or those affected by TB and/or COVID-19 with care. We need to harness the potential of these groups while ensuring effective infection control and protective measures for them. With the outbreak of COVID-19 at the beginning of 2020, to go beyond the line of duty to ensure that people with TB get uninterrupted treatment.

- The COVID-19 pandemic has highlighted the need for more preparedness and solidarity to ensure access to health care in times of crisis. We must learn from this experience and emerge victoriously. The commitments made, and targets set by Heads of State and other leaders to accelerate action to end TB must be kept even in crisis, backed by adequate investments. We need to do this to protect the lives of millions of people struggling with TB each day, and to sustain the gains we have made in the fight against TB. The time is now for solidarity and action. Let us join forces and step up the fight to end TB and COVID-19 – only united will we succeed.
- We have to address both COVID-19 and TB if we are to guarantee an effective response to COVID-19 while ensuring that TB services are maintained. Considering the many *overlaps between TB* and *COVID*-19 *in* disease presentation, transmission and control strategy, the integration of both programmes could be key to making this happen. Moreover, co-infection of both diseases has been reported; clinical experience with concomitant TB and COVID-19 is extremely limited, and high case-fatality rates have been reported.
- Integration of both programmes should be relatively easy. The COVID-19 control programme is based on the same strategy as the TB control programme, i.e., early detection of an infectious case, infection prevention and contact tracing. Both diseases have many clinical and epidemiological characteristics in common. Both primarily attack the lungs and diseased patients show similar clinical symptoms, such as a cough, fever and shortness of breath. Both diseases are transmitted by respiratory aerosols or droplets and spread from person to person through the air via close contact. Both also share the same drivers for transmission: crowding and social mixing. Underlying conditions or risk factors for poor outcomes in either disease include diabetes, immune suppression, old age and COPD
- A serious problem for the integration of a control programme for both diseases is the diversion of health service funding solely towards COVID-19 diagnosis and control. Both financial and workforce resources should instead work together to provide services for both conditions. TB control already has an established infrastructure and a laboratory network that can be used to support the COVID-19 response, while also continuing to respond to TB.
- About diagnosis, testing facilities can be shared and TB laboratory staff could participate in COVID-19 diagnosis. TB laboratories are used to working with a dangerous infectious disease and in general have safety measurements in place to avoid infection by aerosol-generating activities. TB laboratories that culture *Mycobacterium tuberculosis* are Biosafety Level 2 laboratories equipped with a biosafety cabinet as recommended by the WHO, which are also suitable for diagnosing COVID-19. However, direct sputum smear microscopy for TB is considered a low-risk process and can be performed in a well-ventilated laboratory without a biosafety cabinet.
- However, as sputum samples of TB patients and COVID-19 patients may mix in the TB laboratory, such samples should be processed in a safety cabinet. Therefore, future investment in safety features for laboratories equipped for COVID-19 diagnosis should also take into account these "ventilated" TB laboratories. Providing a safety cabinet will establish a *safe* working environment for COVID-19 samples, and also enable the future processing of sputum samples for the culture of *M. tuberculosis*. Also, equipment for the diagnosis of both diseases can be shared and investments in new equipment for COVID-19 diagnosis should be made in a way that ensures their continued usefulness for TB diagnosis.
- An example is GeneXpert (Cepheid, Sunnyvale, CA, USA), which provides real-time data collection for drug-resistant TB testing and which can be used to test for both TB and COVID-19. Laboratories that will be equipped for COVID-19 diagnosis should consider this equipment instead of a real-time quantitative polymerase chain reaction (PCR) apparatus. Sample preparation is straight forward and GeneXpert can report a result within

30 minutes, without the need for a separate RNA isolation step. Real-time PCR diagnosis of COVID-19 requires the isolation of RNA from the patient sample, which is technically demanding and requires trained personnel (not readily available in a rural setting), and which adds additional cost to the diagnosis.

- About patient care, TB doctors and nurses should be trained in COVID-19 diagnosis and management and control as patients will mix. TB specialists and health workers at the primary health care level may be points of reference for patients with pulmonary complications from COVID-19. Doctors evaluating COVID-19 suspects should implement TB orientated testing algorithms, and COVID-19-negative patients with clinical manifestations and/or risk factors for TB should be followed up by TB testing. Chest X-rays used to distinguish pneumonia from COVID-19 should also be evaluated for the presence of lesions typical for TB. SARS-COV-2 infection may mask radiological manifestations of TB.
- The community also has a role to play, and community-wide education may encourage TB testing in case of a negative COVID-19 result. The community should be made aware of the differences between the two diseases but also the similarities. Although the sample types being collected for TB and COVID-19 are different (sputum vs. nasal swabs), research has shown that both diseases can be tested for with one sample type. Saliva and sputum are equivalent, and in some studies superior, to nasal swabs in the detection of SARS-COV-2 and could thus be used for both TB and COVID-19 diagnosis. National reference laboratories and providers of commercial diagnostic tests should validate saliva and sputum samples and authorise the use of these samples for COVID-19 and TB diagnosis.
- Integrating TB and COVID diagnosis can help to overcome the decrease in registered TB cases. The COVID-19 pandemic has created an opportunity for case finding for both diseases at the same time.
- The integration of control programmes for HIV and TB have been successfully established and newly diagnosed TB patients, always tested for HIV before starting on TB treatment. The same integrated approach could be used for COVID-19 and TB. COVID-19 appears to be here to stay – at least for the near future. We should not forget TB is a major infectious and deadly disease in low- to middle-income countries. By integrating funding, the control programmes for both diseases and raising awareness at all levels of health care, we can contain both.
- Last but not least, measles, pneumococcal disease and other respiratory pathogens can also present with similar symptoms and should be tested where relevant (and before de-isolation of patients) to avoid the risk of transmission of these other communicable diseases.

CONCLUSION

COVID - 19 and lockdown restrictions may pose a significant impact in providing and monitoring TB surveillance strategies nationally and globally. The concerns of delay in the treatment of TB patients would deteriorate their disease and hence more extensive management needs to undertake. Furthermore, these TB patients may develop multidrug resistance and superinfection by the Coronavirus. We suggest that an effective and rapid response to both COVID-19 and TB surveillance, monitoring and treatment services should run simultaneously. Finding and treating patients with TB remain the fundamental pillars of TB prevention and care. Remote teleconsultation of the TB patients would help to track and supervise their treatment. There should be no break in the continuity of essential services for people affected with TB during the COVID-19 pandemic and it should not be bulldozed by the COVID-19.

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