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# Tuberculosis in the era of COVID-19 in India

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# ABSTRACT

*Background and aims:* Tuberculosis (TB) still continues to be endemic in various regions of the world, including in India and needs surveillance, clinical assessment, testing, contact tracing, confirmation of diagnosis with supervised or in-supervised treatment regimens for an effective eradication. We assess the challenges due to COVID- 19 pandemic on 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' and 'India' on the search engines of PubMed, Scopus, Google Scholar and Research Gate in the month of May 2020 during the current COVID-19 pandemic to assess the impact of COVID-19 on management of Tuberculosis.

*Results:* We found considerable disruption 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 in the delivery of various tuberculosis prevention, surveillance, and treatment programmes. Lockdown and public health guidelines have resulted in tough challenges in traditional management of tuberculosis and has required reconfiguration of methods to support patients including wider use of remote consultations.

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### 1. Introduction

The COVID-19 pandemic due to novel coronavirus SARS-CoV-2 is predominantly a respiratory illness and ranges from a common cold to more severe disease including pneumonia [1,2]. The mode of human to human transmission is via droplet infections which are either inhaled 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 [3,4].

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 of death of nearly 0.44 million people in India [5]. One third of the global drug-resistant TB cases are in India, according to the World Health Organisation (WHO) [6].

COVID-19 pandemic has presented us with a global health crisis. However national programmes to combat TB need to be actively engaged ensuring an effective, rapid response to COVID-19 whilst maintaining TB services [7].

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 or in-supervised treatment regimens should still 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 lock-down and infection control strategies [8,9].

We assess the impact of COVID- 19 on TB management including surveillance and monitoring and current strategies adopted to mitigate them.

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1.1. Challenges and strategies to manage TB during COVID-19 pandemic

- 1. Drop in 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. Lock down effects during the COVID-19 pandemic
- 9. Personal Protective Equipment concerns
- 10. Prevention of drug resistance TB
- 11. Personal safety of health-care workers
- 12. Effect of COVID-19 pandemic on TB immunization program
- 13. Economic consequences of COVID-19 pandemic

# 2. Drop in diagnosis of new cases of active TB

TB patients have been badly hit by ongoing lockdown due to COVID-19 pandemic. The diagnosis of new TB cases has seen a dramatic drop since the lockdown according to the Central TB Nikshay portal of Government of India [10]. The estimated number of the diagnosis of 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 [10]. Closure of out-patient departments (OPD) at various hospitals, poor access to treatment, refusal by government and private hospitals, difficulty in reaching Direct Observed Therapy programme (DOTS) centres by patient and medical staff due to limited transport have been quoted as reasons for this situation. Patients who are multidrug resistant tuberculosis and are on injectable medications for TB e.g. Amikacin or Streptomycin are facing real challenge for injection administration [11]. Ministry Of Health and Family Welfare (MOHFW), Government of India (GOI) are trying to ensure uninterrupted diagnosis and treatment for TB patients, including steps like supplying drugs for a month but there is terrible hardship [10].

# 3. Out-patient setting challenges

With 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 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 health-care systems, virtual communication platforms such as e-Sanjeevani, a Government of India, integrated telemedicine solution will be helpful in assisting patients [12]. Telemedicine is already playing an emerging role in remote management of chronic illness such as diabetes mellitus [13,14]. In line with World Health Organization (WHO) recommendations, technologies like electronic medication monitors and video-supported therapy can help patients complete their TB treatment [15].

### 4. Community TB challenges

With the lockdown restrictions and reduction in face to face appointments, there has been increasing necessity of finding complementary ways of assisting patients with TB. Telemedicine can help in community management of TB. Case management of patients with TB can take place via video link or tele-conferencing. Should patients require assistance with medications or there be a risk of compliance with medications, patients are enrolled into a DOTS programme [16], 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 healthcare 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 patient is adhering to the treatment [17].

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 severe cavitating disease, adverse treatment outcomes, a higher rate of recurrence following Antitubercular treatment, and a higher risk of mortality from TB than patients with TB alone [18]. Remote management and monitoring of both diabetes mellitus and TB possible with telemedicine will address both diseases [13].

# 5. 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 of distraction of contact tracing services provided for TB programmes [19]. The response to the COVID-19 pandemic should not affect the continuity of essential contact tracing applications (apps) used for people affected by tuberculosis. In fact, lessons learnt from TB contact apps should be used to make COVID-19 app work better.

#### 6. 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 the outreach services to reach patients with TB and the postal delivery of TB medications [17]. In cases of multi-drug resistant TB, a strategy recommended by the World Health Organisation (WHO) includes the shortening of tuberculosis prevention regimens to 1 month daily regimen of Rifapentine and Isoniazid in the prevention of TB in those who are in close contact with active TB patients [7].

More recently, the Government of India has issued advice regarding the provision of TB medications to patients in the outpatient setting, stating that these patients should be provided with TB medications to last 1 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 [16].

### 7. 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 over a shorter period than TB. (Table 1) A positive result for COVID-19 infection does not eliminate the

#### Table 1

Similarities and Difference between COVID19 and tuberculosis (TB).

	COVID 19	Tuberculosis
Differences	-	-
Onset	Acute	Chronic
Transmission	droplet-transmitted, by touching	airborne transmission; by inhalation
Pathogen	Viral disease	Bacterial disease
-	SARS COV2	Mycobacterium tuberculosis
Incubation period (exposure to disease)	Short (5-14 days)	Longer
Clinical feature	Coughing more commonly a dry a	t • Coughing in TB is usually productive of sputum and even blood
	presentation	<ul> <li>fever and cough: much longer period</li> </ul>
	<ul> <li>fever and cough: rapid onset</li> </ul>	<ul> <li>shortness of breath: later stage or as a long-term sequel</li> </ul>
	<ul> <li>shortness of breath: early</li> </ul>	
Testing specimen	nasopharyngeal or oropharyngeal swab	Sputum
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	anti-tuberculosis treatment
National policy adoption	Fast	Slow
Prevention	Current: Self- distancing, hand washing, PPE	Bacille Calmette-Guérin (BCG) vaccination
	strategy	
	Future: Vaccine	
	Bacilli Calmette-Guerin (BCG) vaccination?	
	Role yet to be proved	
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	Find Test, Treat, Monitor and Prevent strategy. DOTS and Monitoring of
	strategy	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,	Elderly, Diabetes, HIV immunosuppression, chronic obstructive
	chronic obstructive pulmonary disease	pulmonary disease
Personal protection measures	basic infection prevention and control, cough	basic infection prevention and control, cough etiquette, patient triage
	etiquette, patient triage, hand washing	
Role of digital health technologies	Yes	Yes

Abbreviations: RT- PCR-Real Time Polymerase Chain Reaction; HIV- Human Immunodeficiency Virus; HCQS-hydroxychloroquine sulphate.

likelihood of concomitant TB, particularly in a TB endemic country like in India.

European Laboratory Initiative has recommended the use of GeneXpert machines for COVID-19 testing without compromising their use for TB [20]. Recently Indian Council of Medical Research (ICMR) also has approved the use of 'TruenatTM beta CoV test on TruelabTM workstation' which were used for testing drug-resistant tuberculosis as a screening test for COVID-19 [21].

# 8. COVID-19 and TB disease

### 8.1. 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 [22,23]. Mathematical model-based forecasting studies from New Delhi, India emphasize the importance of primary prevention measures especially in TB patients and the need of TB centres to prepare for concurrent infections [24].

# 8.2. 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 [25]. 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 [26]. The testing of TB patients for COVID -19 is applicable to both patients at home as well as patients who are inpatients, including those who are deemed high risk i.e. HIV positive patients [27]. Nigeria Ministry of Health has identified TB as one of the risk factors for severe COVID-19 infection and death [28]. Nigeria has similar profile of endemic presence of TB like India.

### 8.3. 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 [28]. Adewole, O points out the significant impact of 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. Similar dramatic drop since the lockdown according to the Central TB Nikshay portal of Government of India [10]. As 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 [29].

# 8.4. Course and complications of concomitant COVID-19 and TB infection

Tandolini et al. [30] 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 does not fit classical clinical features of either disease. Motta et al. [31] highlight the importance of awareness of possibility of concomitant COVID-19 and TB infection with a serious course and fatality associated in 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 nosocomial infection in the early phases of 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.

# 9. Lock down effects and interruption of supply chain in health care during COVID-19 pandemic

Non-COVID-19 health services like TB surveillance has been hampered with focus on the emergency planning for the pandemic including improving rates of COVID-19 testing and organising quarantine facilities [8]. There is a concern that there may be a surge in 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 COVID-19 pandemic [32].

# 10. Personal protective equipment (PPE)

There has been a worldwide concern about the availability of PPE and paucity of protective materials such as hand sanitizers, mask, and gowns. PPEs shortage in health centres make it impossible for health care workers to provide safe regular health-care services for patient with tuberculosis [33]. This affects sampling of patients with active TB and their transport to central government laboratory since health workers are reluctant taking samples due lack of appropriate PPE.

# 11. 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 [7]. People-centered outpatient and community-based care should be strongly preferred over hospital treatment for TB patients as this will not only prevent patient from a in-hospital visit, but also allow monitoring of uptake of anti-TB drugs. This will reduce chances of drug resistant TB [27]. TB patients likely to be at increased risk of COVID-19 infection so it is advisable that TB patients should continue treatment and take precautions like social distancing, mask, and hand hygiene to protect themselves from COVID-19. Recent study showed there are cases of multidrug-resistant TB cases not put on treatment after being diagnosed due to COVID-19 [34].

### 12. Concerns of safety 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 [35,36].

### 13. Effect of COVID-19 on TB immunization program

Bacille Calmette-Guérin vaccine (BCG) has protective effect against tuberculosis. Due to COVID-19 pandemic lock down, 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 [37]. There has been rising debate about the role of BCG in reducing the impact of COVID-19 [38].

# 14. Economic consequences of COVID-19 pandemic

Together the social, economic, and biomedical consequences of the COVID-19 pandemic have created a perfect storm with respect to tuberculosis disease management [39]. A recent study from 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 [40]. 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 [39].

# 15. Conclusion

COVID - 19 and lockdown restrictions may pose 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 super infection by Corona virus. 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 tele-consultation of the TB patients would help tracking and supervising 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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# **Competing interests**

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# **Disclosure statement**

Nothing to disclose.

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None.

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