Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Tuberculosis in the era of COVID-19 in India

Vijay Kumar Jain a, *, Karthikeyan P. Iyengar b, David Ananth Samy b, Raju Vaishya c

a Department of Orthopaedics, Atal Bihari Vajpayee Institute of Medical Sciences, Dr Ram Manohar Lohia Hospital, New Delhi, 110001, India
b Southport and Ormskirk NHS Trust, Southport, PR8 6PN, UK
c Department of Orthopaedics, Indraprastha Apollo Hospital, Sarita Vihar, Mathura Road, 110076, New Delhi, India

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 lockdown 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.
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 Anti-tubercular 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
likelihood of concomitant TB, particularly in a TB endemic country like 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 Truenat™ beta CoV test on Truelab™ 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

### Table 1

| Similarities and Difference between COVID-19 and tuberculosis (TB). |
|---------------------------------------------------------------|
| **Differences**                                               | **COVID 19**                              | **Tuberculosis**                               |
| Onset                                                         | Acute                                     | Chronic                                       |
| Transmission                                                  | droplet-transmitted, by touching          | airborne transmission; by inhalation          |
| Pathogen                                                      | Viral disease                             | Bacterial disease                             |
| Incubation period (exposure to disease)                       | Short (5-14 days)                         | Mycobacterium tuberculosis                    |
| Clinical feature                                              | • Coughing more commonly a dry presentation | • coughing in TB is usually productive of sputum and even blood                                    |
|                                                              | • fever and cough: rapid onset            | • fever and cough: much longer period                                                   |
|                                                              | • shortness of breath: early              | • shortness of breath: later stage or as a long-term sequel                                |
| 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 strategy | Bacille Calmette-Guerin (BCG) vaccination |
|                                                              | Future: Vaccine                           | Role yet to be proved                         |
|                                                              | Bacilli Calmette-Guerin (BCG) vaccination? |                                               |
| **Similarities**                                              | Lung                                      | Lung                                          |
| Organ affected                                                | Yes                                       | Yes                                           |
| Genetic and non-genetic factors - lack of knowledge for individual susceptibility | 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-Real Time Polymerase Chain Reaction; HIV- Human Immunodeficiency Virus; HCQS-hydroxychloroquine sulphate.
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. PPE 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

Providing 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 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 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.

Statement of ethics

Not required.
Funding statement

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Disclosure statement

Nothing to disclose.

Declaration of competing interest

None.

References

[1] World Health Organisation Dashboard Coronavirus. 2020. https://experience.arcgis.com/apps/arcgisExperienceMap/index.html#/bda75947474185f40da79ef8fa8d3e2d
[2] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu C, Gao C. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382. https://doi.org/10.1056/NEJMoa2001017
[3] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course, and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single centered, retrospective, observational study. Lancet Respir Med 2020. https://doi.org/10.1016/S2213-2600(20)30079-5
[4] Abe DG, Shin HJ, Kim MH, et al. Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19). J Microbiol Biotechnol 2020;30(3):313–24. https://doi.org/10.4014/jmb.2003.03011
[5] TB Statistics India. Available from: https://tbstats.org.in/tb-statistics-india/. [Accessed 10 July 2020]. Accessed.
[6] World Health Organisation (WHO). Global TB Report 2019. https://www.who.int/tb/publications/global_report/en/. [Accessed 10 July 2020]. Accessed.
[7] World Health Organisation (WHO). Tuberculosis and COVID-19. Available from: https://www.who.int/docs/default-source/documents/tuberculosis/infonote-tb-covid-19.pdf. [Accessed 11 May 2020]. Published.
[8] The Lancet. India under COVID-19 lockdown. Lancet 2020;395(10233):1315. https://doi.org/10.1016/S0140-6736(20)30937-5
[9] COVID-19 India. https://www.mohfw.gov. [Accessed 10 July 2020]. Accessed.
[10] Indian Council of Medical Research (ICMR. ). ICMR Approves Use of Diagnostic Machine used for drug-resistant TB for COVID-19. Available from: https://www.icmr.nic.in/news/impact-of-covid-19-on-tb-care-experiences-of-a-treatment-centre-in-delhi. [Accessed 10 July 2020]. Accessed.
[11] Motta I, Centris R, Ambrosio LD, et al. Tuberculosis, COVID-19, and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts. Pulmonology 2020. https://doi.org/10.1016/j.pulmoe.2020.05.002.
[12] Nikhaya Aushadhi, Government of India. Available from. https://www.mohfw.gov.in. [Accessed 10 July 2020]. Accessed.
[13] Houghton C, Meskell P, Delaney H, et al. Barriers and facilitators to healthcare workers’ adherence with infection prevention and control (IPC) guidelines for routine infectious diseases: a rapid qualitative evidence synthesis. Cochrane Database Syst Rev 2020;4(4):CD013582. https://doi.org/10.1002/14651858.CD013582. Published 2020 Apr 21.
[14] Chatterjee PK. Community preparedness for COVID-19 and frontline health workers in Chhattisgarh. Indian Public Health J 2020;64:510–4.
[15] COVID-19: Indian government vows to protect health care workers from violence amid rising cases. BMJ 2020;369. https://doi.org/10.1136/bmj.m1631. [Accessed 23 April 2020]. Published.
[16] Vaishya R, Vaish A. The plight of Health Care Workers in India during COVID-19 pandemic. BMJ 4th April 2020. Published on, https://www.bmj.com/content/369/bmj.m1324/rc-4.
[17] World Health Organisation (WHO) Regional Office for Europe. Guidance on Routine Immunization Services During COVID-19 Pandemic in the WHO European Region. http://www.euro.who.int/__data/assets/pdf_file/0004/435813/Guidance-routine-immunization-services-COVID-19-pandemic.pdf?ua=1. [Accessed 15 July 2020]. Accessed.
[18] Curtis N, Sparrow A, Ghebreyesus TA, Netea MG. Considering BCG vaccination to reduce the impact of COVID-19. Lancet 2020. https://doi.org/10.1016/S0140-6736(20)31025-4 [published online ahead of print, 2020 Apr 30]. S0140-6736(20)31025-4. [Accessed 10 July 2020]. Accessed.
[19] Saunders MJ, Evans CA. COVID-19, tuberculosis and poverty: preventing a perfect storm. Eur Respir J 2020;56(1). 2001348.
[20] Sumner A, Hoy C, Ortiz-Juarez E. Estimates of the Impact of COVID-19 on Global Poverty. WIDER Working Paper 2020/43. Helsinki: UNU-WIDER; 2020. Available from: https://www.wider.unu.edu/publication/estimates-impact-covid-19-global-poverty. [Accessed 14 July 2020]. Accessed.

Antimicrob 2020;19:21. https://doi.org/10.1186/s12941-020-00363-1.

Government of India. Ministry of Electronics and Information Technology. Ayogya Setu. https://www.aayogya.gov.in/. [Accessed 10 July 2020]. Accessed.

World Health Organisation (WHO). COVID-19 Strategy Update 14 April 2020. https://doi.org/10.1016/S0140-6736(20)31025-4 [published online ahead of print, 2020 Apr 30]. S0140-6736(20)31025-4. [Accessed 10 July 2020]. Accessed.

Diabetes Metab Syndr 2020;14(4):273–6. https://doi.org/10.1016/j.dsx.2020.04.001 [published online ahead of print, 2020 Apr 4].