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TUBERCULOSIS DURING THE COVID-19: IMPACT, CHALLENGES AND MANAGEMENT

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ABSTRACT

The corona virus disease 2019 (COVID-19) has caused substantial disruptions to health services due to overburdening the health system. Hence, there are severe obstructions in tuberculosis (TB) services in India's primary health care and hospital settings. Several restrictions, such as lockdown, self-isolations, and other public health guidelines to prevent viral transmission, impacted the delivery of essential facilities for TB management. A significant reduction in tuberculosis testing in the public health sector has been noticed, which is an alarming situation in India. However, there are several risks in managing TB due to rising cases of COVID-19 but maintaining the most critical prevention activities and healthcare services for tuberculosis could substantially reduce the overall impact of the COVID-19 pandemic. This review focuses on the impact and challenges of COVID-19 on tuberculosis. Further, the strategies to eradicate tuberculosis in the era of COVID-19 are also discussed.

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1 Introduction

Coronaviruses (CoVs) have been associated with several disease outbreaks in several parts of the world. The severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) began to emerge in 2002 and 2012, respectively. Recently, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), appeared in late 2019, and it has posed a high global health threat, causing an ongoing pandemic all around the world (Dhama et al., 2020a; Malik et al., 2020a).

The outbreak of COVID-19, which was declared as an emergency in March 2020, has employed a substantial negative impact on the healthcare systems and socio-economic structures of countries across the globe. The disease, caused by a novel SARS-CoV-2, has infected millions and killed hundreds of thousands of people in essentially every country in the world (WHO Dashboard, 2020; Dhama et al., 2020b). Adverse effects of the COVID-19 epidemic on access to health services have emerged (Hogan et al., 2020), and there is a serious concern that possible disruptions in Tuberculosis (TB) programmes due to COVID-19 could impact TB-related mortality and new infections (Figure 1).

TB is a deadly disease, with more than 4,000 deaths a day worldwide, making it a highly infectious disease globally. It is not yet clear whether having a disease like TB will increase disease severity from coronavirus infection. However, evidence suggests that having underlying health conditions such as a chronic respiratory disease will increase the chance of exacerbating symptoms and negatively impact a person's health contracted with COVID-19.

Moreover, the COVID-19 pandemic led to a global reduction of 25% in expected TB detection in the last few months – an inevitable consequence has been observed in many countries, which results in a 13% increase in TB deaths, bringing us back to TB mortality levels of the year 2015. This study can be a conservative estimate as it does not include other factors such as treatment interruptions and poorer outcomes in patients with TB and COVID-19 infection (Glaziou, 2020). From 2020 to 2025, an additional 1.4 million TB deaths could be registered due to the COVID-19 pandemic (WHO Information Note, 2020).

However, India accounts for more than one-fourth of the world's TB cases. This amounts to about 2.6 million cases out of 10 million cases worldwide. TB has been the reason for the death of nearly 0.44 million people in India. According to the World Health Organization (WHO), one-third of the global drug-resistant TB cases are in India, and the COVID-19 pandemic has presented us with a global health crisis. India is a high TB burden country with a massive number of patients with post TB lung sequel, and the outcome of COVID-19 in such patients is unknown so far. However, national programs to combat TB need to be actively engaged, ensuring an effective, rapid response to COVID-19 while maintaining TB services (Jain et al., 2020). In this study, we aim to provide information on the potential impact of the COVID-19 epidemic on TB. Further, this review focuses on the challenges and strategies to manage TB during the era of COVID-19.
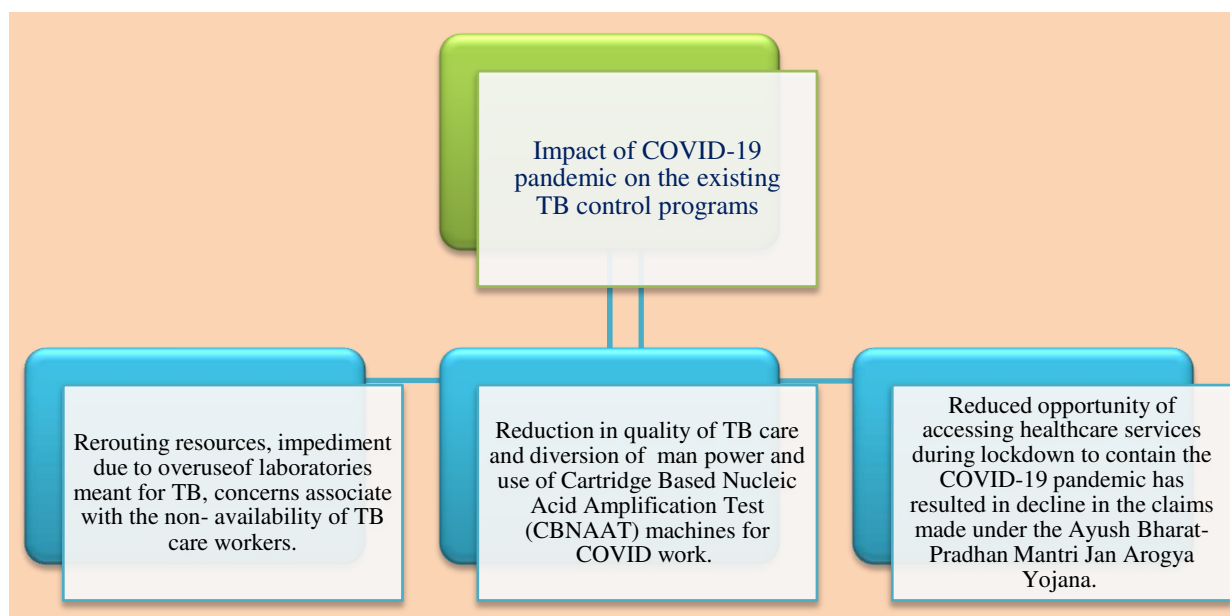

Figure 1 Impact of COVID-19 on TB management

2 COVID-19 and TB relationship:

COVID-19 and TB both attack the lungs primarily, and patients with both diseases develop similar symptoms such as cough, fever, and difficulty breathing. Although both biological agents transmit via close contact, the incubation period from TB disease exposure is more prolonged, often with a slow onset. COVID-19 and TB are emerging, and early evidence suggests that patients with latent TB and established disease have an increased risk of the SARS-CoV-2 infection and predisposition towards developing severe COVID-19 associated pneumonia. Moreover, TB patients with COVID-19 may have poorer treatment outcomes, especially if TB treatment is interrupted. TB patients should take more precautions as advised by health authorities to be protected from COVID-19 and continue their TB treatment as prescribed (WHO guidelines, 2020).

The main concern about the co-infection of TB and COVID-19 is the mortality associated with it. A study showed a mortality of 12.3% in patients with dual infection, which is much higher than isolated Covid-19 disease (Guan et al., 2020). However, this apparent higher mortality can't be attributed to the dual infection from this cohort as the majority of fatal patients had proven risk factors of mortality that might have deviated from the actual results.

Irrespective of the probable temporal association between COVID-19 and TB, both infectious diseases may have a synergistic impact on social and economic impact worldwide. This is because both the diseases are expected to spread in overcrowded areas with a poor and undernourished population (Wingfield et al., 2018). High TB burden countries have a huge number of patients with post TB treatment, and the outcome of COVID-19 in such patients is unknown so far. It is important to understand that in the fight against the COVID-19 pandemic, we should not forget to manage TB appropriately, which is still one of the leading infectious diseases in the world (Khurana & Aggarwal, 2020).

3 Reduction in TB testing

Due to COVID-19, people with TB are likely to face less access to diagnostic and treatment services because of extreme pressures on health systems, resulting in adverse outcomes. TB patients have been badly hit by ongoing lockdown due to the 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 the Government of India (Government of India TB report, 2020). The estimated number of diagnoses of several new tuberculosis cases detected as of September 2020 in government healthcare centers saw a significant fall (Figure 2).

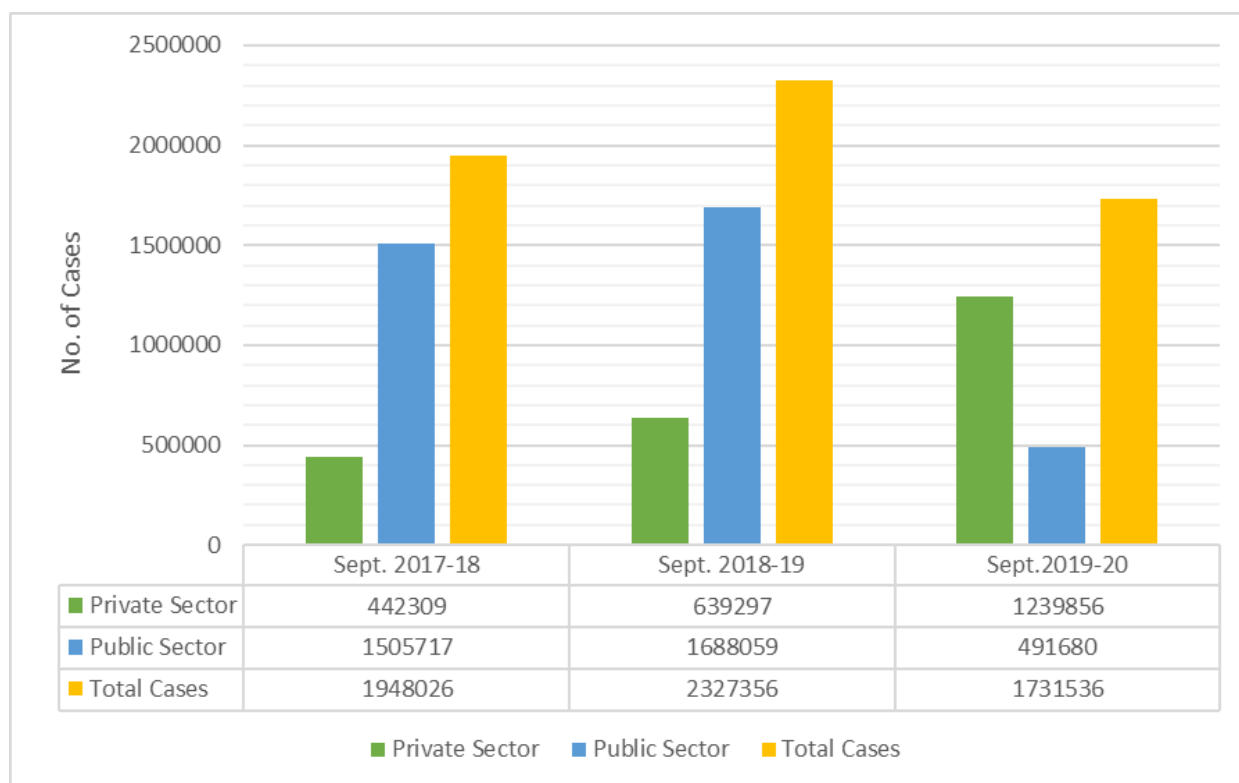|	Sept. 2017-18	Sept. 2018-19	Sept.2019-20
Private Sector	442309	639297	1239856
Public Sector	1505717	1688059	491680
Total Cases	1948026	2327356	1731536

Figure 2 Drastic drop in Testing of TB in the Public sector and reduction in total cases. (Data obtained from Nikshay Portal of Government of India).

4 Challenges and Risks in combating the Tuberculosis

4.1 Substandard primary healthcare infrastructure in the rural regions of India.

The poor condition of India's rural areas' healthcare system is entirely ascribed to the degraded and corrupted system, which leads to missed opportunities for diagnosis and poor treatment outcomes. The root causes of health inequities lie in the economic, social, and political systems that lead to social hierarchy according to the occupation, income, education, and gender (WHO, 2008). The rural healthcare facilities are combating with scarceness of efficient infrastructure and limited manpower (Chilimuntha et al., 2013). Several studies from local regions of India suggest that a considerable percentage of TB patients were found at government health care facilities but fail to be diagnosed with TB or fail to start TB treatment even if they are correctly diagnosed (Subbaraman et al., 2016). It has been reported that India has about 1 million "missing" tuberculosis patients, who may not have given effective care. There are several barriers to the diagnosis and treatment of TB in India (Figure 3).

4.2 Pressure on struggling healthcare systems in the COVID era

COVID-19 pandemic has put unprecedented demands on the healthcare system, and this pressure has decreased access to medicines and diagnostics for those with other critical life-threatening conditions. The resources and manpower are rerouted and are assigned to various other activities to control the outbreak (Behera, 2020). During this pandemic, detection and medication of TB, or TB and COVID-19 co-infection, are expected to be compromised. The current state of affairs has escalated the number of deaths from TB in recent times (Prasad et al., 2020). Preliminary studies have suggested that TB infection rates were comparatively higher among COVID-19 patients and TB infection status is a specific risk factor for SARS-COV-2 infection (Liu et al., 2020).

4.3 Delay in Diagnosis

Diagnosis of COVID-19 is the most pressing matter nowadays, leading to TB's treatment delay. Utilization of established TB sanatoriums and hospitals for admitting COVID-19 patients bounded health infrastructure (ventilators, hospital beds, and respiratory barriers), reduced manufacturing capacity of drugs has resulted in the exhaustion of stocks, interrupted transportation facilities, and lack of streamline health policy has significantly increased TB cases.

Malnutrition, poverty, and low-income in unauthorized colonies such as slums, are also rampant in a densely populated country like India (1.35 million), thus creating a significant hindrance to the containment plan. All these factors will be responsible for delay in treating both TB and COVID-19, which can lead to a shoot in both diseases and increased transmission of infection in the community.

5 Possible strategies to manage tuberculosis during the COVID-19 pandemic

While there are several trials under the development of the COVID-19 vaccine (Rabaan et al., 2020; Yatoo et al., 2020), there is no evidence that the existing Bacille Calmette-Guerin (BCG) vaccine protects the people suffering from TB with the infection of
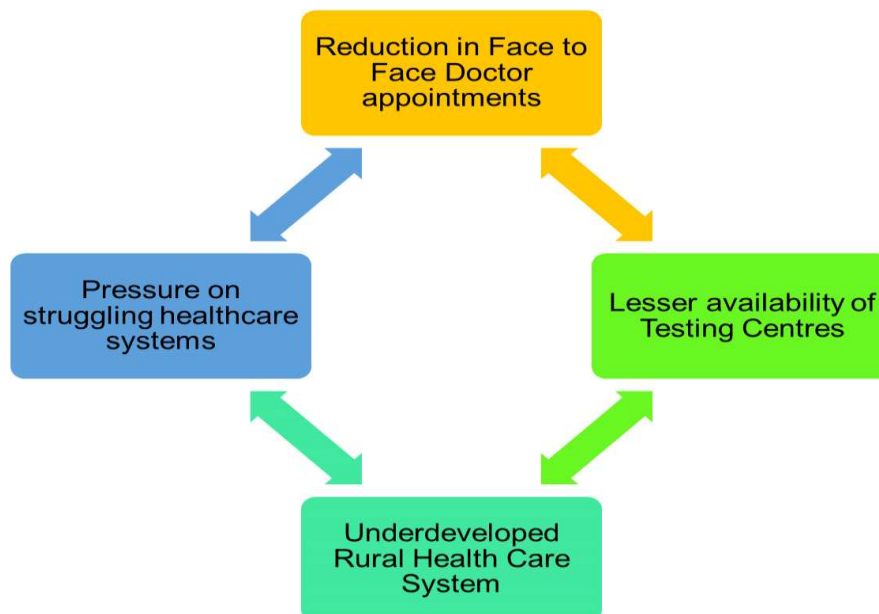

Figure 3 Challenges and risks in combatting the TB during Pandemic.

COVID-19, though BCG vaccination has been suggested to reduce the morbidity and mortality amidst COVID-19 pandemic (Alene et al., 2020; Malik et al., 2020b; Miller et al., 2020; Miyasaka, 2020; Singh et al., 2020). Different strategies can be implemented to lessen the impact of COVID-19 on TB control to overcome this situation. As the COVID-19 pandemic spreads into high TB burden settings, countries must put strategies like advising the people to stay at home until the situation comes under fully controlled (Anderson et al., 2020); social distancing; maintaining proper hygiene through sanitization, provide TB research and related information through various platforms viz. seminars, workshops, conferences; decentralizing the TB treatment facility; apply room ventilation (through natural and mechanical ways, recirculated air through high-efficiency particulate air (HEPA) filters); provide short-term training for health professionals to work on TB programs; providing community awareness of the importance of TB services to ease pressure on health systems and mitigate disruption in routine health services. The current social distancing and stay-at-home measures made it more challenging for TB programs to provide diagnosis, treatment, and care for low-income countries and communities with a high TB burden. The TB programs should create and rely on newer technologies to avoid obstructions in TB management. These technologies include virtual care, digital health services, and community- monitoring solutions. In today's scenario, it is the need of the hour to provide these technologies as close as possible to the people and communities, which is affected by TB (Figure 4).

5.1 Strategies to control at household levels during COVID-19 pandemic

TB can be overcome with COVID-19 under different levels. The initial preventive measures should be taken at the household level. All the countries are advised to stay at home to prevent the COVID-19 until the situations come under control (Anderson et al., 2020; Xiao et al., 2020). Furthermore, this measure is also beneficial for the transmission of TB because extended contact at the household level is the primary factor for increasing the transmission of TB (Acuna et al., 2018). Singh et al. (2005) reported the important risk factors such as younger age, severe malnutrition, absence of BCG vaccination, contact with an adult who was sputum positive, and exposure to environmental tobacco smoke for transmission of TB. These researchers also reported that household infection is increased significantly with prolonged household contact with sputum positive adults than the general population.

To limit household transmission of TB, necessary control measures, recommended by the WHO for health care facilities and high-risk settings, can be implemented at home (WHO, 2019). The patients should follow the cough etiquette, personal protective equipment, etc. To avoid TB diagnosis and treatment delay due to COVID-19, the use of virtual care and digital health technologies, decentralizing TB treatment to community health workers, and supporting private health sectors and academic research institutions to provide TB testing and treatment might all be required.
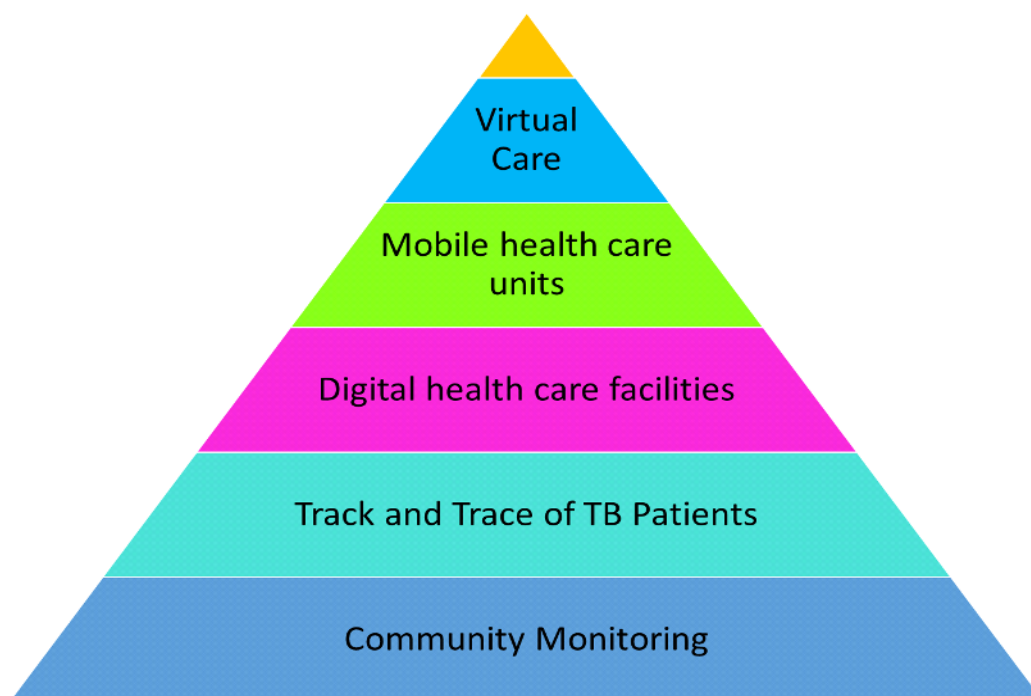

Figure 4 Strategies to reduce the impact of COVID-19 on TB management in India.

5.2 Continuity of essential TB services during COVID-19 pandemic

Necessary measures should be introduced to limit transmission of TB and COVID-19 in congregate settings and health care facilities, as per WHO guidelines. The most important measures are that the TB disease controlling staff should share their expertise and knowledge for technical and logistic support with their excellent working experience and contact tracing. TB can cure in this pandemic by supporting the patients through well communication, care, and counseling using digital health technologies (WHO guidelines, 2020).

5.3 Continuous supply of human resources

The supply of human resources includes well trained Respiratory physicians, pulmonology staff, TB specialists, and health workers at the primary health care level should be available and appointed at points of reference for patients with pulmonary complications of COVID-19. In the context of worldwide restriction on the population's movements, the COVID-19 patients are advised to be retained isolated and placed into the quarantine centers. To overcome this gap, communication between health care staff and patients should be maintained, and their health services should be provided continuously. These healthcare services include nutritional and mental health support, restocking of medicines, and managing adverse drug responses.

A sufficient amount of TB medicines should be provided to those who will not come out from their houses until the next visit to overcome TB management's hindrance. There should be some mechanisms for delivering the medicines and also collecting their specimens for proper follow-up from their homes. The Government of India should start mobile health care units to battle with tuberculosis during the era of COVID-19. Home-based TB treatment has become more common during the COVID-19 pandemic. These alternative arrangements reduced continuous clinic visits, and lead to avoid exposure to other clinic attendees, using digital technologies to maintain treatment support.

At present, it is well known that both the diseases, TB, and COVID-19 are linked with social stigma and have produced a lot from health education and medications. Efforts are made by the Govt. of India to start again routinely services across the country, and NTEP mainly follows it. It also ensures that all laboratory services, including public and private, should continue their services like sputum collection with safety precautions. They must follow preventive and control measures (Prasad et al., 2020).

In this COVID-19 pandemic, the other useful strategy is self-administered therapy, which is provided at home. To manage tuberculosis during the pandemic, the measures should be adopted,

such as evading daily checkups for the outpatient department (OPD) visits, and only serious patients should be admitted. There should be shifting of health care workers.

It is well known that BCG is the only vaccine for proper dissemination of TB, but for COVID-19, trials are ongoing for vaccines and still under development. Efforts have been made continuously by many countries for vaccine production, and many of them are in the last stage of trials (Yatoo et al., 2020).

According to Miller et al., 2020 and Hegarty et al., 2020, Asian and African countries fully adopted BCG vaccination than Europe and the USA. That is why they have a high mortality rate for COVID-19. The causative agent of COVID-19 is the novel virus SARS-CoV-2, whereas, for TB, it is *Mycobacterium tuberculosis*. As both the diseases have similar respiratory symptoms, but in COVID-19, their progression is high. Therefore, this is a ray of new hope for India, where BCG revaccination practices provide additional protection against severe COVID-19.

This is doubtless that India will also get assistance in fulfilling the dream of proper diminishing the TB by 2025. There is a high requirement for proper investigation and the use of advanced technologies for the development of vaccines as well as drugs for both the diseases.

In Last, different strategies are adopted for reducing epidemics of both TB and COVID-19, which can complement each other and leads to a decrease in the level of mortality. So, for this time, we need to reframe our health policies. To accomplish these policies, there should be coordination between government, public, and private health sectors.

Conclusion and future perspectives:

In conclusion, the interruptions caused by COVID-19 in National TB management programmes of several developing countries could lead to a substantial number of additional deaths. COVID-19 has created a threatening situation for high TB burden countries like India, Pakistan, and Africa. It is essential to understand that in the fight against the COVID-19 pandemic, the government should not forget to manage TB efficiently, which is still one of the most severe infectious diseases. There are several challenges in managing TB during the era of COVID-19 in India, such as the lack of adequate resources and outreach of essential medicines. However, the use of the virtual health care system, mobile care facilities, and the continuous supply of TB medicines can reduce the negative impact of COVID-19 on TB management, especially in India's rural regions.

Ethics approval and consent to participate:

Not applicable

Consent for publication

All the authors have agreed for publication.

Availability of data and materials

All the analyzed data of this work are included in this manuscript is available at (https://tbcindia.gov.in/).

Competing interests

The authors declare that they have no competing interests.

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Author's contribution

All authors contributed equally and approved the manuscript.

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References

Acuna-Villaorduna, C, Jones-Lopez EC, Fregona G, Marques-Rodrigues P, Gaeddert M, Geadas C, Ribeiro-Rodrigues R (2018) Intensity of exposure to pulmonary tuberculosis determines risk of tuberculosis infection and disease. European Respiratory Journal 51(1):1701578 https://doi.org/10.1183/13993003.01578-2017.

Alene KA, Wangdi K, Clements AC (2020) Impact of the COVID-19 Pandemic on Tuberculosis Control: An Overview. Tropical Medicine and Infectious Disease *5*(3): 123. https://doi.org/10.3390/tropicalmed5030123.

Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD (2020) How will country-based mitigation measures influence the course of the COVID-19 epidemic? The Lancet 395: (10228): 931-934.

Behera D (2020) TB control in India in the COVID era. Indian Journal of Tuberculosis, https://doi.org/10.1016/j.ijtb.2020.08.019.

Chilimuntha, Anil K, Kumudini RT, Jeremiah SM (2013) Disadvantaged Rural Health– Issues and Challenges: A Review. National Journal of Medical Research 3(1): 80-82.

Dhama K, Khan S, Tiwari R, Sircar S, Bhat S, Malik YS, Singh KP, Chaicumpa W, Bonilla-Aldana DK, Rodriguez-Morales AJ (2020a) Coronavirus Disease 2019-COVID-19. Clinical Microbiology Reviews 33(4): e00028-20. https://doi.org/10.1128/CMR.00028-20.

Dhama K, Patel SK, Pathak M, Yatoo MI, Tiwari R, Malik YS, Singh R, Sah R, RabaanAA,. Bonilla-Aldana DK, RodriguezMorales AJ (2020b) An update on sars-cov-2/covid-19 with particular reference to its clinical pathology, pathogenesis, immunopathology and mitigation strategies. Travel Medicine and Infectious Disease https://doi.org/10.1016/j.tmaid.2020.101755

Glaziou P (2020) Predicted impact of the COVID-19 pandemic on global tuberculosis deaths in 2020. Epidemiology: https://doi.org/10.1101/2020.04.28.20079582. .

Government of India. Central Tuberculosis Division. India TB report 2020: Available on https://tbcindia.gov.in/ access on 19th September 2020.

Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX (2020) Clinical characteristics of Coronavirus disease 2019 in China. The New England Journal of Medicine 382:1708-1720.

Hegarty PK, Kamat AM, Zafirakis H, Dinardo A (2020) BCG vaccination may be protective against Covid-19. Preprint https://doi.org/10.13140/RG.2.2.35948.10880.

Hogan AB, Jewell B, Sherrard-smith E, et al. (2020) The Potential Impact of the COVID-19 Epidemic on HIV, TB and Malaria in Low- and Middle-Income Countries. London, Imperial College London, DOI: https://doi.org/10.25561/78670.

Jain VK, Iyengar KP, Samy DA, Vaishya R (2020) Tuberculosis in the era of COVID-19 in India Diabetes & Metabolic Syndrome. Clinical Research & Reviews 14: 1439-1443. https://doi.org/10.1016/j.dsx.2020.07.034

Khurana AK, Aggarwal D (2020) The (in)significance of TB and COVID-19 co-infection. European Respiratory Journal 56 (2) 2002105   DOI: https://doi.org/10.1183/13993003.02105-2020.

Liu Y, Bi L, Chen Y (2020) Active or latent tuberculosis increases susceptibility to COVID-19 and disease severity. medRxiv, DOI: https://doi.org/10.1101/2020.03.10.20033795.

Malik YS, Kumar N, Sircar S, Kaushik R, Bhat S, Dhama K, Gupta P, Goyal K, Singh MP, Ghoshal U, El Zowalaty ME, O R V, Yatoo MI, Tiwari R, Pathak M, Patel SK, Sah R, Rodriguez-Morales AJ, Ganesh B, Kumar P, Singh RK (2020a). Coronavirus disease pandemic (COVID-19): Challenges and a global perspective. Pathogens 29(7):519. doi: 10.3390/pathogens9070519.

Malik YS, Ansari MI, Ganesh B, Sircar S, Bhat S, Pande T, Vinodhkumar OR, Kumar P, Yatoo MI, Tiwari R, Touil N,

Patel SK, Pathak M, Sharun K, Dhama K (2020b). BCG vaccine: a hope to control COVID-19 pandemic amid crisis. Human Vaccines & Immunotherapeutics. DOI: https://doi.org/10.1080/21645515.2020.1818522

Miller A, Reandelar MJ, Fasciglione K, Roumenova V, Li Y, Otazu GH (2020). Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: an epidemiological study. MedRxiv DOI: https://doi.org/10.1101/2020.03.24.20042937.

Miyasaka M (2020) Is BCG vaccination causally related to reduced COVID-19 mortality? EMBO Molecular Medicine 12(6):e12661. doi: 10.15252/emmm.202012661.

Prasad R, Singh A, Gupta N (2019) Tuberculosis and COVID-19 in India: Challenges and opportunities. Lung India 37(4): 292.

Rabaan AA, Al-Ahmed SH, Sah R, Tiwari R, Yatoo MI, Patel SK, Pathak M, Malik YS, Dhama K, Singh KP, Bonilla-Aldana DK, Haque S, Martinez-Pulgarin DF, Rodriguez-Morales AJ, Leblebicioglu H (2020). SARS-CoV-2/COVID-19 and advances in developing potential therapeutics and vaccines to counter this emerging pandemic. Annals of Clinical Microbiology and Antimicrobials 19(1):40. doi: 10.1186/s12941-020-00384-w.

Singh M, Mynak ML, Kumar L, Mathew JL, Jindal SK (2005) Prevalence and risk factors for transmission of infection among children in household contact with adults having pulmonary tuberculosis. Archives of disease in childhood 90(6): 624-628.

Singh BR, Gandharva R, Karthikeyan R, Singh SV, Yadav A, Vinodh Kumar OR, Sinha DK, Jayakumar V, Dhama K, Kumar D, Gandharava S (2020). Epidemiological determinants of acute respiratory syndrome coronavirus-2 disease pandemic and the role of the Bacille-Calmette-Guerin vaccine in reducing morbidity and mortality. Journal of Pure and Appl Microbiology. 14(suppl 1):1007-1016. doi: 10.22207/JPAM.14.SPL1.39

Subbaraman R, Nathavitharana RR, Satyanarayana S, Pai M, Thomas BE, Chadha VK (2016) The Tuberculosis Cascade of Care in India's Public Sector: A Systematic Review and Meta-analysis. PLoS Medicine 13(10): e1002149.

World Health Organization (2020) Tuberculosis and COVID-19. Available from: https://www.who.int/docs/default-source/documents/tuberculosis/infonote-tb-covid19.pdf

WHO Coronavirus disease 2019 (COVID-19) Situation report (2020) World health Organization, Geneva, Switzerland, 2020.

WHO Guidelines (2020) WHO operational Handbook on Tuberculosis: Module1: Prevention: Tuberculosis Preventive Treatment, World health Organization, Geneva, Switzerland 2020.

Wingfield T, Tovar MA, Datta S, Saunders MJ, Evans CA (2018) Addressing social determinants to end tuberculosis. Lancet 391: 1129–1132. https://doi.org/10.1016/S0140-6736(18)30484-7.

World Health Organization Dashboard Coronavirus (2020) https://experience.arcgis.com/experience/685d0ace521648f8a5bee eee1b9125cd   [Accessed 11Sept 2020].

World Health Organisation (2008) Report of the Commission on Social Determinants of Health

Xiao Y, Torok M E (2020) Taking the right measures to control COVID-19. The Lancet Infectious Diseases 20(5): 523-524.

Yatoo MI, Hamid Z, Parray OR, Wani AH, Ul Haq A, Saxena A, Patel SK, Pathak M, Tiwari R, Malik YS, Sah R, Rabaan AA, Rodriguez Morales AJ, Dhama K (2020) COVID-19 - Recent advancements in identifying novel vaccine candidates and current status of upcoming SARS-CoV-2 vaccines. Human Vaccines and Immunotherapeutics 1-14. doi: 10.1080/21645515.2020.1788310.