

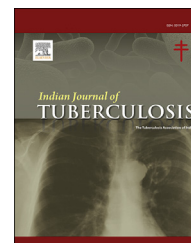


Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.journals.elsevier.com/indian-journal-of-tuberculosis/>

Viewpoint

Tobacco use, tuberculosis and Covid-19: A lethal triad

Parul Mrigpuri^a, Amitesh Gupta^b, Ritika Jha^b, Pranjal Singla^c,
Rupak Singla^{b,*}^a Department of Pulmonary Medicine, Vallabh Patel Chest Institute, University of Delhi, New Delhi, 110007, India^b Department of Tuberculosis and Chest Diseases, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, 110030, India^c iDEFEAT TB Project, International Union Against Tuberculosis and Lung Diseases, India

ARTICLE INFO

Article history:

Received 4 August 2021

Accepted 6 August 2021

Available online 12 August 2021

Keywords:

Smoking

Tuberculosis

COVID-19

ABSTRACT

Smoking, TB and Covid-19 are high prevalence entities with public health consequences. All three of them have a possible complex interaction at cellular level. Smoking behavior makes it difficult to maintain infection control measures. Smoking is known to increase TB infection and also adversely affect treatment outcomes in TB. There is also upcoming evidence which suggests that smoking and TB increase the risk of severe Covid-19 symptoms. Simple infection control measures like, social distancing, cough etiquette, isolation, hand hygiene, quarantine, use of masks etc. play a pivotal role in prevention of these diseases. There is need of strengthening of the public health policies and incorporation of the Covid-19 safety awareness measures into the various national programmes.

© 2021 Tuberculosis Association of India. Published by Elsevier B.V. All rights reserved.

The habit of smoking is centuries old and tobacco addiction is no less than an epidemic. The epidemiological data of 2019 by World Health Organization (WHO) reported that tobacco was responsible for 8 million deaths worldwide.¹ WHO factsheet 2018 of India reported more than 1 million deaths which was about 9.5% of all the deaths.¹ Tuberculosis (TB) as a disease also has a very high burden. An estimated 10 million people developed TB in 2019 with 1.2 million TB deaths. India alone reported 2.64 million cases in 2019.² The Coronavirus disease (Covid-19) caused by severe acute respiratory syndrome

corona virus 2 (SARS-CoV-2) has spread throughout the world. Globally, by 28th July 2021, there have been 195,992,087 confirmed cases of Covid-19, including 4,193,169 deaths indicating a very high burden of infection. In India alone there has been 31,484,605 cases with 422,054 deaths.³ The association between the three entities is presently undefined and studies are needed to establish a clear association. The epidemiological picture however undoubtedly clarifies that smoking, TB and Covid-19, all three have a high burden with public health concerns.

* Corresponding author. Department of Tuberculosis and Chest Diseases, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, 110030, India. Tel.: +91 9891168908.

E-mail address: drrupaksingla@yahoo.com (R. Singla).

<https://doi.org/10.1016/j.ijt.2021.08.010>

0019-5707/© 2021 Tuberculosis Association of India. Published by Elsevier B.V. All rights reserved.

1. Possible etio-pathogenetic link of smoking, TB and Covid-19 infection

Smoking, TB and Covid-19 have complex interaction at cellular level. Smoking has a damaging effect on lungs. It alters the immune response by hindering the functioning of immune cells like macrophages, monocytes and CD4 lymphocytes and affects the ciliary function.⁴ These factors are responsible for increased susceptibility of smokers to TB. Smoking is known to increase the risk of various other infections. Risk for pneumococcal, legionella, and mycoplasma pneumonia infection is about 3–5-times higher in smokers than non-smokers. Studies though scarce have shown increased risk of mortality and increased disease severity in smokers with Middle Eastern respiratory syndrome coronavirus.⁵ It also hinders the cytokine release and results in upregulation of the angiotensin converting enzyme 2 (ACE-2) receptor, which is the main receptor used by SARS-CoV-2 for entry to the mucosa.⁵ SARS-CoV-2 infection has been implicated in the reactivation of dormant TB by activating the cell mediated defense mechanism and its role in predisposing for TB is also proposed in view of its ability to initiate inflammation by increasing cytokine release. Moreover, the virus affects the host immunity because of mutations in Interferon- γ and Interleukin-12 signaling pathways.⁶

2. Clinical convergence and possible interactions

Smoking is a known risk factor for getting infected with *Mycobacterium tuberculosis* and developing a severe form of the disease. It has also been linked to poor TB treatment outcomes.⁴ Smokers have been found to be more likely to contract the flu and smoking has been found to be consistently associated with a higher risk of hospital admissions after influenza infection. Smoking is also primary etiological factor behind chronic obstructive pulmonary diseases (COPD) and exacerbations of COPD are strongly linked to respiratory viruses.⁵ Some studies have shown smoking to be associated with severe Covid-19.⁷ While one meta-analysis did not associate smoking with severity of coronavirus disease.⁸

Smoking is not yet established as a risk factor for acquiring SARS-CoV-2 infection, but it might increase the disease severity. Also, smoking is an established causative factor for many chronic diseases which are themselves a risk factor for increased disease severity in Covid-19.⁹

The co-existence of Covid-19 and TB pandemic had given rise to various concerns. Firstly, as both primarily affect lungs leading to overlapping symptoms, there were concerns about a diagnostic difficulty. Secondly, there was worry regarding delay in TB diagnosis and treatment because of Covid-19 restrictions and lockdown. Number of patients registered for TB treatment and notification of cases declined. To combat the effects of the pandemic on tuberculosis services in India National TB Elimination Program (NTEP) announced a rapid

response plan and a plan for bi-directional screening. Under this all diagnosed patients with TB are to be screened for Covid-19, and all Covid-19-positive patients are to be screened for TB.⁹ Thirdly, there was apprehension regarding increased disease severity and mortality. The frequent use of drugs like Tocilizumab further complicated the situation as it reduces the macrophage and cytotoxic cell differentiation thus leading to decreased anti-mycobacterial activity.⁶ Currently available evidence is insufficient to support that TB increases the susceptibility to Covid-19 but evidence support that TB may lead to increased risk of complications from Covid-19.⁶

3. Preventive strategies and suggestions

Both TB and Covid-19 are known to spread to contacts through droplet nuclei of aerosols. Thus, simple infection control measures like, social distancing, cough etiquette, isolation, hand hygiene, quarantine, use of masks etc. play a pivotal role in prevention of these diseases.⁶ Strict implication of the infection control measures to prevent Covid-19 has certainly increased the awareness of the infection control measures among the general population.

Smoking behavior makes it difficult to maintain infection control measures. Smokers tend to gather in closed environments and smoking can make the user cough/sneeze thus releasing large number of aerosols. Even smokeless tobacco can contribute in the spread of the diseases as it is finally spit out with saliva and might carry the pathogen. Home isolation policies to curtail the spread of the disease led to increase in symptoms of panic and anxiety urging smokers to use tobacco.¹⁰ There is a need to identify the importance of tobacco control, particularly during the Covid-19 epidemic. Public awareness campaigns about the risks of tobacco use and the benefits of quitting should be encouraged and also incorporated into Covid-19 prevention strategies.

Also, there is a need to strengthen telemedicine services in India. The ministry of health and family welfare, Government of India, runs the National Tobacco Quit Line services to provide telephone-based tobacco cessation counseling.¹¹ Such already established platforms can be used to spread awareness of the infection control measures among smokers.

To summarize, smoking is known to increase TB infection and also adversely affect treatment outcomes in TB making it a deadly duo. Growing evidence suggest that smoking and TB increase the risk of severe Covid-19 symptoms. Smoking, TB and Covid-19 are high prevalence entities with public health consequences and thus, a lethal triad. There is a need for strengthening of the public health policies and incorporation of the Covid-19 safety awareness measures into the various national programmes.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. WHO report on the global tobacco epidemic 2019: offer help to quit tobacco use. [cited 2021 Aug 1]. Available from: <https://www.who.int/publications-detail-redirect/9789241516204>.
2. TB Facts - TB Statistics, India. TB Facts. [cited 2021 Aug 1]. Available from: <https://tbfacts.org/tb-statistics-india/>.
3. COVID Live Update: 198,597,091 Cases and 4,234,090 Deaths from the Coronavirus - Worldometer. [cited 2021 Aug 1]. Available from: <https://www.worldometers.info/coronavirus/>.
4. Alavi-Naini R, Sharifi-Mood B, Metanat M. Association between tuberculosis and smoking. *Int J High Risk Behav Addiction*. 2012;1(2):71–74.
5. van Zyl-Smit RN, Richards G, Leone FT. Tobacco smoking and COVID-19 infection. *Lancet Respir Med*. 2020 Jul;8(7):664–665.
6. Singh A, Prasad R, Gupta A, Das K, Gupta N. Severe acute respiratory syndrome coronavirus-2 and pulmonary tuberculosis: convergence can be fatal. *Monaldi Arch Chest Dis*. 2020 Jul 22;90(3) [cited 2021 Aug 1]. Available from: <https://www.monaldi-archives.org/index.php/macd/article/view/1368>.
7. Gülsen A, Yigitbas BA, Uslu B, Drömann D, Kilinc O. The effect of smoking on COVID-19 symptom severity: systematic review and meta-analysis. *Pulm Med*. 2020 Sep 9;2020:1–11.
8. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). *Eur J Intern Med*. 2020 May;75:107–108.
9. Shrinivasan R, Rane S, Pai M. India's syndemic of tuberculosis and COVID-19. *BMJ Glob Health*. 2020 Nov;5(11), e003979.
10. Xie J, Zhong R, Wang W, Chen O, Zou Y. COVID-19 and Smoking: what evidence needs our attention? *Front Physiol*; 2021 Mar 18;12:603850. <https://doi.org/10.3389/fphys.2021.603850>.
11. National Tobacco Control Programme. [cited 2021 Aug 1]. Available from: https://ntcp.nhp.gov.in/national_tobacco_quit_line_services.