



Effects of COVID-19 on tuberculosis control: past, present, and future

Denise Rossato Silva¹, Fernanda Carvalho de Queiroz Mello²,
Giovanni Battista Migliori^{3,4}

As we celebrate the World Tuberculosis Day on the 24th of March, the biggest challenge faced in tuberculosis control is the COVID-19 pandemic.⁽¹⁾ According to the latest report by the WHO, the number of newly diagnosed tuberculosis cases fell from 7.1 million in 2019 to 5.8 million in 2020; the number of drug-resistant tuberculosis (DR-TB) cases also decreased from 177,100 to 150,359, respectively, and the number of patients on tuberculosis preventive treatment reduced from 3.6 million to 2.8 million.⁽²⁾ In fact, the Global Tuberculosis Network coordinated a multicentric study⁽³⁾ and demonstrated that the COVID-19 pandemic has substantially affected tuberculosis services in many countries around the globe. In 2020, as compared with in 2019, there was an overall decrease in the total number of diagnosed and treated active tuberculosis cases, fewer DR-TB cases were managed, fewer latent tuberculosis cases were treated, and there was an increase in telehealth/internet-based visits.⁽³⁾

In this issue of the *Jornal Brasileiro de Pneumologia*, another Global Tuberculosis Network study⁽⁴⁾ evaluated country-specific lockdown measures during the first year of the COVID-19 pandemic. Although in the pre-COVID-19 vaccination period (i.e., during the first three waves of the pandemic) lockdown measures were important in reducing transmission, limiting the pressure on hospital departments and ICUs, public health measures taken to contain the spread of COVID-19 clearly had an impact on tuberculosis control.^(2,5)

In fact, in a letter to the editor,⁽⁶⁾ the authors showed a reduction of confirmed tuberculosis cases reported in Brazil in 2020, as compared with the period from 2017 to 2019. The reduction in diagnosis compromises the WHO goals for tuberculosis elimination. At the present time and over the next few years, raising awareness about tuberculosis will be critical to diagnosing as many tuberculosis cases as possible. In this sense, new diagnostic tools might facilitate prompt tuberculosis diagnosis. Santos et al.⁽⁷⁾ described a decision tree classifier model for the diagnosis of pleural tuberculosis, including clinical characteristics and cellular/biochemical pleural fluid testing. Considering that pleural tuberculosis is the most frequent extrapulmonary form of tuberculosis and that its diagnosis is generally difficult due to its paucibacillary nature, a predictive model with only three variables and high sensitivity and specificity that can be easily used in basic health care units is very advantageous.

The diagnosis of latent tuberculosis infection (LTBI) was also negatively impacted by the COVID-19 pandemic.⁽²⁾

In order to reach the End TB Strategy target of reducing tuberculosis incidence by 90% through preventive tuberculosis treatment,⁽¹⁾ it will be critical to intensify efforts to diagnose and treat LTBI cases. For this reason, some individuals should be given high priority for LTBI testing and treatment. In this issue of the Journal, a prospective study⁽⁸⁾ evaluated the prevalence of LTBI in patients with interstitial lung diseases requiring immunosuppression. The authors found a prevalence of LTBI of 9.1%, highlighting the importance of screening for LTBI in this group of patients.

Delayed tuberculosis diagnosis and treatment due to the COVID-19 pandemic can contribute to increasing the burden of tuberculosis, including that of multidrug-resistant tuberculosis (MDR-TB), in the years to come. The treatment success rate of MDR-TB is low (approximately 50%), and, therefore, the development of new drugs and shorter regimens could significantly improve tuberculosis treatment outcomes.⁽⁹⁾ Bedaquiline is a new drug that has been used in regimens recommended by the WHO for the treatment of MDR-TB. Hatami et al.⁽¹⁰⁾ conducted a systematic review and meta-analysis on the use of bedaquiline in MDR-TB treatment. They found that culture conversion and treatment success rates were high in bedaquiline-containing regimens, even in extensively drug-resistant tuberculosis cases.

As we see a great number of undiagnosed and untreated tuberculosis cases due to the COVID-19 pandemic, it is possible that these patients will more frequently experience pulmonary sequelae due to delayed diagnosis and treatment and/or the development of DR-TB. Thus, we can expect an increased number of patients with post-tuberculosis lung disease (PTLD) in the future. According to clinical standards for the assessment, management, and rehabilitation of PTLD,⁽¹¹⁾ these patients should be evaluated as soon as possible at the end of tuberculosis treatment. Furthermore, it is important to know the prevalence and severity of PTLD in different populations. A comparison of three cohorts (from Brazil, Italy, and Mexico) was published in the Journal this month.⁽¹²⁾ It was demonstrated that the three cohorts had variable pulmonary function test results and that patients with DR-TB had more severe disease. In addition, in the Brazilian cohort, pulmonary function test results decreased over time, reinforcing the importance of pulmonary rehabilitation in those patients.

In summary, for the past two years we have been living with the COVID-19 pandemic, witnessing successive waves and its effects on global health. Currently, we are

1. Faculdade de Medicina, Universidade Federal do Rio Grande do Sul – UFRGS – Porto Alegre (RS) Brasil.

2. Instituto de Doenças do Tórax – IDT – Faculdade de Medicina, Universidade Federal do Rio de Janeiro – UFRJ – Rio de Janeiro (RJ) Brasil.

3. Servizio di Epidemiologia Clinica delle Malattie Respiratorie, Istituti Clinici Scientifici Maugeri – IRCCS – Tradate, Italia.

4. Blizard Institute, Queen Mary University of London, London, United Kingdom.

still facing the rise of new variants and dealing with the post-COVID-19 syndrome. At the same time, we can see COVID-19 disrupting tuberculosis control, reducing the number of tuberculosis diagnoses and patients on tuberculosis preventive treatments. At the moment and during the next few years, we will have to be prepared to diagnose more cases of tuberculosis and LTBI, and to be aware of the possible increase in MDR-TB and PTLT cases.

ACKNOWLEDGMENTS

This study was conducted under the auspices of the European Respiratory Society (ERS)/*Asociación Latinoamericana de Tórax* (ERS/ALAT) and ERS/

Sociedade Brasileira de Pneumologia e Tisiologia (SBPT) collaborative projects and the operational research plan of the WHO Collaborating Centre for Tuberculosis and Lung Diseases (Tradate, ITA-80, 2017-2020-GBM/RC/LDA), as well as those of the Global Tuberculosis Network, hosted by the World Association for Infectious Diseases and Immunological Disorders.

AUTHOR CONTRIBUTIONS

All of the authors equally contributed to the writing and reviewing of the manuscript.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. TB/COVID-19 Global Study Group. Tuberculosis and COVID-19 co-infection: description of the global cohort. *Eur Respir J*. 2022;59(3):2102538. <https://doi.org/10.1183/13993003.02538-2021>
2. World Health Organization [homepage on the Internet]. Geneva: WHO; c2022 [cited 2022 Mar 10]. Global Tuberculosis Report 2021. 57p. Available from: <https://apps.who.int/iris/rest/bitstreams/1379788/retrieve>
3. Migliori GB, Thong PM, Alffenaar JW, Denholm J, Tadolini M, Alyaquobi F, et al. Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study. *Eur Respir J*. 2021;58(5):2101786. <https://doi.org/10.1183/13993003.01786-2021>
4. Migliori GB, Thong PM, Alffenaar JW, Denholm J, Tadolini M, Alyaquobi F, et al. Country-specific lockdown measures in response to the COVID-19 pandemic and its impact on tuberculosis control: a global study. *J Bras Pneumol*. 2022; 48(2):e20220087.
5. Migliori GB, Thong PM, Akkerman O, Alffenaar JW, Álvarez-Navascués F, Assao-Neino MM, et al. Worldwide Effects of Coronavirus Disease Pandemic on Tuberculosis Services, January-April 2020. *Emerg Infect Dis*. 2020;26(11):2709-2712. <https://doi.org/10.3201/eid2611.203163>
6. Maia CMF, Martelli DRB, Silveira DMML, Oliveira EA, Martelli Jr H. Tuberculosis in Brazil: the impact of the COVID-19 pandemic. *J Bras Pneumol*. 2022;48(2):e20220082.
7. Santos AP, Ribeiro-Alves M, Corrêa R, Lopes I, Silva MA, Mafort TT, et al. Hypoxemia and cellular/biochemical characteristics of pleural fluid as predictive variables on a model for pleural tuberculosis diagnosis. *J Bras Pneumol*. 2021;48(2):e20210245.
8. Dias VL, Storrer KM. Prevalence of latent tuberculosis infection among patients with interstitial lung disease requiring immunosuppression. *J Bras Pneumol*. 2022;48(2):e20210382.
9. Silva DR, Mello FCQ, Migliori GB. Shortened tuberculosis treatment regimens: what is new?. *J Bras Pneumol*. 2020;46(2):e20200009. <https://doi.org/10.36416/1806-3756/e20200009>
10. Hatami H, Sotgiu G, Bostanghadiri N, Abadi SSD, Mesgarpour B, Goudarzi H, et al. Bedaquiline-containing regimens and multidrug-resistant tuberculosis: a systematic review and meta-analysis. *J Bras Pneumol*. 2022; 48(2):e20210384.
11. Migliori GB, Marx FM, Ambrosino N, Zampogna E, Schaaf HS, van der Zalm MM, et al. Clinical standards for the assessment, management and rehabilitation of post-TB lung disease. *Int J Tuberc Lung Dis*. 2021;25(10):797-813. <https://doi.org/10.5588/ijtld.21.0425>
12. Silva DR, Freitas AA, Guimarães AR, D'Ambrosio L, Centis R, Muñoz-Torrico M, et al. Post-tuberculosis lung disease: a comparison of Brazilian, Italian, and Mexican cohorts. *J Bras Pneumol*. 2022; 48(2):e20210515.