



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.



EDITORIAL

Investigating the response to COVID-19 and understanding severe TB cases: The 2022 Pulmonology TB series



Some discoveries in prevention, diagnosis and treatment of tuberculosis (TB) and subsequent implementation led to speed-up of progress towards the modern management of this disease, which in 2020 still killed 1.5 million people and caused suffering to another 8.5 million, of whom 3.3 million were women and 1.1 million children.¹

It is important to remember we fight an ancient foe. The agent responsible for the “white plague”, discovered by Robert Koch, was presented in Berlin on 24th March 1882, nowadays known as World TB Day.² We also remember other important discoveries, which among many others included the introduction of X-rays (Wilhelm Conrad Röntgen, 1885), of the Bacillus Calmette-Guérin (BCG) vaccination with an attenuated strain of *Mycobacterium bovis* (which Albert Calmette and Camille Guérin introduced into clinical practice in 1921) and of treatment with streptomycin (William H. Feldman and Horton Corwin Hinshaw- first case treated with the new drug in 1944).

Pulmonology was in the frontline of the fight against TB with its TB series published in 2018^{3–11} and in 2021,^{12–14} the latter focused on the COVID-19 pandemic and its relationship with TB. TB is essentially one of the main ‘victims’ of the COVID-19 pandemic, for several reasons including the direct interaction between the two diseases in terms of morbidity and mortality,^{12,15–19} the shifting of specialised staff from TB services to manage the COVID-19 emergency and the effects of fear on patients and staff, the impact of lockdown/social distancing measures and the re-organization of health services among others.^{20–24}

Importantly, the further perspective of this deadly interaction, including the potential risk of developing post-TB and post-COVID-19 sequelae hampering the quality of life and requiring rehabilitation services must be considered.^{12,25–29}

The topic of the 2022 World TB day is “Invest to end TB. Save lives”.³⁰

Pulmonology is happy to contribute to the fight against TB by publishing three relevant articles, which complete what was done in previous years, by covering the area of health services organization and management of severe cases of TB.

The first article of the series by Rodrigues et al. is aimed at investigating how infection control norms and standards were applied during the different waves of the COVID-19 pandemic in the out-patient centers in Portugal and globally, and how these centers, which are responsible for diagnosis, treatment, screening and prevention of TB responded during the pandemic.³¹ The study is comprehensive and representative, and offers the possibility of reflecting on the need for health services to adapt in order to prevent further transmission of COVID-19 (but also of TB) while continuing to manage and control TB to prevent a future resurgence and increased mortality from the disease, a scenario which the World Health Organization has forecasted.¹

An area that is still poorly understood is how to optimize management of severe cases of TB with or without COVID-19, admitted to an Intensive Care Unit (ICU), given their challenging management and poor prognosis.³²

Pulmonology has previously published an interesting contribution from developing countries to create a simple score to predict which patients are likely to deteriorate and die rapidly if not transferred to ICU.³³

The second paper of the Pulmonology TB series 2022 is a systematic review by Galvin et al. which investigated 529 articles in the literature to raise important questions on the topic.³⁴ The study identified an average mortality rate exceeding 50% among the severe TB patients admitted to ICU, ranging from 29% to 95%. In addition, the study demonstrated that mortality in high TB prevalence/limited-resource settings is 23.4% higher than in low TB prevalence ones. Interestingly, the existing severity scores investigated underestimate the actual mortality. Other significant findings of the study are that acute respiratory failure is the

<https://doi.org/10.1016/j.pulmoe.2022.01.018>

2531-0437/© 2022 Sociedade Portuguesa de Pneumologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

leading cause of admission to ICU and that negative predictors of outcome exist, including hospital-acquired infections, the need for mechanical ventilation and vasopressors, delay in anti-TB treatment, more than one organ failure and worse severity scores.

Still on the same page, an original study based on an extensive data set of 448 patients from 9 countries in Europe, Latin America and Asia investigated the characteristics of the severe TB patients admitted to ICU, including the cause of admission (the most frequent being intubation) and the description of their clinical management and outcome (in press). Interestingly, about half of the patients initiated anti-TB treatment in the ICU. The study findings indicate that a substantial proportion of patients had malabsorption necessitating intravenously administered anti TB drugs. The study demonstrated a positive correlation between the predictive scores and the patients' mortality in terms of prognosis. The probability of treatment success was significantly associated with a longer duration of intravenous anti-TB treatment.

This is the most extensive study on the topic so far, its strengths being also in its global representativeness.

We hope this contribution of Pulmonology to the World TB Day and the fight against the White Plague will be appreciated by our readers and that the findings of these three studies will help to end TB in the COVID-19 pandemic era.

Declaration of Competing Interest

None.

References

- World Health Organization. Global tuberculosis report 2021. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/publications/digital/global-tuberculosis-report-2021>. [accessed 21 January 2022].
- Migliori GB, Caminero Luna JA, Kurhasani X, van den Boom M, Visca D, D'Ambrosio L, et al. History of prevention, diagnosis, treatment and rehabilitation of pulmonary sequelae of tuberculosis. *Press. Méd.* 2022; Feb 3:104112. doi: 10.1016/j.lpm.2022.104112.
- Duarte R, Migliori GB, Zumla A, Cordeiro CR. Strengthening tuberculosis control to advance towards elimination: the 2018 Rev. Port. Pneumol. (RPP) TB series. *Pulmonology.* 2018;24:67–8. <https://doi.org/10.1016/j.pulmoe.2018.01.002>.
- Lopes F, Duarte R, Migliori GB, Araújo R. Tuberculosis in the news: how do Portuguese media cover TB. *Pulmonology.* 2018;24:69–72. <https://doi.org/10.1016/j.pulmoe.2018.02.004>.
- García-Basteiro AL, DiNardo A, Saavedra B, Silva DR, Palmero D, Gegia M, et al. Point of care diagnostics for tuberculosis. *Pulmonology.* 2018;24:73–85. <https://doi.org/10.1016/j.rppnen.2017.12.002>.
- Tiberi S, Muñoz-Torrico M, Duarte R, Dalcolmo M, D'Ambrosio L, Migliori GB. New drugs and perspectives for new anti-tuberculosis regimens. *Pulmonology.* 2018;24:86–98. <https://doi.org/10.1016/j.rppnen.2017.10.009>.
- Rendon A, Centis R, Zellweger JP, Solovic I, Torres-Duque CA, Robalo Cordeiro C, et al. Migration, TB control and elimination: whom to screen and treat. *Pulmonology.* 2018;24:99–105. <https://doi.org/10.1016/j.rppnen.2017.11.007>.
- Carvalho I, Goletti D, Manga S, Silva DR, Manissero D, Migliori GB. Managing latent tuberculosis infection and tuberculosis in children. *Pulmonology.* 2018;24:106–14. <https://doi.org/10.1016/j.rppnen.2017.10.007>.
- Duarte R, Lönnroth K, Carvalho C, Lima F, Carvalho ACC, Muñoz-Torrico M, et al. Tuberculosis, social determinants and co-morbidities (including HIV). *Pulmonology.* 2018;24:115–9. <https://doi.org/10.1016/j.rppnen.2017.11.003>.
- Chalmers JD, Aksamit T, Carvalho ACC, Rendon A, Franco I. Non-tuberculous mycobacterial pulmonary infections. *Pulmonology.* 2018;24:120–31. <https://doi.org/10.1016/j.pulmoe.2017.12.005>.
- D'Ambrosio L, Bothamley G, Caminero Luna JA, Duarte R, Guglielmetti L, Muñoz Torrico M, et al. Team approach to manage difficult-to-treat TB cases: experiences in Europe and beyond. *Pulmonology.* 2018;24:132–41. <https://doi.org/10.1016/j.rppnen.2017.10.005>.
- Visca D, Ong CWM, Tiberi S, Centis R, D'Ambrosio L, Chen B, et al. Tuberculosis and COVID-19 interaction: a review of biological, clinical and public health effects. *Pulmonology.* 2021;27(2):151–65. <https://doi.org/10.1016/j.pulmoe.2020.12.012>.
- Duarte R, Aguiar A, Pinto M, Furtado I, Tiberi S, Lönnroth K, et al. Different disease, same challenges: social determinants of tuberculosis and COVID-19. *Pulmonology.* 2021;27(4):338–44. <https://doi.org/10.1016/j.pulmoe.2021.02.002>.
- Migliori GB, Visca D, van den Boom M, Tiberi S, Silva DR, Centis R, et al. contributing members of the global tuberculosis network. Tuberculosis, COVID-19 and hospital admission: consensus on pros and cons based on a review of the evidence. *Pulmonology.* 2021;27(3):248–56. <https://doi.org/10.1016/j.pulmoe.2020.12.016>.
- Tadolini M, Codecasa LR, García-García JM, Blanc FX, Borisov S, Alffenaar JW, et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur. Respir. J.* 2020;56(1). <https://doi.org/10.1183/13993003.01398-2020.15:2001398>.
- Motta I, Centis R, D'Ambrosio L, García-García JM, Goletti D, Gualano G, et al. Tuberculosis, COVID-19 and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts. *Pulmonology.* 2020;26(4):233–40. <https://doi.org/10.1016/j.pulmoe.2020.05.002>.
- Migliori GB, Thong PM, Alffenaar JW, Denholm J, Tadolini M, Alyaquobi F, et al. Global tuberculosis network. 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>.
- TB/COVID-19 Global Study Group. Tuberculosis and COVID-19 co-infection: description of the global cohort. *Eur. Respir. J.* 2021;2102538. <https://doi.org/10.1183/13993003.02538-2021>. Nov 11.
- McQuaid CF, Vassall A, Cohen T, Fiekert K, White RG. The impact of COVID-19 on TB: a review of the data. *Int. J. Tuberc. Lung Dis.* 2021;25(6):436–46. <https://doi.org/10.5588/ijtld.21.0148>.
- Alvesa A, Aguiar A, Migliori GB, Duarte R. COVID-19 related hospital re-organization and trends in tuberculosis diagnosis and admissions: reflections from Portugal. *Arch. Bronconeumol. (Engl Ed).* 2021. <https://doi.org/10.1016/j.arbres.2021.09.005>. Epub ahead of print. PMID: 34602700.
- Migliori GB, Thong PM, Alffenaar JW, Denholm J, Tadolini M, Alyaquobi F, et al. Country-specific lockdown measures in response to COVID-19 pandemic and its impact in tuberculosis control: a global study. *J. Bras. Pneumol.* 2022. In press.
- Gigante AR, Sousa M, Aguiar A, Pinto M, Gaio R, Duarte R. The impact of COVID-19 on the TB response: data from the field. *Int. J. Tuberc. Lung Dis.* 2021;25(9):769–71. <https://doi.org/10.5588/ijtld.21.0149>.
- Min J, Kang JY, Kim J, Yang J, Kwon Y, Shim E, et al. Impact of COVID-19 on TB services in Korea. *Int. J. Tuberc. Lung Dis.* 2021;25(5):400–2. <https://doi.org/10.5588/ijtld.20.0942>.
- Dara M, Kuchukhidze G, Yedilbayev A, Perehinets I, Schmidt T, Van Grinsven WL, et al. Early COVID-19 pandemic's toll on tuberculosis services, WHO European region, January to June 2020.

- Eurosurveillance. 2021;26(24):2100231. <https://doi.org/10.2807/1560-7917.ES.2021.26.24.2100231>.
25. 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>.
 26. Visca D, Zampogna E, Sotgiu G, Centis R, Saderi L, D'Ambrosio L, et al. Pulmonary rehabilitation is effective in patients with tuberculosis pulmonary sequelae. *Eur. Respir. J.* 2019;53(3):1802184. <https://doi.org/10.1183/13993003.02184-2018>.
 27. Visca D, Centis R, Muñoz-Torrico M, Pontali E. Post-tuberculosis sequelae: the need to look beyond treatment outcome. *Int. J. Tuberc. Lung Dis.* 2020;24(8):761–2. <https://doi.org/10.5588/ijtld.20.0488>.
 28. Visca D, Centis R, D'Ambrosio L, Muñoz-Torrico M, Chakaya JM, Tiberi S, et al. The need for pulmonary rehabilitation following tuberculosis treatment. *Int. J. Tuberc. Lung Dis.* 2020;24(7):720–2. <https://doi.org/10.5588/ijtld.20.0030>.
 29. Silva DR, Freitas AA, Guimarães AR, D'Ambrosio L, Centis R, Muñoz-Torrico M, et al. Post-tuberculosis lung disease: comparison of Brazilian, Italian, and Mexican cohorts. *J. Bras. Pneumol.* 2022. <https://doi.org/10.36416/1806-3756/e20210515>.
 30. World Health Organization. World TB day 2022. <https://www.who.int/campaigns/world-tb-day/2022>. [accessed 21 January 2022].
 31. Rodrigues I, Aguiar A, Migliori GB, Duarte R. Impact of the COVID-19 pandemic on tuberculosis services. *Pulmonology.* 2022. <https://doi.org/10.1016/j.pulmoe.2022.01.015>.
 32. Sieow YFN, Goh JTK, Gokhale RS, Tan YH. Characteristics, risk factors and outcomes of critically ill patients with active tuberculosis. *Int. J. Tuberc. Lung Dis.* 2022. <https://doi.org/10.5588/ijtld.21.0723>.
 33. Singla R, Raghu B, Gupta A, Caminero JA, Sethi P, Tayal D, et al. Risk factors for early mortality in patients with pulmonary tuberculosis admitted to the emergency room. *Pulmonology.* 2021;27(1):35–42. <https://doi.org/10.1016/j.pulmoe.2020.02.002>.
 34. Galvin J, Tiberi S, Akkerman O, Kerstjens HAM, Kunst H, Kurhanski X, et al. Pulmonary tuberculosis in intensive care setting, with a focus on the use of severity scores, a multinational collaborative systematic review. *Pulmonology.* 2022. <https://doi.org/10.1016/j.pulmoe.2022.01.016>.

G.B. Migliori^{a,*}, S. Tiberi^{b,c},
R. Duarte^{d,e,f,g}

^a *Servizio di Epidemiologia Clinica delle Malattie Respiratorie, Istituti Clinici Scientifici Maugeri IRCCS, Via Roncaccio 16, Tradate, Tradate, Varese 21049, Italy*

^b *Department of Infection, The Royal London Hospital, Barts Health NHS Trust, London, United Kingdom*

^c *Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University, London, United Kingdom*

^d *ICBAS-UP, Instituto de Ciências Biomédicas de Abel Salazar, Universidade do Porto, Portugal*

^e *ISPUP, Instituto de Saúde Pública da Universidade do Porto, Portugal*

^f *Unidade de Investigação Clínica, Administração Regional de Saúde do Norte, Portugal*

^g *Serviço de Pneumologia, Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal*

* Corresponding author at: Servizio di Epidemiologia Clinica delle Malattie Respiratorie, Istituti Clinici Scientifici Maugeri IRCCS, Via Roncaccio 16, Tradate, Tradate, Varese 21049, Italy.

E-mail address: giovannibattista.migliori@icsmaugeri.it (G.B. Migliori).

Received 25 January 2022; Accepted 25 January 2022
Available online 8 February 2022