The Lancet Regional Health - Europe 3 (2021) 100059

Contents lists available at ScienceDirect

The Lancet Regional Health - Europe

journal homepage: www.elsevier.com/lanepe



Commentary

Trend towards reduction in COVID-19 in-hospital mortality

Annalisa Ruggeri[a,*], Giovanni Landoni[b,c], Fabio Ciceri[a,c]

[a] Hematology and Bone Marrow Transplant Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[b] Anesthesia and Intensive Care Department, IRCCS San Raffaele Scientific Institute, Milan, Italy
[c] Vita-Salute San Raffaele University, Milan, Italy

ARTICLE INFO

Article History:
Received 11 February 2021
Accepted 12 February 2021
Available online 26 February 2021

SARS-CoV2 outbreak hit the entire world in late winter/early spring 2020, with a dramatic mortality rate in hospitalized patients across countries. While the pandemic has been continuing to hit on a global scale, the mortality rates started to decline with respect to the initial observed levels. In the current issue, Carolina Garcia Vidal and colleagues [1] report a decrease in COVID-19 mortality in a consecutive cohort of patients admitted over a period of six months (from March to September 2020) to the Hospital Clinic of Barcelona, Spain. According to this study, overall mortality decreased from 11·6% in March 2020 to 1·4% in September 2020 in the overall cohort, with the reduction being observed particularly in those older than 70 years. Importantly, the authors report a concomitant decrease in the intensive care unit (ICU) mortality from 19·1% in March 2020 to no mortality in the September 2020. The study describes other important findings, namely the changes over time in patient characteristics at hospital admission, as well as in treatment approaches. In March 2020 the clinical presentation of patients was characterized by signs of hyperinflammation, high D-Dimer levels, high CRP and low absolute lymphocyte count. Along the same lines, during the more recent months, the medical treatments for COVID-19 patients changed significantly, with an earlier use of remdesivir after symptoms onset replacing lopinavir/ritonavir, a more frequent use of dexamethasone and a decrease in the use of antibiotics. Patients admitted with shorter duration of symptoms before hospital admission experienced higher mortality. This may be in part related to the high viral load which may affect clinical outcome, highlighting the need of prompt intervention on such patients, as recently demonstrated by Marks et al. [2].

A drop in hospital mortality rates of COVID-19 patients has been reported for the first time in Italy in April-May 2020 [3] and then confirmed in several other countries. Italy was hit by the first wave of the pandemic earlier than other European countries, and the development of dedicated areas for management of COVID-19 within hospitals, together with the large use of respiratory protective equipment, implementation of lockdowns and other social distancing measures were promptly organized. Training of healthcare workers in intensive care medicine was a major effort and multidisciplinary teams were organized to rapidly provide support and adequate management during hospital overflow [3].

Several different factors [4, 5] have been identified as associated with COVID19 mortality, in particular, older age, history of comorbidities, ARDS severity and features of hyperinflammation at disease onset. The reduction in mortality due to COVID-19 is multifactorial and reflects the changes in disease management from health policy makers, as well as the global effort to rapidly share knowledge on disease characteristics, pathogenesis risk factors and treatments.

Treatment of COVID-19 evolved rapidly thanks to the increased knowledge on the pathophysiology and to the availability of the results of clinical trials, which may have played a role in the reduction of mortality. The use of antivirals changed after demonstration of a possible effectiveness of the early use of remdesivir in reducing mortality [6]. Anti-inflammatory drugs and immunomodulation therapies to reduce the cytokine release storm induced by COVID-19 were extensively used, targeting different pathways of inflammations. In addition, dexamethasone was more frequently used, replacing the use of other corticosteroids [7]. Furthermore, dysregulated inflammation and endothelial cell direct injury promote the expression of coagulation initiating factors, like tissue factor, on cell surfaces, thereby causing downstream activation of coagulation, common in COVID-19 patients with ARDS. The rapid start of anticoagulant regimens [7] with low molecular weight heparin for prevention of COVID-19 related complications is also reflected by the significant decrease of D-dimer levels reported over the months in the present study. Other important factors contributing to the improvement of COVID-19 management included the availability of Extra Corporeal Membrane Oxygenation (ECMO) and the possibility of performing continuous positive airway pressure (CPAP) outside the ICU, together with the beneficial effect of prone positioning.

The current study focuses on an urban population treated in a university hospital in Barcelona, Spain and these results should be evaluated considering that metropolitan areas have been deeply affected by excess of mortality, rather than other types of regions [8]. Overall, not only the higher density in the population, but also the increased air pollution, which is a contributor of the airborne transmission of

DOI of original article: http://dx.doi.org/10.1016/j.lanepe.2021.100041.
* Corresponding author.
E-mail address: annalisaruggeri80@hotmail.com (A. Ruggeri).

https://doi.org/10.1016/j.lanepe.2021.100059
2666-7762/© 2021 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

SARS-CoV-2, may be responsible of the excess in mortality in the metropolitan areas [8].

To continue the global COVID-19 exit strategy, efforts should be done to closely track the virus population diversity [9]. The emergence of new SARS-CoV-2 variants with high transmissibility represents a new global emergency and a high level of vigilance should be maintained. The vaccination campaign should proceed at large scale and strict adherence to the vaccine protocols validated by the available clinical trials is of outmost importance [10] to ensure efficacy at a global level.

Declaration of Interests

The authors declare no conflict of interest.

Author Contributions

AR wrote the manuscript, GL and FC provided comments and critical review.

References

[1] Garcia- Vidal C, Cozar-Llisto A, Meira F, et al. Trends in mortality of hospitalised COVID-19 patients: a single centre observational cohort study from Spain. Lancet Reg Health Europe 2021. doi: 10.1016/j.lanepe.2021.100041.
[2] Marks M, Millat-Martinez P, Ouchi D, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. Lancet Infect Dis 2021 S1473-3099(20)30985-3.
[3] Ciceri F, Ruggeri A, Lembo R, et al. Decreased in-hospital mortality in patients with COVID-19 pneumonia. Pathog Glob Health 2020;114(6):281–2.
[4] Ciceri F, Castagna A, Rovere-Querini P, et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol 2020;217:108509.
[5] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
[6] Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-374 19 - final report. N Engl J Med 2020 published online Oct.375. doi: 10.1056/NEJMoa2007764.
[7] Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA 2020.
[8] OECD. OECD regions and cities at a glance 2020. OECD Publishing Paris; 2020. doi: 10.1787/26173212.
[9] Priesemann V, Balling R, Brinkmann MM, et al. An action plan for pan-European defence against new SARS-CoV-2 variants. Lancet 2021;397(10273):469–70.
[10] Heaton P M. The Covid-19 vaccine-development multiverse. N Engl J Med 2020;383:1986–8. doi: 10.1056/NEJMe2025111.