



Letter to the Editor

Lactate dehydrogenase, COVID-19 and mortality

*Lactato deshidrogenasa, COVID-19 y mortalidad*

Dear Editor:

Outbreaks of the COVID-19 epidemic have been causing worldwide health concerns since November 2019. Until today, over 200 countries have been affected by the COVID-19 disease with over six million confirmed cases leading to over 370,000 deaths. Spectrum of the SARS-CoV-2 coronavirus disease (COVID-19) ranges from minimally symptomatic (fever, cough, myalgia, sputum production, headache, haemoptysis, diarrhea, dyspnea) to severe pneumonia and acute respiratory distress syndrome (ARDS).¹

Due to the fact that all these subjective clinical symptoms are not specific to COVID-19, they should be interpreted more confidently with the use of biological markers (biomarkers). Unfortunately, there is no currently available prognostic biomarker to distinguish patients that require immediate medical intervention from those that can be treated more conservatively and at the same time to estimate their associated mortality rate. The ability to identify cases that are in imminent danger of death has thus become an urgent necessity. Recently we read with great interest the article published by Zhu and co-workers in 'Medicina Clínica', which assessed organ function in 102 patients with severe COVID-19.² On the occasion of this article, we would like to point out and draw attention to a specific laboratory test which can be probably used as prognostic factors of the disease. This is lactate dehydrogenase (LDH).

What we know so far? So far we had known that LDH is an enzyme involved in energy production and that is found in almost all cells in the body. Tests that measure the concentration of LDH in the blood are commonly used to monitor tissue damage associated with a wide range of disorders, including liver disease and interstitial lung disease. The increase of LDH reflects tissue/cell destruction and is regarded as a common sign of tissue/cell damage, suggesting viral infection or lung damage, such as the pneumonia induced by SARS-CoV-2. We also know that serum LDH has been identified as an important biomarker for the activity and severity of idiopathic pulmonary fibrosis.³ More specifically, in patients with severe pulmonary interstitial disease, the increase of LDH is significant and is one of the most important prognostic markers of lung injury.

There is convincing evidence linking high LDH levels in critically ill patients, through COVID-19, with increasing activity and extent of lung injury.⁴ It would not be an exaggeration to say that all the studies so far have reported supporting evidence correlating the extent of tissue damage and inflammation with increasing levels

of LDH. Recently, Yan and co-workers analyzed 75 clinical features, including the concentrations of markers in the blood of 485 infected individuals in Wuhan, and developed a mortality prediction model using machine learning tools.⁵ Their modeling identified three indicators (blood-borne markers) that together classified the mortality of individual patients more than 10 days in advance with more than 90% accuracy (LDH, lymphocytes and hs-CRP). One of these markers alone, level of lactate dehydrogenase (LDH) in the blood, was highly indicative of COVID-19 mortality.

Based on these observations, serum LDH may represent a rapidly measured, efficacious, affordable, and widely available biomarker that may predict patients at the highest risk, allowing them to be prioritized and potentially reducing the mortality rate. Clinical trials in the direction of identification of this seemingly robust and meaningful biomarker of mortality risk in COVID-19 patients are urgently needed.

Conflict of interest

None.

References

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497–506. [http://dx.doi.org/10.1016/S0140-6736\(20\)30183-5](http://dx.doi.org/10.1016/S0140-6736(20)30183-5).
- Zhu Y, Du Z, Zhu Y, Li W, Miao H, Li Z. Evaluation of organ function in patients with severe COVID-19 infections. *Med Clin (Barc)*. 2020. <http://dx.doi.org/10.1016/j.medcli.2020.05.012>. S0025-7753(20)30339-0.
- Kishaba T, Tamaki H, Shimaoka Y, Fukuyama H, Yamashiro S. Staging of acute exacerbation in patients with idiopathic pulmonary fibrosis. *Lung*. 2014;192:141–9. <http://dx.doi.org/10.1007/s00408-013-9530-0>.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–20. <http://dx.doi.org/10.1056/NEJMoa2002032>.
- Yan L, Zhang H, Goncalves J, Xiao Y, Wang M, Guo Y, et al. An interpretable mortality prediction model for COVID-19 patients. *Nat Mach Intell*. 2020;2:283–8. <http://dx.doi.org/10.1038/s42256-020-0180-7>.

Konstantinos Bartzioakas*, Konstantinos Kostikas

Respiratory Medicine Department, University of Ioannina School of Medicine, Ioannina, Greece

* Corresponding author.

E-mail address: bartzioakas@gmail.com (K. Bartzioakas).<https://doi.org/10.1016/j.medcli.2020.07.043>

0025-7753/© 2020 Elsevier España, S.L.U. All rights reserved.