



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.



Contents available at [ScienceDirect](https://www.sciencedirect.com)

Diabetes Research
and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres



International
Diabetes
Federation



Editorial

Hyperglycemia and the worse prognosis of COVID-19. Why a fast blood glucose control should be mandatory



Evidence in the COVID-19 pandemic shows that hyperglycemia, not only in people with diabetes, worsens the prognosis and increases the risk to die [1,2]. It is, moreover, emerging that particularly the hyperglycemia at the admission in the hospital is a very bad prognostic factor [1,2], suggesting that hyperglycemia in the very early phase of the disease may play a particular role in determining the seriousness of the prognosis.

There are at least two reasons why hyperglycemia, particularly an acute one, can be very dangerous during the SARS-CoV-2 infection. One is that an acute increase of glycemia is accompanied by a huge increase of inflammatory mediators [3].

Clearly, knowing the role of the “cytokines storm” in the COVID-19 this is an effect that must be avoided. Another reason seems to be very specific for COVID-19 and it is related to the binding of SARS-CoV-2 to ACE2 [4]. The glycosylation, a reaction that can be induced by hyperglycemia, of the ACE2 is needed for the linkage of the virus to this cellular receptor [4]. Therefore, high and aberrantly glycosylated ACE2 in the tissue in uncontrolled hyperglycemia could favor the cellular intrusion of SARS-CoV2, thus leading to a higher propensity to COVID-19 infection and a higher disease severity [4]. It is also likely that it is the amount of glycosylated ACE2 receptor, and not simply the amount of ACE2 alone, that is responsible for virus binding and fusion [4]. It is well known, however that the hyperglycemia-related process of glycosylation is at the beginning a reversible process, going through the so called “labile glycosylation”, which is reversible also in vivo [5].

Therefore, it is conceivable that a fast normalization of hyperglycemia during COVID-19 may result in a decrease of inflammatory cytokines release and in a lower ACE2 binding capacity for the virus, two facts which consistently might help in improving the prognosis in people affected by SARS-CoV-2.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

- [1] Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, et al. Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. *J Diabetes Sci Technol*; 2020 [in press]. <https://www.bloomberg.com/press-releases/2020-04-17/covid-19-study-shows-more-than-4-times-in-hospital-mortality-rate-and-increased-length-of-stay-for-patients-with-diabetes-and>.
- [2] Iacobellis G, Penaherrera CA, Bermudez LE, Mizrahi EB. Admission hyperglycemia and radiological findings of SARS-CoV2 in patients with and without diabetes. *Diab Res Clin Pract* 2020;164:108185.
- [3] Ceriello A, Zarich SW, Testa R. Lowering glucose to prevent adverse cardiovascular outcomes in a critical care setting. *J Am Coll Cardiol* 2009;53(5 Suppl):S9–S13.
- [4] Brufsky A. Hyperglycemia, hydroxychloroquine, and the COVID-19 epidemic. *J Med Virol* 2020. <https://doi.org/10.1002/jmv.25887>.
- [5] Ceriello A, Paolisso G, Dello Russo P, Giugliano D, Sgambato S. Influence of labile glucose adducts on glycosylated protein assay by aminophenylboronic acid affinity chromatography: in vivo studies. *Acta Diabetol Lat* 1985;22:81–2.

Antonio Ceriello
IRCCS MultiMedica, Via Milanese 300,
20099 Sesto San Giovanni, Milan, Italy
E-mail address: antonio.ceriello@hotmail.it

Available online 29 April 2020