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.

Journal of Infection and Public Health 13 (2020) 1887

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

Letter to the Editor

Hypocalcemia and hypoalbuminemia during COVID-19 infection: Opportunities for therapeutic intervention

Dear Editor,

We write about the article "*Prevalence and predictive value of hypocalcemia in severe COVID-19 patient*" [1] by Liu et al., published in the June 2020 issue of your journal. Here the authors noted a positive correlation between serum calcium and albumin, lymphocyte counts, and a negative correlation with IL-6 levels during COVID-19 infection. This letter provides a mechanism that (unlike vitamin D deficiency [2]), reproduces this spectrum, and discusses its therapeutic relevance.

Hypocalcemia [3], hypoalbuminemia [4], and the cytokine storm [5] including IL-6 elevation [4,6] can be induced by the unbound [4] unsaturated fatty acids [7] released during severe COVID-19 infection. This occurs due to adipose lipolysis (in agreement with obesity worsening COVID-19 [8]), and causes distributive shock, renal failure and arrhythmias via endothelial, epithelial and cardiomyocyte injury respectively [4]. These unbound fatty acids are elevated in respiratory failure [4], when fatty acid carriers and antagonists; i.e. albumin and calcium are depleted [4]. Calcium and albumin normally bind these fatty acids with favorable enthalpies of −20 KJ/mol [3] and −230 KJ/mol respectively [4], and prevent lipotoxicity [3]. Acute lipolysis of large adipose tissue amounts in obese patients can overwhelm the ability of calcium and albumin to bind these fatty acids, lower calcium and albumin, cause widespread mitochondrial injury [9], organ failure and death.

The therapeutic relevance in COVID-19 lies in early supplementation of calcium and albumin to maintain their normal levels before organ failure. Such supportive care may prevent severe COVID-19 infection later, since late supplementation after organ failure is pointless [10].

Funding

RO1 DK119646, funded by the NIDDK, NIH PR151612 from the Department of Defense.

Competing interests

None declared.

Ethical approval

Not required.

References

[1] Liu J, Han P, Wu J, Gong J, Tian D. Prevalence and predictive value of hypocalcemia in severe COVID-19 patients. J Infect Public Health 2020;13(9):1224–8.
[2] Holick MF. Vitamin D deficiency. N Engl J Med 2007;357(3):266–81.
[3] Khatua B, Yaron JR, El-Kurdi B, Kostenko S, Papachristou GI, Singh VP. Ringer's lactate prevents early organ failure by providing extracellular calcium. J Clin Med 2020;9(1).
[4] El-Kurdi B, Khatua B, Rood C, Snozek C, Cartin-Ceba R, Singh VP, on behalf of the Lipotoxicity in COVID-19 Study. Mortality from Covid-19 Increases with unsaturated fat, and may be reduced by early calcium and albumin supplementation. Gastroenterology 2020;159(3):1015–8.
[5] Hegyi P, Szakacs Z, Sahin-Toth M. Lipotoxicity and cytokine storm in severe acute pancreatitis and COVID-19. Gastroenterology 2020.
[6] de Oliveira C, Khatua B, Noel P, Kostenko S, Bag A, Balakrishnan B, et al. Pancreatic triglyceride lipase mediates lipotoxic systemic inflammation. J Clin Invest 2020;130(4):1931–47.
[7] Thomas T, Stefanoni D, Reisz JA, Nemkov T, Bertolone L, Francis RO, et al. COVID-19 infection alters kynurenine and fatty acid metabolism, correlating with IL-6 levels and renal status. JCI Insight 2020;5(14).
[8] Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, et al. Lille Intensive Care C and Obesity study g. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity (Silver Spring) 2020;28(7):1195–9.
[9] Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ, Shiva SS, et al. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. Sci Transl Med 2011;3(107):107ra110.
[10] Caironi P, Tognoni G, Masson S, Fumagalli R, Pesenti A, Romero M, et al. Albumin replacement in patients with severe sepsis or septic shock. N Engl J Med 2014;370(15):1412–21.

Vijay P. Singh *
Biswajit Khatua
Department of Medicine, Mayo Clinic, Scottsdale, AZ, United States

Bara El-Kurdi
University of Texas San Antonio, San Antonio, TX, United States

* Corresponding author at: Division of Gastroenterology and Hepatology Mayo Clinic, Scottsdale, AZ 85259, United States.
E-mail address: singh.vijay@mayo.edu (V.P. Singh)

21 August 2020

https://doi.org/10.1016/j.jiph.2020.09.019
1876-0341/© 2020 The Author(s). Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).