

CORRESPONDENCE

New-Onset Diabetes in Covid-19

TO THE EDITOR: There is a bidirectional relationship between Covid-19 and diabetes. On the one hand, diabetes is associated with an increased risk of severe Covid-19. On the other hand, new-onset diabetes and severe metabolic complications of preexisting diabetes, including diabetic ketoacidosis and hyperosmolarity for which exceptionally high doses of insulin are warranted, have been observed in patients with Covid-19.¹⁻³ These manifestations of diabetes pose challenges in clinical management and suggest a complex pathophysiology of Covid-19–related diabetes.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19, binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in key metabolic organs and tissues, including pancreatic beta cells, adipose tissue, the small intestine, and the kidneys.⁴ Thus, it is plausible that SARS-CoV-2 may cause pleiotropic alterations of glucose metabolism that could complicate the pathophysiology of preexisting diabetes or lead to new mechanisms of disease.

There are also several precedents for a viral cause of ketosis-prone diabetes, including other coronaviruses that bind to ACE2 receptors.⁵ Greater incidences of fasting glycemia and acute-onset diabetes have been reported among patients with SARS coronavirus 1 pneumonia than among those with non-SARS pneumonia.⁵

In the aggregate, these observations provide support for the hypothesis of a potential diabetogenic effect of Covid-19, beyond the well-recognized stress response associated with severe illness. However, whether the alterations of glucose metabolism that occur with a sudden onset in severe Covid-19 persist or remit when the infection resolves is unclear. How frequent is the phenomenon of new-onset diabetes, and is it classic type 1 or type 2 diabetes or a new type of diabetes? Do these patients remain at higher risk for diabetes or diabetic ketoacidosis? In patients with preexisting diabetes, does Covid-19 change the underlying pathophysiology and the natural history of the disease? Answering these questions in order

to inform the immediate clinical care, follow-up, and monitoring of affected patients is a priority.

To address these issues, an international group of leading diabetes researchers participating in the CoviDIAB Project have established a global registry of patients with Covid-19–related diabetes (covidiab.e-dendrite.com). The goal of the registry is to establish the extent and phenotype of new-onset diabetes that is defined by hyperglycemia, confirmed Covid-19, a negative history of diabetes, and a history of a normal glycated hemoglobin level. The registry, which will be expanded to include patients with preexisting diabetes who present with severe acute metabolic disturbance, may also be used to investigate the epidemiologic features and pathogenesis of Covid-19–related diabetes and to gain clues regarding appropriate care for patients during and after the course of Covid-19. Given the very short history of human infection with SARS-CoV-2, an understanding of how Covid-19–related diabetes develops, the natural history of this disease, and appropriate management will be helpful. The study of Covid-19–related diabetes may also uncover novel mechanisms of disease.

Francesco Rubino, M.D.

Stephanie A. Amiel, M.D.

King's College London
London, United Kingdom
francesco.rubino@kcl.ac.uk

Paul Zimmet, M.D.

Monash University
Melbourne, VIC, Australia

George Alberti, M.D.

Imperial College London
London, United Kingdom

Stefan Bornstein, M.D.

Technical University of Dresden
Dresden, Germany

Robert H. Eckel, M.D.

University of Colorado Anschutz Medical Campus
Aurora, CO

Geltrude Mingrone, M.D.

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Rome, Italy

Bernhard Boehm, M.D.

Nanyang Technological University
Singapore, Singapore

Mark E. Cooper, Ph.D.

Zhonglin Chai, Ph.D.

Monash University
Melbourne, VIC, Australia

Stefano Del Prato, M.D.

University of Pisa
Pisa, Italy

Linong Ji, M.D.

Peking University
Beijing, China

David Hopkins, M.D.

King's Health Partners
London, United Kingdom

William H. Herman, M.D.

University of Michigan
Ann Arbor, MI

Kamlesh Khunti, M.D.

University of Leicester
Leicester, United Kingdom

Jean-Claude Mbanya, M.D.

University of Yaounde 1
Yaounde, Cameroon

Eric Renard, M.D.

University of Montpellier
Montpellier, France

Drs. Rubino, Amiel, and Zimmet contributed equally to this letter.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on June 12, 2020, at NEJM.org.

1. Chee YJ, Ng SJH, Yeoh E. Diabetic ketoacidosis precipitated by Covid-19 in a patient with newly diagnosed diabetes mellitus. *Diabetes Res Clin Pract* 2020 April 24 (Epub ahead of print).
2. Li J, Wang X, Chen J, Zuo X, Zhang H, Deng A. COVID-19 infection may cause ketosis and ketoacidosis. *Diabetes Obes Metab* 2020 April 20 (Epub ahead of print).
3. Ren H, Yang Y, Wang F, et al. Association of the insulin resistance marker TyG index with the severity and mortality of COVID-19. *Cardiovasc Diabetol* 2020;19:58.
4. Hamming I, Timens W, Bultuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus: a first step in understanding SARS pathogenesis. *J Pathol* 2004;203:631-7.
5. Yang J-K, Lin S-S, Ji X-J, Guo L-M. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta Diabetol* 2010;47:193-9.

DOI: 10.1056/NEJMc2018688

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