

New-onset diabetes in “long COVID”

Dear Editor,

Studies published in the *Journal of Diabetes* and elsewhere demonstrate the increased likelihood of new-onset diabetes (NOD) during the acute phase¹⁻⁷ or shortly after recovering from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),⁸⁻¹⁰ the virus causing coronavirus disease 2019 (COVID-19). Findings from these studies are supported by a recent Mendelian randomization analysis establishing a causal link between SARS-CoV-2 infection and NOD.¹¹ Emerging evidence shows that NOD is also observed in the post-acute COVID-19 phase, the so-called long COVID.^{12,13} In a retrospective cohort study of 47 780 discharged COVID-19 patients (mean age 65 years) in England, the rate of NOD was 29 (95% CI, 26-32) per 1000 person-years over a mean follow-up of 4.6 months.¹⁴ In another retrospective cohort study of three data sources from a large United States health plan, among 193 113 COVID-19 patients aged ≤ 65 years, NOD was the sixth most common post-acute clinical sequelae over a median follow-up of 2.9 months.¹⁵

Possible mechanisms explaining the occurrence of NOD with SARS-CoV-2 infection during the acute phase are cytolytic effects of the virus on pancreatic β -cells,¹⁶ activation of the hypothalamic-pituitary-adrenal and sympathoadrenal axes causing an increase in counterregulatory hormones, activation of the renin-angiotensin system resulting in unopposed deleterious actions of angiotensin II, and enhanced autoimmunity.^{17,18} However, it is yet to be determined whether these mechanisms persist in the post-acute phase for the development of NOD in long COVID.

It is essential to screen COVID-19 patients for NOD during acute illness and after recovery for several reasons. Globally, 50% of adults remain undiagnosed, and this figure reaches up to 60% in some low- and middle-income countries.¹⁹ Therefore, some of the NOD in hospitalized COVID-19 patients could reflect previously undiagnosed diabetes discovered incidentally by increased testing.⁵ Secondly, acute infections can cause stress hyperglycemia, which may resolve once the infection and the coexistent inflammation subside.²⁰ Further, COVID-19 patients are increasingly being treated with glucocorticoids that are known to induce hyperglycemia.²¹ As with stress hyperglycemia, blood glucose levels

may return to the pre-illness stage after stopping steroids. Finally, autoantibodies against pancreatic β -cells triggered by respiratory viral infections usually develop over several months or years to cause type 1 diabetes.²²

The COVID-19 pandemic has now persisted for over a year, and researchers across the globe are studying its long-term effects.^{2,12-15,23,24} It is now high time to consider NOD as a metabolic clinical sequela of SARS-CoV-2 infection to understand the role of COVID-19 in driving the diabetes pandemic.

KEYWORDS

COVID-19, diabetes, long COVID, SARS-CoV-2, new-onset diabetes

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