

COVID-19 may trigger hyperglycemia and worsen disease by harming fat cells

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COVID-19 may bring high risks of severe disease and death in many patients by disrupting key metabolic signals and thereby triggering hyperglycemia, according to a new study from researchers at Weill

Cornell Medicine and NewYork-Presbyterian.

In the study, reported Sept. 15 in *Cell Metabolism*, the researchers found that hyperglycemia—having high blood sugar levels—is common in hospitalized COVID-19 patients and is strongly associated with worse outcomes. The researchers also found evidence suggesting that SARS-CoV-2, the coronavirus that causes COVID-19, can induce hyperglycemia by disrupting fat cells' production of adiponectin, a hormone that helps regulate blood sugar levels.

"We normally don't think that fat cells are very active, but in fact they synthesize many protective proteins for your body—and it appears that SARS-CoV-2 may disable that protection in many patients," said Dr. James Lo, an associate professor of [medicine](#) in the Weill Center for Metabolic Health and the Cardiovascular Research Institute at Weill Cornell Medicine and a cardiologist at NewYork-Presbyterian/Weill Cornell Medical Center.

Hyperglycemia, the core feature of diabetes, is associated with inflammation and weakened immunity against infections, and was recognized as a significant risk factor for severe COVID-19 early in the pandemic. However, doctors later began finding evidence that COVID-19 is associated with hyperglycemia in patients who have no history of diabetes.

To better understand this important but mysterious aspect of COVID-19, Dr. Lo and colleagues analyzed the records of 3,854 patients who were hospitalized with COVID-19 at NewYork-Presbyterian /Weill Cornell Medical Center, NewYork-Presbyterian Queens and NewYork-Presbyterian Lower Manhattan Hospital. in the first few months of the pandemic in the United States.

They found that a remarkably high proportion (49.7 percent) of these

patients presented with hyperglycemia or developed it during their hospital stays.

Hyperglycemia in these COVID-19 patients was also strikingly associated with worse outcomes. Compared to patients with normal blood sugar levels, the patients with hyperglycemia were 9 times more likely to develop severe lung dysfunction (acute respiratory distress syndrome, or ARDS), 15 times more likely to be given mechanical ventilation, and 3 times more likely to die.

Surprisingly, the researchers found that hyperglycemia and the dire risks it brings also occur in other, non-COVID-19 forms of severe lung dysfunction. They found it in the same proportion in ARDS cases associated with COVID-19 and in ARDS cases from non-COVID-19 causes such as severe influenza or bacterial pneumonia. However, hyperglycemia in the latter cases appeared to be caused mostly by the death or dysfunction of beta cells that produce insulin, the principal hormone that regulates blood sugar levels. "In contrast, hyperglycemia in COVID-19 patients is mainly caused by [insulin resistance](#), in which insulin is present but the tissues it normally acts upon are no longer sensitive to it," said first author Dr. Moritz Reiterer, a postdoctoral fellow in Dr. Lo's laboratory.

Further tests revealed that the COVID-19 ARDS patients had severe declines in blood levels of adiponectin, a hormone produced by fat cells which normally has a protective effect against diabetes by enhancing insulin sensitivity.

How SARS-CoV-2 disrupts fat cells' production of adiponectin isn't yet clear. It may do so indirectly, by raising the general level of inflammation, which in turn disrupts fat cells. But the researchers demonstrated that SARS-CoV-2 can infect human and mouse fat cells, hinting at the possibility that the virus disrupts adiponectin

production in this direct way in COVID-19 patients.

The results open up a novel perspective on COVID-19, offering, among other things, a new explanation for why some people have worse COVID-19 outcomes.

"Patients with obesity, for example, may be more vulnerable to COVID-19 because they may already have some degree of insulin resistance and fat cell dysfunction, and possibly their fat cells are more susceptible to infection," Dr. Lo said.

The findings also suggest that a class of diabetes drugs called thiazolidinediones, which boost adiponectin production, may be useful in treating COVID-19 when it includes hyperglycemia. Further research is needed before this becomes clinically actionable.

Dr. Lo is now investigating whether COVID-19-induced [hyperglycemia](#) persists and develops into diabetes even after the recovery from COVID-19.

More information: Moritz Reiterer et al, Hyperglycemia in Acute COVID-19 is Characterized by Insulin Resistance and Adipose Tissue Infectivity by SARS-CoV-2, *Cell Metabolism* (2021). [DOI: 10.1016/j.cmet.2021.09.009](#)

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