

Could higher carnitine levels in the blood protect against severe COVID-19?

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The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causes mild to moderate illness in most individuals. However, some people are at a higher risk of developing severe illness due to advanced age, underlying health conditions or immunodeficiencies.

Severe COVID-19 is characterized by a hyperactive immune response. In the most severe cases, this overreaction leads to a cytokine storm, wherein various proinflammatory cytokines are produced at a much higher rate than normal. Cytokine overproduction causes positive feedback on other immune cells, allowing recruitment to the injury site. In worse cases, this can cause multiple organ damage.

Carnitine and acetyl-carnitine can downregulate proinflammatory cytokines, and so some scientists believe that these nutrients may help prevent disease progression.



Study: Mendelian randomization analyses show that higher acetyl-carnitine and carnitine levels in blood protect against severe Covid19. Image Credit: Eugeniusz Dudzinski / Shutterstock



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Researchers at the MRC Integrative Epidemiology Unit (IEU), Bristol Medical School, University of Bristol, Bristol, UK, found that carnitine and its derivative acetyl-carnitine provide a protective effect against severe COVID-19. Doubling of carnitine or acetyl-carnitine is tied to a 40-percent reduction risk of disease progression.

The study, which appeared on the pre-print server *medRxiv*^{*}, also showed that acetyl-carnitine had the largest protective effect when comparing hospitalized COVID-19 patients and those infected with SARS-CoV-2, but not admitted to the hospital.

The study findings underscore the therapeutic potential of carnitine and acetyl-carnitine in preventing severe COVID-19. Carnitine (also known as L-carnitine) is a chemical similar to an amino acid

produced in the body.

The body converts carnitine into other chemicals such as acetyl-carnitine and propionyl-carnitine. It is essential for brain and heart function, muscle movement, and other bodily processes.

Severe COVID-19

Most people who contract SARS-CoV-2 experience either no obvious symptoms or only mild symptoms, and recover within one to two weeks. Some individuals, however, are at a higher risk of developing severe illness. Those who develop severe illness are often admitted to the hospital, and in critical cases, require support in an intensive care unit (ICU).

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Aside from corticosteroids that are used to control inflammation, acetyl-carnitine has also been hypothesized as a potentially effective agent against COVID-19. However, large-randomized trials are expensive and time-consuming, while small trials may not fully provide the real effect.

In the current study, the researchers used Mendelian randomization, wherein genetic variants tied to the exposure or treatment of interest are used as proxies for the exposure, which is inexpensive and easier to do.

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To arrive at the study findings, the team performed a two-sample Mendelian randomization evaluation of acetyl-carnitine and carnitine on COVID-19 risk by using publicly available data from the genome-wide association study (GWAS). The team considered the link between the two nutrients and infection, hospitalization due to COVID-19, and very severe COVID-19.

Further, the team also sought to determine whether carnitine was tied to comorbidities usually found among patients with severe COVID-19.

The researchers found some evidence to suggest that carnitine and its derivative protected against progression to very severe COVID-19. They found that a doubling of acetyl-carnitine concentration in the blood could thus reduce the risk of severe COVID-19 by 40 percent.

The risk for hospitalized COVID-19 patients to develop severe infection dropped by 67 percent for acetyl-carnitine. Also, the team noted that with a 43-percent increase in acetyl-carnitine levels in the body, the risk of developing severe COVID-19 reduced by 23 percent.

Meanwhile, the results were similar for carnitine levels. Doubling in blood carnitine levels may decrease the risk of any SARS-CoV-2 infection by 19 percent; being admitted to the hospital due to COVID-19 by 18 percent; and being infected but not hospitalized by 20 percent, and could reduce the risk of severe COVID-19 by 44 percent.

In summary, we found strong protective effects of both blood acetyl-carnitine and carnitine levels on severe COVID-19. Carnitine and acetyl-carnitine may therefore be effective treatments in those who have contracted COVID-19," the researchers concluded in the study.

However, the team warned that genetic predisposition to higher carnitines might increase the risk of coronary heart disease and type 2 diabetes. They recommend only short-term treatment with carnitines to reduce inflammation and severe COVID-19, without causing harm to the patient's health.

If further studies (including randomized trials) of carnitine's potential to mitigate COVID-19 severity corroborate these findings, this may open up a new avenue to help combat the pandemic.



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- **Preliminary scientific report.** Kazmi, N., Smith, G.D., and Lewis, S. (2021). Mendelian randomization analyses show that higher acetyl-carnitine and carnitine levels in blood protect against severe COVID-19. *medRxiv*. doi: <https://doi.org/10.1101/2021.05.31.21257910>, <https://www.medrxiv.org/content/10.1101/2021.05.31.21257910v1>

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