Drop in convalescent plasma use at US hospitals linked to higher COVID-19 mortality rate

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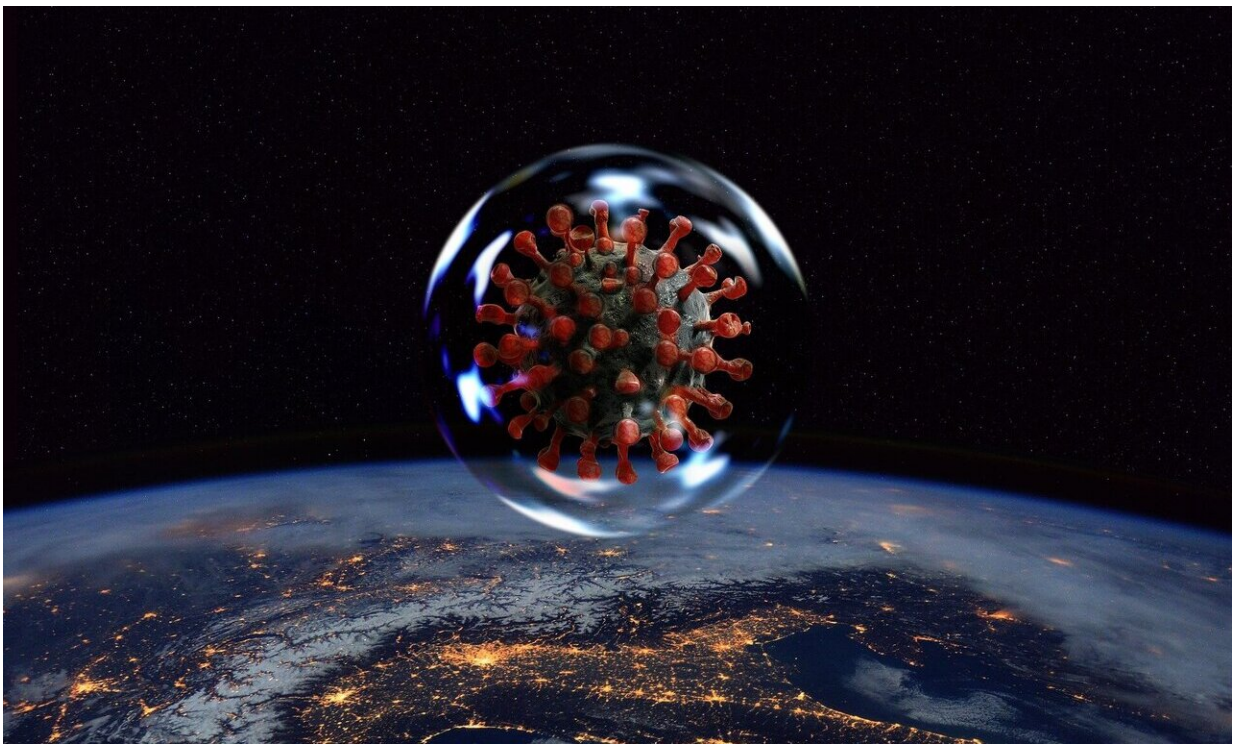

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A new study from researchers at Johns Hopkins Bloomberg School of Public Health and colleagues suggests a slowdown in the use of convalescent plasma to treat hospitalized COVID-19 patients led to a

higher COVID-19 mortality during a critical period during this past winter's surge.

U.S. hospitals began treating COVID-19 patients with convalescent plasma therapy—which uses antibody-rich blood from recovered COVID-19 patients—in the summer of 2020 when doctors were looking to identify treatments for the emerging disease. By the spring of 2021, doctors in the United States had treated over 500,000 COVID-19 patients with convalescent plasma. The use of convalescent plasma started declining late in 2020 after several large clinical trials showed no apparent benefit.

The researchers' analysis suggests that the decline in convalescent plasma use might have led to more than 29,000 excess COVID-19 deaths from November 2020 to February 2021.

The study was published online June 4 in the journal *eLife*.

"Clinical trials of convalescent plasma use in COVID-19 have had mixed results, but other studies, including this one, have been consistent with the idea that it does reduce mortality," says study senior author Arturo Casadevall, MD, Ph.D., Alfred and Jill Sommer Professor and Chair of the Department of the Molecular Microbiology and Immunology at the Bloomberg School.

The study was done in collaboration with researchers at Michigan State University and the Mayo Clinic. Casadevall and colleagues observed that while plasma use was declining late last year, the reported COVID-19 patient mortality rate was rising. That led them to hypothesize that the two phenomena were related.

In the study, the researchers compared the number of units of plasma distributed to U.S. hospitals from blood banks, on a per patient basis, to

the number of reported COVID-19 deaths per hospital admission across the country.

One finding was that while the total use of plasma peaked last December and January during the winter surge in new COVID-19 patients, the use per hospitalized patient peaked in early October 2020—just as deaths per COVID-19 hospital admission bottomed. Thereafter, in the wake of reports of negative results from clinical trials, use of plasma per hospitalized patient fell sharply—and deaths per COVID-19 hospital admission rose.

The researchers analyzed the relationship between these two datasets and found a strong negative correlation, higher use rate being associated with lower mortality and vice versa. They also grouped periods of plasma use into five "quintile" groupings from lowest-use weeks to highest, and found a graded relationship between less use and higher mortality.

A model the researchers generated to fit the data suggested that the COVID-19 case fatality rate decreased by 1.8 percentage points for every 10-percentage point increase in the rate of plasma use. That model implied that there would have been 29,018 fewer deaths, from November 2020 to February 2021, if the peak use rate of early October had held. Moreover, it suggested that the use of plasma on the whole, as limited as it was, prevented about 95,000 deaths through early March of this year.

The researchers analyzed, and then rejected, the possibility that several other factors could explain away the link between less plasma use and more mortality. These factors included changes in the average age of hospitalized patients, and the emergence of new variants of the COVID-19-causing coronavirus.

As for why some clinical trials found no benefit for plasma use, the

researchers note in their paper that many of the clinical trials with negative results had used plasma—mainly considered an antiviral treatment—relatively late in the course of COVID-19, when patients may have been too ill to benefit, and when the disease is driven mainly by immune-related responses rather than the coronavirus itself.

Casadevall notes that convalescent plasma remains under FDA Emergent Use Authorization in the U.S., and that it is readily available. "We hope that physicians, policymakers, and regulators will consider the totality of the available evidence, including our findings, when making decisions about convalescent plasma use in individual COVID-19 patients," Casadevall says.

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