

Criteria to predict cytokine storm in COVID-19 patients identified

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Like a cold front that moves in, setting the stage for severe weather, coronavirus infection triggers showers of infection-fighting immune molecules—showers that sometimes escalate into a chaotic immune

response known as a cytokine storm. About 20 to 30 percent of patients hospitalized with COVID-19 develop severe immune manifestations, in some instances leading to cytokine storm, with life-threatening organ damage and high risk of death.

Predicting which COVID-19 patients will develop [cytokine storm](#) is challenging, owing to the many variables that influence immune function. But now, in breakthrough work, researchers at the Lewis Katz School of Medicine at Temple University (LKSOM) have developed and validated predictive criteria for early identification of COVID-19 patients who are developing hyperimmune responses, raising the possibility for early therapeutic intervention.

"If we can anticipate cytokine storm, we can apply treatment sooner and possibly decrease mortality," explained Roberto Caricchio, MD, Chief of the Section of Rheumatology, Director of the Temple Lupus Program, Professor of Medicine and Microbiology and Immunology at LKSOM, and lead author on the new report.

The report, published online in the *Annals of the Rheumatic Diseases*, is the first to identify criteria that can be readily used in clinical practice to potentially head off the worst of the hyperimmune attack against COVID-19.

The breakthrough is the result of an extensive collaboration between researchers and clinicians across multiple departments in the Lewis Katz School of Medicine and Temple University Hospital, constituting the Temple University COVID-19 Research Group.

According to Dr. Caricchio, large numbers of COVID-19 patients have been treated at Temple since the pandemic emerged in the United States. "We have a significant amount of data in terms of variables to predict cytokine storm," he said.

Since early March, every patient admitted to Temple University Hospital (TUH) has had data on more than 60 different laboratory variables collected daily until the time of recovery or time of death. Among variables measured every day are factors like white blood cell count, metabolic enzyme activity, and markers of inflammation and respiratory function. Importantly these markers are commonly used in hospitals across the globe and therefore are readily available.

The research group carried out statistical analyses on laboratory data for 513 COVID-19 patients hospitalized at TUH in March and April, 64 of whom developed cytokine storm. A genetic algorithm was used to identify cut-off values for each individual laboratory variable to define the predictive requirements for cytokine storm. Genetic algorithms mimic the processes of natural selection and evolution in analyzing the data, and in this case, over multiple iterations, the algorithm turned up variables indicating which patients are most likely to develop cytokine storm.

Overall, the analyses yielded six predictive criteria comprising three clusters of laboratory results relating to inflammation, cell death and tissue damage, and electrolyte imbalance. In particular, patients in cytokine storm exhibited a proinflammatory status and elevated levels of enzymes indicating significant systemic tissue damage. Moreover, patients who met the criteria had extended hospital stays and were at increased risk of death from COVID-19, with almost half of patients who experienced cytokine storm meeting all criteria within the first day of hospitalization.

The researchers validated the criteria in a subsequent cohort of 258 patients admitted to TUH for COVID-19 infection. "The algorithm correctly predicted cytokine storm in almost 70 percent of patients," Dr. Caricchio said.

"The ability to reproduce our results in a second cohort of patients means that our group of variables are effective criteria for cytokine storm diagnosis in COVID-19 patients," he added. The final step now is to have the criteria validated by other centers where COVID-19 patients are admitted for care.

Dr. Caricchio noted that the criteria could be applied to COVID-19 patients at any hospital or level of hospitalization anywhere in the world. "This makes the criteria very valuable for guiding decisions about how to treat COVID-19 patients worldwide," he said. Applied more broadly, the criteria could greatly facilitate early diagnosis and intervention, helping save many lives.

"This was a truly collective effort between frontline clinicians, researchers, and statisticians, and the results are one of the many testaments to the exceptional work Temple University and the Temple University Health System have performed," Dr. Caricchio concluded.

More information: Roberto Caricchio et al, Preliminary predictive criteria for COVID-19 cytokine storm, *Annals of the Rheumatic Diseases* (2020). [DOI: 10.1136/annrheumdis-2020-218323](https://doi.org/10.1136/annrheumdis-2020-218323)

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