

Higher risk of serious COVID-19 complications in children with immunodeficiency

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Children with certain immunodeficiency diseases carry mutations in genes that regulate the body's immune system against viral infections and they have a higher mortality rate due to COVID-19. This is according to a study by researchers from Karolinska Institutet, published in the *Journal of Allergy and Clinical Immunology*.

Most [children](#) infected with the SARS-CoV-2 coronavirus develop a mild illness or show no symptoms at all. But for a small percentage, serious complications may develop.

"Mortality is much higher among children with primary immunodeficiency diseases infected with SARS-CoV-2. Our results indicate that basic immunological examination and [genetic analysis](#) should be conducted in children with severe COVID-19 or multi-inflammatory syndrome (MIS-C). The clinicians will then be able to help these children with more precise therapies based on their [genetic changes](#)," says Qiang Pan-Hammarström, professor at the Department of Biosciences and Nutrition, Karolinska Institutet, who led the study.

How the infection affects patients with primary immunodeficiency diseases (i.e. hereditary and congenital diseases of the immune system) is controversial. Even among these patients, some suffer from severe COVID-19 while others experience mild or no symptoms.

To investigate this more closely, and try to find genetic explanations for severe forms of COVID-19, researchers from Karolinska Institutet have studied [young patients](#) with primary immunodeficiency diseases (also called inborn errors of immunity, IEI) who developed severe or critical SARS-CoV-2 infection. Genetic and immunological analyses were performed.

Opportunity for more targeted therapy

"Our results clarify the molecular mechanism of these immune diseases, which opens up the possibility of developing a more targeted therapy. The knowledge acquired from the study also allows us to develop better strategies for the treatment and prevention of severe COVID-19 disease in these patients," says Qiang Pan-Hammarström.

The study included 31 children aged five months to 19 years. All children had some type of primary immunodeficiency disease without a molecular diagnosis and suffered from severe or critical COVID-19. Participants were recruited from August to September 2020 in Iran. None of the children were vaccinated against COVID-19.

Eleven of the children, more than one-third, died of complications from the infection. Five children, 16%, met the criteria for multi-inflammatory syndrome, MIS-C. Some of the children lacked antibodies to the coronavirus.

"This suggests that many children with this type of

immune disease cannot produce antiviral antibodies and therefore would not have the full benefit of vaccination," says Hassan Abolhassani, assistant professor at the Department of Biosciences and Nutrition, Karolinska Institutet, and the study's first author.

Mutations in immune genes

Genetic analyses showed that more than 90% of the participants, 28 children, had mutations in genes that are important for our immune defense, and that could explain their immunodeficiency. An important mechanism was mutations that affect proteins that regulate the immune system during virus infection, known as interferons.

The analyses of the patients' immune responses showed that children with MIS-C had immunological profiles that differ from the profiles of children with primary immunodeficiency but without MIS-C.

The study also includes a literature review, where the researchers globally found reports of approximately 1,210 patients with primary immunodeficiency disease and COVID-19. About 30% of them were children. The mortality rate among children with primary [immunodeficiency](#) disease and COVID-19 was more than 8%, compared with about 0.01% among children in the general population.

The study is limited to severe cases of COVID-19, infected with the original strain of the virus, and non-vaccinated children. Further studies are needed to evaluate the importance of different virus variants and vaccines in this patient group.

More information: Hassan Abolhassani et al, Genetic and immunological evaluation of children with inborn errors of immunity and severe or critical COVID-19, *Journal of Allergy and Clinical Immunology* (2022). [DOI: 10.1016/j.jaci.2022.09.005](#)

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