

COVID-linked multi-system inflammatory syndrome in children diagnosed more in Black and Latino child

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Multisystem Inflammatory Syndrome in Children (MIS-C) significantly affected more Black and Latino children than white children, with Black children at the highest risk, according to a new observational study of 124 pediatric patients treated at Children's National Hospital in Washington, D.C. Researchers also found cardiac complications, including systolic myocardial dysfunction and valvular regurgitation, were more common in MIS-C patients who were critically ill. Of the 124 patients, 63 were ultimately diagnosed with MIS-C and were compared with 61 patients deemed controls who presented with similar symptoms but ultimately had an alternative diagnosis.

In the study, published in *The Journal of Pediatrics*, researchers provide insight into key features distinguishing MIS-C patients to provide a more realistic picture of the burden of disease in the pediatric population and aid with the early detection of disease and treatment for optimal outcomes. The COVID-linked syndrome has affected nearly 4,000 <u>children</u> in the United States in the past year. Early reports showed severe illness, substantial variation in treatment and mortality associated with MIS-C. However, this study demonstrated that with early recognition and standardized treatment, short-term mortality can be nearly eliminated.

"Data like this will be critical for the development of clinical trials around the long-term implications of MIS-C," says Dr. Roberta DeBiasi, M.D., lead author and chief of the Division of Pediatric Infectious Diseases at Children's National. "Our study sheds light on the demographic, clinical and biomarker features of this disease, as well as viral load and viral sequencing."

Of the 63 children with MIS-C, 52% were critically ill, and additional subtypes of MIS-C were identified including those with and without still detectable virus, those with and without features meeting criteria for Kawasaki Disease, and those with and without detectable cardiac



abnormalities. While median age (7.25 years) and sex were similar between the MIS-C cohort and control group, Black (46%) and Latino (35%) children were overrepresented in the MIS-C group, especially those who required critical care. Heart complications were also more frequent in children who became critically ill with MIS-C (55% vs. 28%). Findings also showed MIS-C patients demonstrated a distinct cytokine signature, with significantly higher levels of certain cytokines than those of controls. This may help in the understanding of what drives the disease and which potential treatments may be most effective.

In reviewing viral load and antibody biomarkers, researchers found MIS-C cases with detectable virus had a lower viral load than in primary SARS-CoV-2 infection cases, but similar to MIS-C controls who had alternative diagnoses, but who also had detectable virus. A larger proportion of patients with MIS-C had detectable SARS-CoV-2 antibodies than controls. This is consistent with current thinking that MIS-C occurs a few weeks after a primary COVID-19 infection as part of an overzealous immune response.

Viral sequencing was also performed in the MIS-C cohort and compared to cases of primary COVID-19 infection in the Children's National geographic population. 88% of the samples analyzed fell into the GH clade consistent with the high frequency of the GH clade circulating earlier in the pandemic in the U.S. and Canada, and first observed in France.

"The fact that there were no notable sequencing differences between our MIS-C and primary COVID cohorts suggests that variations in host genetics and/or immune response are more likely primary determinants of how MIS-C presents itself, rather than virus-specific factors," says Dr. DeBiasi. "As we've seen new variants continue to emerge, it will be important to study their effect on the frequency and severity of MIS-C."



Researchers are still looking for consensus on the most efficacious treatments for MIS-C. In a recent <u>editorial</u> in the *New England Journal of Medicine*, Dr. DeBiasi calls for well-characterized large prospective cohort studies at single centers, and systematic and long-term follow-up for cardiac and non-cardiac outcomes in children with MIS-C. Data from these studies will be a crucial determinant of the best set of treatment guidelines for immunotherapies to treat MIS-C.

Provided by Children's National Hospital

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