# Multisystem Inflammatory Syndrome in Children: A Call for Improving Pediatric COVID-19 Vaccination Rates

Paula Soung, MD

The COVID-19 pandemic continues to loom over the medical community while the visibility of vaccine campaigns is waning. As the peaks and waves of COVID-19 and its variants have hit the American population hard, pediatrics has fared well overall. Children under 18 years account for 0.1% of US deaths related to COVID-19.[1] For the most part, children have experienced relatively milder disease than adults, and arguments in favor of vaccination have been disregarded by many, with societal concerns about safety peaking as approval rolled out for pediatric age groups.[2-4] In Wisconsin, only 60% of children ages 12 to 17 and 26% of children ages 5 to 11 have received at least 1 dose of COVID-19 vaccine.[3] Meanwhile, in addition to protection from acute COVID-19 disease itself, data are emerging about the protection COVID-19 vaccines may provide to children from multisystem inflammatory syndrome in children (MIS-C).

MIS-C is a condition presenting with fever, inflammation, and multisystem organ involvement, typically occurring within 4 weeks of a SARS-CoV-2 infection or exposure.[5] This postinfectious syndrome has set SARS-CoV-2 apart from the viral milieu we are accustomed to in pediatrics. While children with immunocompromised states or comorbidities have been at greatest risk for requiring hospitalization with acute COVID-19 infections, MIS-C has been dragging on the tails of the variant peaks, waiting for mostly healthy children to present. Often, affected children have had asymptomatic or mild acute COVID-19, providing no warning of the sequalae to come. The Centers for Disease Control and Prevention has confirmed over 6,800 cases of pediatric MIS-C and 60 deaths.[1] Data trends show that more than 50% of patients present with hypotension or shock requiring intensive care admission, and cardiac dysfunction is common with more than 30% of patients having pericardial effusion, myocarditis, or coronary artery dilatation or aneurysms.[6] While considered a rare condition associated with COVID-19 and most patients having overall good outcomes, MIS-C still poses a significant risk and morbidity to the pediatric population.[7]

As Wisconsin reports its first MIS-C death, there is a growing body of data demonstrating COVID-19 vaccination is associated with lower MIS-C incidence among adolescents.[8-10] A study in France evaluating the effects of COVID-19 mRNA vaccine on MIS-C outcomes in adolescents 12 years and older admitted to French pediatric intensive care units showed most adolescents with MIS-C had not been vaccinated.[8] To account for the increasing vaccination rate in adolescents over time, hazard ratios (HR) of unvaccinated vs vaccinated adolescents with at least 1 dose of vaccine were estimated using Cox proportional hazard models. Among 38 vaccine-eligible adolescents hospitalized with MIS-C, no patients had been fully vaccinated and 7 had received a single dose with median time between vaccination and onset of MIS-C of 25 days. The hazard ratio for MIS-C was 0.09 (95% CI, 0.04-0.21; $P < .001$).[8] By the end of the study period, eligible adolescent vaccination rates reached 72% fully vaccinated with Pfizer (>95%), Moderna (<5%), and other COVID-19 vaccines (<1%) used. Despite these vaccination rates, most adolescents with MIS-C had not been

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**Author Affiliations:** Medical College of Wisconsin, Milwaukee, Wisconsin (Soung).

**Corresponding Author:** Paula Soung, MD, C560 Children's Corporate Center, PO Box 1997, Milwaukee, WI 53201-1997, phone 414.337.7050; email psoung@mcw.edu.

vaccinated, suggesting COVID-19 mRNA vaccination was associated with a lower incidence of MIS-C.[8]

An additional case-control design study within a multistate US hospital network demonstrated that receipt of 2 doses of the Pfizer-BioNTech vaccine was associated with a high level of protection against MIS-C in patients aged 12 to 18 years.[9] Among 102 MIS-C case patients and 181 hospitalized controls, estimated effectiveness of 2 doses of Pfizer-BioNTech vaccine against MIS-C was 91% (95% CI, 78%-97%).[9] All of the MIS-C patients requiring life support were unvaccinated. Most patients (95%) aged 12 to 18 years hospitalized with MIS-C were unvaccinated. While there are several limitations to the study, it supports evidence that vaccination of children and adolescents is protective against COVID-19 and MIS-C, highlighting the importance of vaccination for all eligible children.[9]

Further data analysis is needed to evaluate the impact of immunization status on younger age groups and additional factors associated with MIS-C. Age ranges for MIS-C have included infants to adolescents, with peak ages 5 to 11 years (> 45%). (Notably, children ages 5 to 11 years old have been able to receive the Pfizer-BioNTech vaccine only since November 2021.[1]) Furthermore, the majority of MIS-C patients have been of Hispanic/Latino or non-Hispanic Black race/ethnicity (59%).[1,11] The same populations are also disproportionately affected by COVID-19, having lower vaccination rates than White, non-Hispanic ethnicities.[1] Further studies of MIS-C are needed to identify why certain racial or ethnic groups may be affected at higher rates and whether this relates to vaccination inequities or other risk factors.[1,11]

While COVID-19 vaccinations are the most effective strategy we have to prevent the serious consequences of COVID-19 in pediatrics, including MIS-C, hospitalizations, and death, pediatric immunization rates are low. Utilizing system improvement to increase opportunities for COVID-19 vaccination, including during planned and unplanned health care visits, may be a step forward to improve pediatric vaccination rates and health inequities.[12,13] With increasing data demonstrating the many benefits of COVID-19 vaccination, hopefully future vaccination campaigns and immunization discussions with patients and families will be bolstered as the waves of this pandemic continue.

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