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Understanding the risk for severe outcomes of youth with COVID-19

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The Global Pediatric Emergency Research Network (PERN)–COVID-19 Study sought to understand risk factors for severe SARS-CoV-2 infections in youth. By conducting a large prospective cohort study that included children seeking emergency department (ED) care, we were able to describe some of the risk factors associated with this particular population.

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During the early stages of the global COVID-19 pandemic, children younger than 18 years of age represented less than 5% of overall reported cases. However, as the pandemic had evolved, young people represented a growing proportion of new COVID-19 cases. Similarly, pediatric hospitalizations due to COVID-19 had increased dramatically from the early days of the pandemic, peaking during the Omicron wave.

Although COVID-19 generally resulted in mild symptoms in children, severe outcomes and deaths have occurred. To better understand the risk of severe outcomes among youth with SARS-CoV-2 infections, early research initiatives examined discrete populations including community-based databases, hospitalized populations, and youth admitted to the intensive care unit (ICU). These studies generated findings that identified varying and often conflicting risk factors for severe COVID-19 in youth that were highly impacted by study design, settings, and region. Thus, our understanding of the risk of COVID infection and risk factors for severe disease in children remained poorly characterized.

The Global Pediatric Emergency Research Network (PERN)–COVID-19 Study sought to understand the risk factors for severe SARS-CoV-2 infections in youth by conducting a large prospective cohort study that included children, with early or mild stages of disease, seeking emergency department (ED) care. The study enrolled 10,382 participants from 38 participating EDs across 8 countries between March 7, 2020, and June 15, 2021. Children and adolescents younger than 18 years who had a PCR-test because of suspected acute infection based on symptoms, or exposure, were eligible to participate. Participants who were tested-negative were included in the study as a comparison group.

At the time of enrollment, the participant's guardian provided information regarding demographic characteristics, epidemiological risk factors, and clinical symptoms. Two weeks later, guardians were contacted to determine if there were subsequent health care visits, treatments, or interventions. A medical record review was completed a minimum of 30 days after the initial ED visit to collect data related to medical care and interventions provided, disposition, and clinical outcomes.

After 14 days of follow-up, among the 3,221 children who tested positive for SARS-CoV-2 infection, 23% had been hospitalized, 3% experienced severe outcomes, and 4 children died. Among the 2,510 SARS-CoV-2–positive youth not hospitalized, only 0.5% had severe outcomes during the follow-up period. Overall, SARS CoV-2–negative youth that also presented to the ED were equally likely to experience a severe outcome. Yet among all subsequently hospitalized children, those who were SARS-CoV-2 positive were more likely to experience severe outcomes.

In support of other pediatric COVID-19 studies**,** this study identified the following risk factors for severe outcomes: older than five years of age, having a pre-existing chronic illness and previous episode of pneumonia. Where this study goes further, is by also identifying that presenting to the ED 4 to 7 days after symptoms started is a risk factor.

In contrast with some studies, our study did not find that very young infants were at a higher risk for severe outcomes. In some studies where young infants were identified at higher risk, the outcome of interest was hospitalization or ICU admission, which was a common precautionary approach taken during the early days of the pandemic. As our study required specific intensive care interventions or complications to occur for the event to be classified as a severe outcome, we therefore reported a lower occurrence rate of such events. Additionally, although asthma has been suggested as a risk factor for severe illness in youths with COVID-19, our study did not confirm this association.

Some studies have shown that Black race and Hispanic ethnicity were associated with increased test-positivity and hospitalizations. However by adjusting for age, comorbidities, and socioeconomic indicators, our analysis did not confirm an increased risk of severe outcomes due to COVID-19 among these groups.

As study participants all sought ED care, the risk of severe outcomes should not be interpreted to reflect the risk faced by children with COVID who do not seek ED care. The study provides an estimate of the risk among an ED-screened pediatric population. Additionally, because participating EDs were in academic pediatric institutions, we cannot generalize our results to all community EDs or to countries beyond those included in our analysis. Finally, as testing for variants of concern was not universal, we were unable to include circulating variants in our model.

The findings from this large global study supports a growing body of literature on the risk of severe outcomes and factors associated with SARS-CoV-2–infected youth presenting to the ED. Risk factors such as older age, underlying chronic illness, and symptom duration are useful for clinicians to consider when evaluating pediatric patients with SARS-CoV-2 infection in their care.