



Published in final edited form as:

Curr Opin Pediatr. 2021 June 01; 33(3): 281–285. doi:10.1097/MOP.0000000000001018.

The clinical epidemiology of coronavirus disease 2019 in children and adolescents mirrors the widening gap in healthcare disparities

Elissa Zirinsky^a, Elijah Paintsil^{a,b,c}, Carlos R. Oliveira^a

^aDepartment of Pediatrics, Section of Infectious Diseases and Global Health, Yale University School of Medicine

^bDepartment of Pharmacology, Yale University School of Medicine

^cDepartment of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connecticut, USA

Abstract

Purpose of review—The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic has exacerbated the longstanding racial/ethnic health disparities in the USA, with a disproportionately negative effect on children of color. This review summarizes recently published studies that describe the clinical epidemiology and racial/ethnic disparities associated with SARS-CoV-2 in children.

Recent findings—Children with SARS-CoV-2 infections manifest with a wide spectrum of disease. Most are either asymptomatic or mildly symptomatic with fever, gastrointestinal, and/or upper respiratory disease. Some children can progress to develop severe lower respiratory disease or a hyper-inflammatory, Kawasaki-like syndrome leading to cardiovascular shock. Although SARS-CoV-2-related deaths in children are rare, more children died within the first nine months of the pandemic than have died during any influenza season over the last decade.

Black and Hispanic children represent less than 41% of the US population but account for three out of every four SARS-CoV-2-related hospitalizations and deaths in the USA. The drivers of these disparities in children are complex and likely a combination of societal, biological, and behavioral influences.

Summary—This pandemic brought to light longstanding health disparities in historically marginalized populations, and minority children have suffered tremendously. It provides an opportunity to understand how a virus hijacked deep-rooted inequities, address these inequities, and work to prevent this outcome in future pandemics/epidemics.

Correspondence to Carlos R. Oliveira, MD, PhD, PO Box 208064=, New Haven, Connecticut 06520, USA. Tel: +1 203 785 5474; carlos.oliveira@yale.edu.

Conflicts of interest

The authors have no conflicts of interest relevant to this article to disclose.

Keywords

coronavirus disease 2019; epidemiology; health disparities; pediatric; severe acute respiratory syndrome coronavirus-2

INTRODUCTION

In December 2019, a novel betacoronavirus emerged as the causative agent of a severe respiratory disease known as coronavirus disease 2019 (COVID-19) [1]. This highly contagious ribonucleic acid virus, known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), spread rapidly and widely across the globe, albeit with an inequitable geographic burden. As of February 2021, over 111 million infections and 2.4 million deaths have been reported worldwide. The United States (US) alone has reported 20% of the global deaths from the pandemic [2]. Although children with COVID-19 have fared better than adults with regard to burden and severity of COVID-19 infection, a significant number have suffered severe life-threatening illness or death [3]. During the first nine months of the pandemic in the US, over 10,660 children were hospitalized, and over 200 died due to SARS-CoV-2. As the virus reached every corner of the US, it took a particularly devastating toll on racial and ethnic minority groups, and with it, brought to the forefront the longstanding and pervasive health disparities many young Americans are facing.

Under normal circumstances, minority children lack equal access to unbiased medical care, effective education, and adequate nutrition. These disparities have only worsened amid a pandemic that has caused disruption to education and housing, rising unemployment, and prolonged social isolation [4,5]. In children and adolescents, SARS-CoV-2 is much like an opportunistic organism, requiring a number of societal, healthcare and comorbid conditions to coincide to cause severe disease, and it is not the first communicable disease to do so [6]. It is reminiscent of the significant disparities seen in the pediatric population during the human immunodeficiency virus pandemic, where the majority of children who acquired human immunodeficiency virus perinatally were Black or Hispanic [7]. In this article, we review studies from March 2020 to February 2021 that assess the impact of SARS-CoV-2 in children, with a particular focus on the racial and ethnic disparities in positivity rates, hospitalization rates, and outcomes.

THE BURDEN OF INFECTION AND CLINICAL MANIFESTATIONS ACROSS THE PEDIATRIC POPULATION

Early in the pandemic, several studies that suggested that the attack and case-fatality rate in children were low [8,9]. However, since children were more commonly either asymptomatic or mildly symptomatic, they were less likely to have been tested early-on, and thus, were under-represented in early incidence estimates [10]. Furthermore, during the early phases of the pandemic, school closures were among the first social-distancing measures implemented by most countries [11,12]. This likely biased the measures of risk in children, as their opportunities for exposure to the virus were largely limited to their

household contacts [13[■]]. As testing capacity increased and schools began to reopen, it became clear that SARS-CoV-2 infection can indeed cause serious consequences in children. By February 2021, the American Academy of Pediatrics (AAP) reported 3,033,370 total pediatric COVID-19 infections and 241 virus-related deaths [14]. As a point of comparison, in a recent analysis of over 10,000 children hospitalized for either COVID-19 or seasonal influenza, the investigators found that the in-hospital mortality for children aged 11–17 years with SARS-CoV-2 was 10 times higher than that of similarly aged children with influenza [15[■]]. Nine months into the pandemic, the pediatric death toll of SARS-CoV-2 had already surpassed that of any influenza season for more than a decade [16].

The clinical features in children were initially thought to be primarily pulmonary. However, as the pandemic progressed, studies identified wide spectra of clinical manifestations and disease severity [17[■],18[■]]. In a prospective cohort of 992 healthy children in the community, half of the infections were asymptomatic. Cough and the loss of taste were reported in only 10% and 7% of cases, respectively [19]. In contrast, gastrointestinal symptoms, such as abdominal pain, loss of appetite, and diarrhea, were the most commonly reported symptoms, occurring in close to one-quarter of cases [20[■]].

In addition to the pulmonary and gastrointestinal phenotypes, children can also manifest with systemic hyperinflammation and rapid onset of circulatory shock. This was first described in Europe in April 2020 in children with past SARS-CoV-2 infection or recent exposures [21[■]]. By May 2020, a similar constellation of signs and symptoms was identified in a cluster of children in New York. Children presented in cardiac failure and appeared to have a physical exam and laboratory findings similar to those seen in Kawasaki Disease (KD), KD shock syndrome, or toxic shock syndrome [22]. On May 14, 2020, the Centers for Disease Control and Prevention (CDC) named this syndrome multisystem inflammatory syndrome in children (MIS-C) [23]. In a systematic review of 953 cases of MIS-C, 73% were admitted to an intensive care unit, 55% were given inotropes, 24% were mechanically ventilated, 4% required extracorporeal membrane oxygenation, and 2% died [24[■]]. Although the majority of children with MIS-C recover within days of admission, several case series have reported that 7–28% of patients have residual cardiac dysfunction or ongoing neurologic symptoms after discharge [25,26,27].

RACIAL AND ETHNIC DISPARITIES IN SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS-2 POSITIVITY RATES AND DIAGNOSIS OF MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN

Historically, data have established that the burden of pediatric infectious diseases in the world is disproportionately borne by those of racial and ethnic minority groups and those of lower socioeconomic status [28]. Unfortunately, this pandemic is no exception. A retrospective study of 4,802 children in Mississippi showed that SARS-CoV-2 positivity rates in Non-Hispanic Black children and Hispanic children were over two and four times higher, respectively, than White children [29[■]]. Similar disparities in positivity rates were noted in Washington, D.C. In a cross-sectional study of 1,000 children, 30% of Black children, 46% of Hispanic children, and 7% of White children tested positive. Positivity

rates also varied by mean family income (MFI); children in homes with the lowest MFI had higher rates of positivity (23.7%) compared to those in the highest MFI households (8.7%) [30[■]].

Epidemiologic studies of MIS-C also found strikingly high incidence rates among racial and ethnic minorities. Among the 2,060 MIS-C patients reported to the CDC as of February 2021, 69% have been Black or Hispanic children [31]. In New York City (NYC), Black children represent 22.2% of the population, but in a cohort of 223 children diagnosed with MIS-C, 34.4% were Black. In comparison, White children constitute 26.1% of the NYC population but only 12.8% of MIS-C patients [32[■]].

There are several hypotheses for the racial and ethnic disparities in the incidence of SARS-CoV-2 infection and MIS-C. First is the issue of increased exposure. It is known that racial and ethnic minority groups are over-represented among the ‘essential worker’ group, which increases the risk of being exposed to SARS-CoV-2 at work and transmitting the virus to children in the home [33]. Second is the disparities in access to diagnostics and treatment. The disproportionate access to testing can lead to a higher prevalence of asymptomatic transmission [34]. Third is the challenge of housing. Racial and ethnic minorities, and families of lower socioeconomic status are far more likely to live in high-density, multigenerational homes [35]. Thus, even if they had equal access to diagnostic testing, living arrangements would make it very difficult to effectively isolate an infected household member. Numerous studies have shown that children are far more likely to be infected from within their household or their community than to be the drivers of infections [36,37[■]]. In effect, children are the reflection of community rates; higher infection rates within communities of color will lead to higher infection rates in children of color.

DISPARITIES IN DISEASE SEVERITY

Hospitalization rates among children tell a similar story of staggering racial and ethnic disparities. In a multicenter study of 315 children with SARS-CoV-2 infections, the majority of children hospitalized (74%) were either Black or Hispanic [38[■]]. These disparities were subsequently validated in an analysis of 576 pediatric COVID-19-associated hospitalizations across 14 states that found 46% of the children were Hispanic, 30% were Black, and 14% were White [39]. Even though Blacks and Hispanics represent less than 41% of the US population, they account for approximately 75% of pediatric deaths from COVID-19 [40].

To date, no genetic or epigenetic markers have been identified to explain the large disparities in disease severity experienced by children of color. However, there are at least three factors contributing to these observed disparities in severity. One major influencer is likely the prevalence of underlying medical conditions. In a study of 576 pediatric COVID-19-associated hospitalizations across the US, 42% of children hospitalized had an underlying medical condition, of which obesity, prematurity, and chronic lung disease were the most common. In particular, obesity occurred in 30.5% of Hispanic, 27.5% of Black, and 6.6% of White children hospitalized with COVID-19 [41[■]]. Similar results have been shown in many other pediatric studies [42]. Notably, these three comorbidities are disproportionately prevalent among Black and Hispanic children. According to recent CDC estimates, one out

of every four Black or Hispanic children is obese, a rate that is nearly double that seen in White children [43]. On average, 17% of Black mothers give birth to a preterm infant in the US, a rate that is 60% higher than that of White infants [44]. Finally, the prevalence of asthma is 14% among Black children, which is more than double of what is seen among White children.

Other likely influencers for the disparities in severity are poverty and barriers healthcare. There is a strong correlation between infectious diseases and poverty. Poverty not only favors the spread of infectious diseases, but also contributes to conditions that make it difficult for children to fully recover once infected [45,46]. Individuals living in poverty or without insurance are more likely to have poorer health outcomes given delays in receiving care out of fears of prohibitive costs. Hispanic children have been particularly affected by these issues. Nearly two-thirds of Hispanic children live in a household that is 250% below the federal poverty level, a rate that is close to double that seen in White children. In 2018, 40% of the uninsured child population in the US were Hispanic, a staggering number considering that they make up 25% of the population [47].

Beyond the wealth gap, Hispanic children face other unique challenges. Approximately one-third of the Hispanic population in the US have limited English proficiency [48]. With limited English proficiency, it is challenging to understand the recommendations from clinicians or public health agencies. They may not be able to effectively communicate their symptoms during medical encounters, and as a result, may experience delays in care or suboptimal care [46]. Finally, as telemedicine became an important health-delivery tool during the pandemic, it also became yet another barrier to care for children who lacked the technology necessary for these visits [49].

CONCLUSION

There is no question that minority children are more likely than their White peers to be infected with and severely affected by SARS-CoV-2. We need more research into the drivers of these disparities at the community, national, and international levels, and data-driven programs to address them. In the immediate future, we need to focus on representing racial and ethnic minority groups in pediatric clinical trials for novel therapeutic agents and vaccines [50]. If found to be efficacious in children, vaccines must be equitably distributed to children without the hurdles seen in the adult vaccine rollout. Uptake and accessibility of the available vaccines within minority communities have been subpar [51]. More research is urgently needed to identify strategies to improve access and acceptability of the vaccines in these populations. In addition, better strategies are needed to increase viral surveillance, as this will be key to reducing community prevalence, monitoring for viral replacement, and ensuring the vaccine remains effective postimplementation. For children, this may be best achieved at the school level when children return to in-person learning. Finally, more research is needed about the long-term effects of the virus in children. There is still much to learn about the effects of SARS-CoV-2 in children but it is clear from the mounting body of evidence that children of color are bearing a disproportionate burden of infections and deaths. Posterity will not forgive us if we do not cease the opportunity to learn from the COVID-19 pandemic and fix the perennial health disparities in our communities.

Financial support and sponsorship

This work was supported, in part, from grants by the National Institutes of Health to E.Z. (gT32AI007210), E.P. (R01 HD103512-01 and D43 TW011526-01), and C.R.O. (KL2TR001862). Contents are solely the responsibility of the authors and do not necessarily represent the official views of NIH.

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KEY POINTS

- SARS-CoV-2 infection in children is often asymptomatic or mildly symptomatic but some children develop severe respiratory and/or hyperinflammatory disease.
- The pandemic has not only highlighted but also exacerbated longstanding racial/ethnic health disparities in children.
- Black and Hispanic children have higher rates of SARS-CoV-2 infection, hospitalization, and death than White children.