

## The curious case of coronavirus disease 2019 (COVID-19) in children



### To the Editor:

The pediatric population has classically been viewed to be highly vulnerable to infectious diseases. Consequently, this cohort deserves diligent observation during an infectious outbreak. The US Centers for Disease Control and Prevention considers children, especially those younger than 5 years of age, as a high-risk category for influenza-related disease.<sup>1</sup> During the last influenza A pandemic (H1N1 2009), 13% of the infected individuals were younger than 5 years.<sup>2</sup>

The age distribution of patients in the coronavirus disease 2019 (COVID-19) pandemic is incongruent with that of the H1N1 pandemic of 2009. At our tertiary care center, 215 individuals been evaluated for COVID-19 through April 10, 2020. Of those tested, all 22 individuals younger the age of 18 years were negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In a systematic review of 45 datasets, Ludvigsson found that less than 5% of COVID-19 cases occurred in children younger than 18 years of age.<sup>3</sup> Two other novel coronavirus diseases, severe acute respiratory syndrome and Middle East respiratory syndrome, also show similarly low rates of infection in the pediatric population.<sup>4</sup> Furthermore, retrospective studies to date suggest that children infected with SARS-CoV-2 generally have mild or no symptoms. In a study of 2143 COVID-19 cases in children, disease manifestations were found to be greatest in age younger than 1 year, with a falling trend in severity with increasing age up to 18 years.<sup>5</sup>

A number of hypotheses have been proposed for the relative sparing of children in the COVID-19 pandemic: a more likely stimulus-naïve immune system, immaturity of angiotensin-converting enzyme 2 receptors, and underdeveloped humoral and cellular immune responses resulting in milder inflammation.<sup>5,6</sup> It also is hypothesized that recurrent viral infections that typify childhood may induce greater or more frequent innate and adaptive responses, such as to leading to greater total immunoglobulin levels that might be protective against a novel virus.<sup>5</sup>

We present the epidemiologic differences among 3 coronavirus diseases (severe acute respiratory syndrome, Middle East respiratory syndrome, and COVID-19) and the influenza pandemic (H1N1 2009) disease in the [Table](#).<sup>2-4,6-17</sup> Although we present data about the H1N1 pandemic that were amassed during the decade that has passed since, the landscape of SARS-CoV-2 infection and COVID-19, especially in children, is evolving, and a more mature analysis may unearth a different trend. Although the current figures are encouraging, the true burden of COVID-19 pandemic on children is yet unknown.

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**Table. Epidemiologic differences in 3 coronavirus diseases (SARS, MERS, and COVID-19) and H1N1-influenza pandemic (2009)**

Epidemiologic factor	SARS <sup>4,7,8</sup>	MERS <sup>4</sup>	H1N1 pandemic 2009 <sup>2,9-14</sup>	COVID-19 <sup>3,6,15-17</sup>
Percentage of positive cases that were children (0-18 y)	<5%	0.1%-4%	73% (0-24 y)	PRC: 2.4% ITA: 1.2% US: 5%
Percentage of positive cases that were children (0-9 y)	SDN	SDN	13% (0-4 y)	PRC: 1% ITA: 0.5% US: SDN
Percentage of patients with severe or critical illness children	5%	SDN	SDN	PRC: 2.7% ITA: SDN US: 2%
Percentage of children requiring mechanical ventilation	<1%	<1%	SDN	PRC: <1% ITA: <1% US: <1%
Percentage children among hospitalized individuals	SDN	SDN	40%	PRC: 10% ITA: <0.1% US: <1%
Mortality rate in children	<1%	6%	0.002%-0.013%	PRC: <0.1% ITA: <0.1% US: <0.1%
Mortality rate in ICU admissions children	SDN	SDN	6.3%-11.6%	PRC: <0.1% ITA: <1% US: <0.1%

ICU, intensive care unit; ITA, Italy; MERS, Middle East respiratory syndrome; PRC, China; SARS, severe acute respiratory syndrome; SDN, sufficient data are not available.

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## Severe neutropenia in infants with severe acute respiratory syndrome caused by the novel coronavirus 2019 infection



### To the Editor:

Infection with severe acute respiratory syndrome caused by the novel coronavirus 2019 (SARS-CoV-2) and resulting coronavirus disease 2019 (COVID-19) is a global pandemic.<sup>1</sup> Pediatric cases have some peculiarities, such as milder clinical manifestations and different laboratory abnormalities.<sup>2</sup> A systematic review on laboratory data identified 12 articles, with a total of 66 pediatric patients.<sup>3-15</sup> Lymphopenia was found in only 3% of children, whereas lymphopenia often is described in adult patients.<sup>16,17</sup> Neutropenia was recorded in 6% of cases, but it was never less than  $0.500 \times 10^9/L$  in this population.<sup>3</sup>

We describe a 23-day-old and a 39-day-old infant with mild COVID-19 and severe neutropenia who were cared for at our tertiary care referral pediatric hospital. They both came to medical attention with low-grade fever and mild respiratory symptoms with a history of contact with an infected person or persons. At admission, leukocyte and neutrophil counts were normal, nasopharyngeal swab tested positive for COVID-19, and co-infection with influenza-like viruses was excluded. On the fifth day and days after the beginning of symptoms, the 39-day-old girl and the 23-day-old girl developed severe neutropenia, with a nadir of  $0.244 \times 10^9/L$  neutrophils and  $0.482 \times 10^9/L$  neutrophils, respectively (Figure). No other alterations on routine examinations were recorded and the neutrophil values improved without clinical complications.

The presence of isolated severe neutropenia has not been described in children with COVID-19. This finding is noteworthy, because postinfectious transient neutropenia has been associated with many other viral infections in infancy, which might share pathogenic mechanisms.<sup>18,19</sup> Moreover, the evidence of neutropenia in neonates and infants could be another manifestation