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Perspectives

Are children less susceptible to COVID-19?

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Emerging at the end of 2019, coronavirus disease 2019 (COVID-19) has become a public health threat to people all over the world. The lower airway is the primary target of the infection for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Pneumonia is always present in patients with severe COVID-19.[1,2] Available reports to date show that COVID-19 seems to be uncommon in children.[3–6] Recent data reported from the Chinese Centers for Diseases Control and Prevention indicated that among the 44,672 confirmed cases of COVID-19 as of February 11, 2020, 416 (0.9%) were aged 0–10 years and 549 (1.2%) aged 10–19 years.[7] Exploring the underlying reasons may help understand the pathogenesis of COVID-19.

One possible reason is that children have fewer outdoor activities and undertake less international travel, making them less likely to contract the virus. The number of pediatric patients may increase in the future and a lower number of pediatric patients at the beginning of a pandemic does not necessarily mean that children are less susceptible to the infection. In fact, infants can be infected by SARS-CoV-2.[8]

During the 1918 outbreak of "Spanish flu," those ≥65 years old and children ≤15 years experienced little or no change in excess mortality as compared with that of the previous influenza season. Nevertheless, those aged 15–24 and 25–44 years experienced sharply elevated death rates.[9]

Similarly, at the beginning of the 2009 pandemic H1N1 influenza outbreak, the percentage age distributions for mortality and morbidity for patients with severe pneumonia show a marked shift to persons between the ages of 5 and 59 years, as compared with distributions observed during previous periods of epidemic influenza.[10]

On the other hand, several infectious diseases are well known to be less severe in children. Paralytic polio occurred in approximately 1 in 1000 infections among infants, in contrast to approximately 1 in 100 infections among adolescents.[11] As compared with young children, teenagers and adults tend to have symptomatic rubella more frequently and have systemic manifestations.[11] The overall case-fatality rate of severe respiratory distress syndrome (SARS)

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ranges from 7% to 17%. Persons with underlying medical conditions and those older than 65 years of age had mortality rates as high as 50%. However, there was no mortality in children or in adults younger than the age of 24 years.[11]

The reasons for the relative resistance of children to some infectious diseases remains obscure. It was suggested that maturational changes in the axonal transport system may explain the relative resistance of immature mice to poliovirus-induced paralysis.[12] Other suggested reasons include children having a more active innate immune response, healthier respiratory tracts because they have not been exposed to as much cigarette smoke and air pollution as adults, and fewer underlying disorders. A more vigorous immune response in adults may also explain a detrimental immune response that is associated with acute respiratory distress syndrome.[11]

A difference in the distribution, maturation, and functioning of viral receptors is frequently mentioned as a possible reason of the age-related difference in incidence. The SARS virus, SARS-CoV-2, and human coronavirus-NL63 (HCoV-NL63) all use the angiotensin-converting enzyme-2 (ACE2) as the cell receptor in humans.[13,14] Previous studies demonstrated that HCoV-NL63 infection is more common in adults than in children.[15,16] This finding suggests there may indeed be relative resistance to SARS-CoV-2 in children.

ACE2 expression in rat lung has been found to dramatically decrease with age.[17] This finding may not be consistent with a relatively low susceptibility of children to COVID-19. However, studies show that ACE2 is involved in protective mechanisms of the lung. It may protect against severe lung injury induced by respiratory virus infection in an experimental mouse model and in pediatric patients. ACE2 also protects against severe acute lung injury that can be triggered by sepsis, acid aspiration, SARS, and lethal avian influenza A H5N1 virus infection.[18]

These intriguing findings suggest that children may really be less susceptible to COVID-19. It is important to elucidate the underlying mechanism that may help to manage COVID-19 patients.

Declaration of Competing Interest

The author declares no conflicts of interest.

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