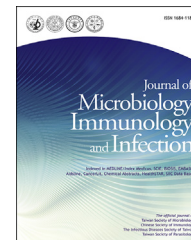


Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

Perspectives

Are children less susceptible to COVID-19?

Ping-Ing Lee ^{a,*}, Ya-Li Hu ^b, Po-Yen Chen ^c,
Yhu-Chering Huang ^d, Po-Ren Hsueh ^{e,f}

^a Department of Pediatrics, National Taiwan University Children's Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

^b Department of Pediatrics, New Taipei City Hospital, New Taipei City, Taiwan

^c Department of Pediatrics, Section of Infection, Taichung Veterans General Hospital, Taichung, Taiwan

^d Department of Pediatrics, Chang Gung Memorial Hospital and Chang Gung University College of Medicine at Linkou, Taoyuan, Taiwan

^e Department of Laboratory Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan

^f Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan

Received 21 February 2020; accepted 21 February 2020

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)

* Corresponding author. Department of Pediatrics, National Taiwan University, Children's Hospital No. 8, Chung Shan S. Rd., Taipei, 10041, Taiwan.

E-mail address: pinging@ntu.edu.tw (P.-I. Lee).

<https://doi.org/10.1016/j.jmii.2020.02.011>

1684-1182/Copyright © 2020, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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.

References

- Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents* 2020 Feb 17. <https://doi.org/10.1016/j.ijantimicag.2020.105924>.
- Lee PI, Hsueh PR. Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. *J Microbiol Immunol Infect* 2020 Feb 4;(20):30011–6. <https://doi.org/10.1016/j.jmii.2020.02.001>. pii: S1684-1182.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J1, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *J Am Med Assoc* 2020 Feb 7. <https://doi.org/10.1001/jama.2020.1585> [Epub ahead of print].
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020. <https://doi.org/10.1056/NEJMoa2001316> [Epub ahead of print].
- Ko WC, Rolain JM, Lee NY, Chen PL, Huang CT, Lee PI, et al. Remdesivir for SARS-CoV-2 pneumonia. *Int J Antimicrob Agents* 2020 [in press].
- Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China, 2020. CCDC weekly* 2020;2. *Zhonghua Liu Xing Bing Xue Za Zhi* 2020. p. 145–51 [in Chinese].
- Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang ZJ. Novel coronavirus infection in hospitalized infants under 1 year of age in China. *J Am Med Assoc* 2020. <https://doi.org/10.1001/jama.2020.2131>.
- Olson DR, Simonsen L, Edelson PJ, Morse SS. Epidemiological evidence of an early wave of the 1918 influenza pandemic in New York City. *Proc Natl Acad Sci U S A* 2005;102:11059–63.
- Chowell G, Bertozzi SM, Colchero MA, Lopez-Gatell H, Alpuche-Aranda C, Hernandez M, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. *N Engl J Med* 2009;361:674–9.
- Kliegman RM, St Geme JW, Blum NJ, Shah SS, Takser RC, Wilson KM. *Nelson textbook of pediatrics*. Edition 20. Philadelphia, PA: Elsevier; 2020.
- Jubelt B, Narayan O, Johnson RT. Pathogenesis of human poliovirus infection in mice. II. Age-dependency of paralysis. *J Neuropathol Exp Neurol* 1980;39:149–59.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8).
- Hofmann H, Pyrc K, van der Hoek L, Geier M, Berkhout B, Pöhlmann S. Human coronavirus NL63 employs the severe acute respiratory syndrome coronavirus receptor for cellular entry. *Proc Natl Acad Sci USA* 2005;102:7988–93.
- Huang SH, Su MC, Tien N, Huang CJ, Lan YC, Lin CS, et al. Epidemiology of human coronavirus NL63 infection among hospitalized patients with pneumonia in Taiwan. *J Microbiol Immunol Infect* 2017;50:763–70.
- Lee KH, Yoo SG, Cho Y, Kwon DE, La Y, Han SH, et al. Characteristics of community-acquired respiratory viruses infections except seasonal influenza in transplant recipients and non-transplant critically ill patients. *J Microbiol Immunol Infect* 2019. <https://doi.org/10.1016/j.jmii.2019.05.007> [Epub ahead of print].
- Xie X, Chen J, Wang X, Zhang F, Liu Y. Age- and gender-related difference of ACE2 expression in rat lung. *Life Sci* 2006;78: 2166–71.
- Gu H, Xie Z, Li T, Zhang S, Lai C, Zhu P, et al. Angiotensin-converting enzyme 2 inhibits lung injury induced by respiratory syncytial virus. *Sci Rep* 2016;6:19840.