

Age-varying susceptibility to the Omicron variant (B.1.1.529) of SARS-CoV-2

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Article

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Abstract

The Omicron variant (B.1.1.529) is estimated to be more transmissible than previous strains of SARS-CoV-2 especially among children, potentially resulting in croup which is characteristic disease in children. However, there have been no reports confirming the relative susceptibility of different age groups to SARS-CoV-2. In this study, we estimated the age-specific susceptibility during the 5th (Omicron driven), 4th (Delta driven), and 3rd (pre-Delta) waves in South Korea, using the age-structured compartmental model. Even after adjusting for contact pattern, vaccination status, and waning of vaccine effectiveness, the susceptibility among age group 0–19 years was approximately 5 times higher during the 5th wave (Omicron driven) than that during the 3rd wave (pre-Delta), and 3 times higher than that during the 4th wave (Delta driven). Here, we found that children are indeed more susceptible to the Omicron variant compared with the previous strains of SARS-CoV-2.

Full Text

As Omicron variant of SARS-CoV-2 drives new surge in coronavirus disease 2019 (COVID-19) cases globally, increasing proportion of pediatric cases is noteworthy.¹ According to the nationwide study in the United States (US), the seroprevalence of infection-induced SARS-CoV-2 antibodies among children aged 0–11 years increased from 44.2% to 75.2% during December 2021 to February 2022, recording the highest among all age groups (overall US seroprevalence increased from 33.5% to 57.7%).² In England, pediatric admissions with COVID-19 infections began to rise since December 26, 2021, from an average of 40 admissions per day to 120 per day, a 3-fold rise in 2 weeks.³

The rise in pediatric cases might be attributed to the elderly-prioritized vaccination strategy against COVID-19, and relatively higher contact rates among school-aged children than adults. As of May 31, 2022, World Health Organization (WHO) authorized COVID-19 vaccines could be administered safely to individuals aged 18 years and older, and only one vaccine could be used for individuals from 5 years of age, which let children more vulnerable to COVID-19.⁴ Otherwise, children might genuinely be more susceptible to contacting the Omicron infections than adults. Identifying the age-specific susceptibility to SARS-CoV-2 is of much interest for effective public health strategies and vaccination policy. However, it is often not easy to clarify the age-specific susceptibility to an infection due to the lack of sufficient data.

Given that South Korean government has posted age-stratified COVID-19 incidences daily based on vigorous contact tracing, along with the solid report of vaccination rates, it could be a suitable country to elucidate this topic. We utilized the concept in force of infection to investigate the age-specific susceptibility to SARS-CoV-2 in this study. Briefly, the force of infection is the product of (i) susceptibility of a population who is at risk of becoming infected, (ii) the number of infectious individuals, and (iii) their contact rates.⁵ Since we know the age-stratified incidence of COVID-19 at discrete time, transition time distribution to the next infection stage, and the age-specific contact matrix for South Korea, we could infer the age-specific susceptibility using Bayesian inference method (see **Methods**).^{6–9} More precisely, we removed individuals who were vaccinated from the susceptible population in accordance with the vaccine effectiveness against the Delta and the Omicron variants.¹⁰ The waning of vaccine effectiveness was also considered.¹¹

In South Korea, the biggest 5th wave has been driven by the Omicron variant since January 2022, following the 4th wave by Delta variant and the 3rd wave by original SARS-CoV-2 virus (**Figure 1**). Here, we inferred the age-specific susceptibility to the Omicron variant compared to the Delta and pre-Delta strains using the epidemiologic data of those three waves.

Uncertainties regarding the age-specific contact patterns, the proportion of asymptomatic individuals, and vaccine effectiveness were also evaluated with sensitivity analyses.

The age distribution of COVID-19 cases during 3rd (pre-Delta), 4th (Delta) and 5th (Omicron) waves in South Korea is shown in **Figure 2**. The proportion of COVID-19 cases among those aged 19 years or less were 11.02%, 16.72%, and 28.55% during the 3rd, 4th, and 5th waves respectively. Meanwhile, the proportion of cases among those aged 60 years or more were 28.47%, 10.16%, and 10.04% during the 3rd, 4th, and 5th waves respectively. Considering the age demographics (age skewed older in South Korea), the proportion of cases among those aged 19 years or less was 13.28%, 23.43%, and 36.95% during the 3rd, 4th, and 5th waves respectively.

The age-specific susceptibility to COVID-19 is shown in **Figure 2**. Both the 3rd (pre-Delta) and 4th (Delta) waves showed a similar age-dependent increase, whereas the 5th (Omicron) wave showed an inverted bell curve with bimodal peaks. A significant difference between the susceptibility to the Omicron and that to the Delta and pre-Delta variants was found in the younger age group. The rise in susceptibility to the Omicron/pre-Delta variant was highest in the 10–15 years age group (5.28 times [95% CI, 4.94–5.60]), whereas in those aged 50 years or more, the susceptibility to the Omicron/pre-Delta remained stable at approximately two-fold, scoring the lowest value of 1.12 (95% CI, 1.09–1.14) among those aged 75 years or more. The rise in susceptibility to the Omicron/Delta variant was highest in the 15–19 years age group (3.21 times [95% CI, 3.12–3.31]), and lowest in those aged 75 years or more (0.93 times [95% CI, 0.89–0.97]).

Varying the contact patterns, proportion of asymptomatic cases, and vaccine effectiveness, the rise in susceptibility to the Omicron/pre-Omicron was not changed, recording the higher values in the 0–19 years age groups than in other age groups (**Extended Data**).

Even after adjusting for contact pattern, vaccination status, and waning of vaccine effectiveness, the age-specific susceptibility among age group 0–19 years was approximately 5 times higher during the 5th wave (Omicron driven) than that during the 3rd wave (pre-Delta), and 3 times higher than that during the 4th wave (Delta driven). Indeed, children are more susceptible to the Omicron variant compared with the previous strains of SARS-CoV-2. According to the US Centers for Disease Control and Prevention report, the hospitalization rates among individuals aged 12–17 years were 3.5 times as high during the peak week of the Omicron period than during the Delta period.¹² This finding is in line with our result, although the increased susceptibility to the infection is not necessarily correlated with the increased hospitalization rates.

Considering that the Omicron variant has shifted tropism to the upper respiratory tract from the lower respiratory tract, children whose upper airway is immature and relatively smaller than those in adults could be much more easily affected.^{13,14} Likewise, increasing cases of croup, an acute laryngotracheobronchitis characterized by barking cough, were noted in South Korea, during the Omicron surge.¹⁵ What is more, the endocytic entry which Omicron prefer over angiotensin-converting enzyme 2 (ACE2) dependent pathway, could also explain the higher number of pediatric cases since children have a lower number of ACE receptors.^{16,17}

An experimental study compared the replication competence of wild type, pre-Delta variants (D614G, Alpha and Beta), Delta, and Omicron in human bronchi and lungs.¹³ The result showed that Delta variant replicated significantly more than pre-Delta variants in human bronchi, and Omicron did even more than the Delta variant. In lung tissues, higher replication was noted with wild type virus compared with the Delta and Omicron variants. Likewise, the age-specific susceptibility among children to Delta variant was higher than that to pre-Delta, and susceptibility to Omicron variant was even higher than that to the Delta in this study. Taken together, our finding is in accordance with both epidemiological and biological observations.

There are several limitations in this study. First, the contact matrix in this study was not of our own empirical data, but instead mathematically estimated data.⁶ Second, although we attempted to reflect the social distancing policy into our model, the implementation of nonpharmaceutical interventions, which could change the effective contact rates, was not considered in this study. Third, the exact proportion of asymptomatic infections by age groups remains unclear. To overcome this hurdle, we adopted the result from a prospective cohort study and further conducted a sensitivity analysis with variable ranges of asymptomatic proportions.¹⁸

In conclusion, large-scale testing, prompt epidemiological survey, and vaccination status records in a national register in South Korea, allowed us to analyse the age-stratified susceptibility to SARS-CoV-2. Generally, the Omicron variant of SARS-CoV-2 was estimated to spread more easily among children than the Delta and pre-Delta strains. At the beginning of SARS-CoV-2 pandemic, an increased number of cases and a greater risk of severe disease with increasing age were notable. We might now see the course of adaptation of novel SARS-CoV-2 to humans. These age-affinity seems to be similar with influenza that we include both the youngest and the elderly as target groups for vaccination. Although it is not yet clear whether children could be key driver groups in SARS-CoV-2 transmission hereafter, additional efforts for vaccinating children might be considered to reducing the pandemic's impact in whole community.

Declarations

Data availability

Age-stratified daily COVID-19 incidence (<http://ncov.mohw.go.kr/>) and vaccine uptake rates (<https://ncv.kdca.go.kr/>) have been reported by the Ministry of Health and Welfare of South Korea. More refined vaccination data of doses and manufacturers were provided by Korea Disease Control and Prevention Agency. Age-structured population data was obtained from the Statistics Korea (<https://kosis.kr/index/index.do>).

Code availability

Code to reproduce the analyses is available at <https://github.com/Hwichang/Age-varying-susceptibility-to-the-Omicron-variant-of-SARS-CoV-2>.

Ethics statement

All the data used in this study were deidentified and were regarded exempt from institutional review board assessment of the National Cancer Center (NCC2022-0127).

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Author contributions

J.Y.C. and Y.K. conceived of the study, and H.J. performed the analysis. J.Y.C. and H.J. wrote the first draft of the manuscript. Y.K. reviewed and edited the manuscript. All authors interpreted the findings, contributed to writing the manuscript, and approved the final version for publication.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- 1 Belay, E. D. & Godfred-Cato, S. SARS-CoV-2 spread and hospitalisations in paediatric patients during the omicron surge. *The Lancet. Child & adolescent health* **6**, 280-281, doi:10.1016/s2352-4642(22)00060-8 (2022).
- 2 Clarke, K. E. N. *et al.* Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies - United States, September 2021-February 2022. *MMWR Morb Mortal Wkly Rep* **71**, 606-608, doi:10.15585/mmwr.mm7117e3 (2022).
- 3 UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 34.* 2022. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1046853/technical-briefing-34-14-january-2022.pdf (May 31 2022).
- 4 World Health Organization. *Coronavirus disease (COVID-19): Vaccines.* 2022. [https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-\(covid-19\)-vaccines?gclid=Cj0KCQjwnNyUBhCZARIsAI9AYIHnDfAcWT3iDzLuyWVH6I-b8NIWhv5MuWbBKUqT86kpJmKbUUNtc30aAtEeEALw_wcB&topicsurvey=v8kj13](https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-vaccines?gclid=Cj0KCQjwnNyUBhCZARIsAI9AYIHnDfAcWT3iDzLuyWVH6I-b8NIWhv5MuWbBKUqT86kpJmKbUUNtc30aAtEeEALw_wcB&topicsurvey=v8kj13) (May 31 2022).
- 5 Vynnycky, E. & White, R. *An introduction to infectious disease modelling.* (OUP oxford, 2010).
- 6 Prem, K. *et al.* Projecting contact matrices in 177 geographical regions: An update and comparison with empirical data for the COVID-19 era. *PLoS computational biology* **17**, e1009098, doi:10.1371/journal.pcbi.1009098 (2021).
- 7 *Coronavirus Disease-19, Republic of Korea.* <http://ncov.mohw.go.kr/> (April 23 2022).
- 8 *Press Release: Korea COVID-19 Update.* <https://www.kdca.go.kr/board/board.es?mid=a20501010000&bid=0015> (April 23 2022).

- 9 Chun, J. Y., Jeong, H. & Kim, Y. Age-Varying Susceptibility to the Delta Variant (B.1.617.2) of SARS-CoV-2. *JAMA Netw Open* **5**, e223064, doi:10.1001/jamanetworkopen.2022.3064 (2022).
- 10 *COVID-19 Vaccination*. <https://ncv.kdca.go.kr/> (April 23 2022).
- 11 Andrews, N. *et al.* Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. *The New England journal of medicine* **386**, 1532-1546, doi:10.1056/NEJMoa2119451 (2022).
- 12 Marks, K. J. *et al.* Hospitalizations of Children and Adolescents with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, July 2021-January 2022. *MMWR Morb Mortal Wkly Rep* **71**, 271-278, doi:10.15585/mmwr.mm7107e4 (2022).
- 13 Hui, K. P. Y. *et al.* SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo. *Nature* **603**, 715-720, doi:10.1038/s41586-022-04479-6 (2022).
- 14 Peacock, T. P. *et al.* The SARS-CoV-2 variant, Omicron, shows rapid replication in human primary nasal epithelial cultures and efficiently uses the endosomal route of entry. 2021.2012.2031.474653, doi:10.1101/2021.12.31.474653 %J bioRxiv (2022).
- 15 Choi, Y. Y. *et al.* Croup as a Manifestation of SARS-CoV-2 Omicron Variant Infection in Young Children. *Journal of Korean medical science* **37**, e140, doi:10.3346/jkms.2022.37.e140 (2022).
- 16 Willett, B. J. *et al.* The hyper-transmissible SARS-CoV-2 Omicron variant exhibits significant antigenic change, vaccine escape and a switch in cell entry mechanism. 2022.2001.2003.21268111, doi:10.1101/2022.01.03.21268111 %J medRxiv (2022).
- 17 Zimmermann, P. & Curtis, N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Archives of disease in childhood*, doi:10.1136/archdischild-2020-320338 (2020).
- 18 Dawood, F. S. *et al.* Incidence Rates, Household Infection Risk, and Clinical Characteristics of SARS-CoV-2 Infection Among Children and Adults in Utah and New York City, New York. *JAMA pediatrics* **176**, 59-67, doi:10.1001/jamapediatrics.2021.4217 (2022).

Figures

Figure 1

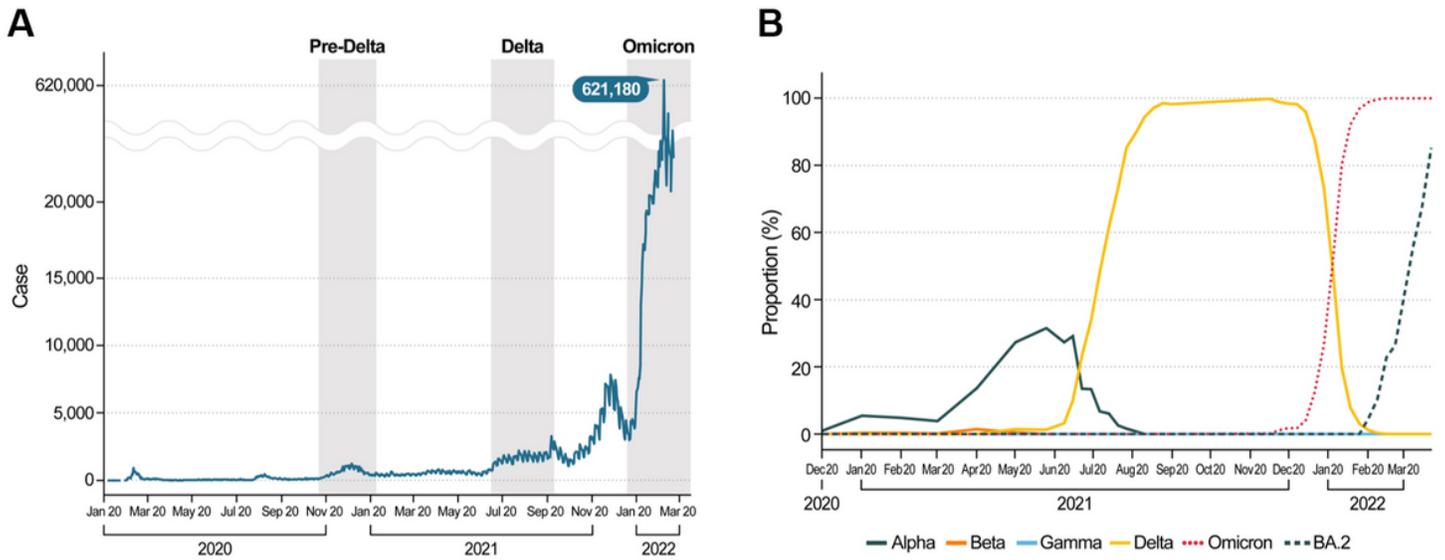


Figure 1

Characteristics of the SARS-CoV-2 outbreak in South Korea: (A) Epidemic curve, (B) Domestic composition of variant strains during the study period.

Figure 2

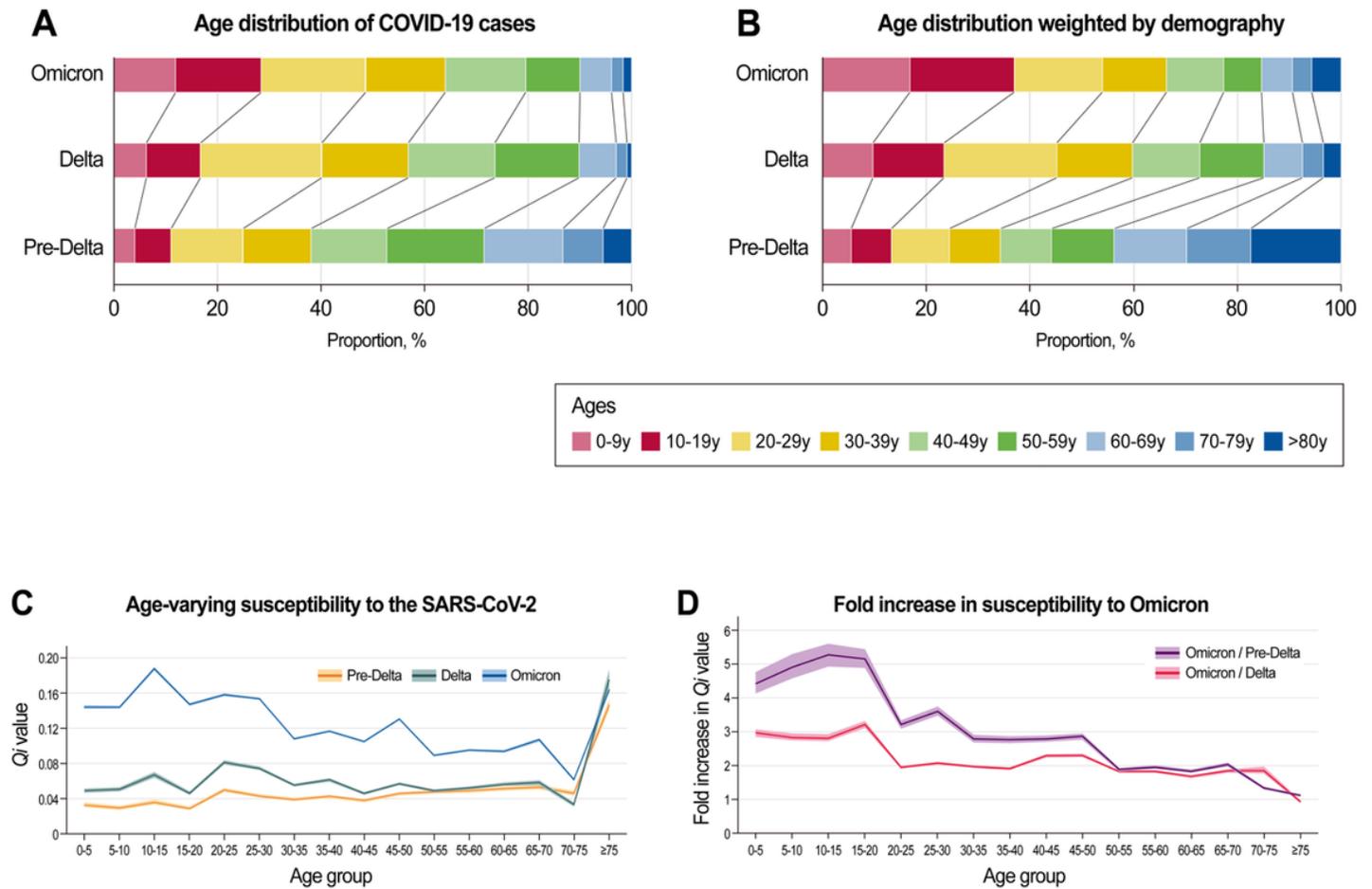


Figure 2

Age distribution of COVID-19 cases (A) during the 3rd, 4th, and 5th wave in South Korea, and (B) those weighted by the demographic structure. The age-varying susceptibility to SARS-CoV-2 (C) during the 3rd (pre-Delta), 4th (Delta), and 5th (Omicron) wave in South Korea, and (D) the fold-rise in susceptibility to the Omicron/Delta and Omicron/pre-Delta by age groups. The shadow indicates the 95% confidence intervals.

Supplementary Files

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