

Review Article

The Comparison of Susceptibility to SARS-CoV-2 Infection between Pediatric and Adults

Milad Zandi ^{1,2} Ph.D., Saber Soltani ^{1,2} Ph.D., Mona Fani ³ Ph.D.,
Haniye Shafipour ¹ M.Sc., Samaneh Abbasi ^{4*} Ph.D.

¹ Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

² Research Center for Clinical Virology, Tehran University of Medical Sciences, Tehran, Iran

³ Department of Pathobiology and Laboratory Sciences, Faculty of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran

⁴ Department of Microbiology, Faculty of Medicine, Abadan University of Medical Sciences, Abadan, Iran

ABSTRACT

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SARS-CoV-2 causes coronavirus disease 2019 (COVID-19) and is responsible for the recent pandemic in the world. It has been recently recognized as a challenge for public health and a significant cause of severe illness in all age groups. Young children and older people are susceptible to SARS-CoV-2 infection. However, children usually present mild symptoms compared to adult patients. The relationship between age, severity, and COVID-19 transmission is compared to determine whether there is any reasonable relationship between age and COVID-19. It should be mentioned that some risk factors may increase the probability of developing severe COVID-19 by advancing age, such as pathophysiological changes in the respiratory system, angiotensin-converting enzyme 2 expression in the nasopharynx, and smoking. Susceptibility to SARS-CoV-2 infection is independent of age, but the mortality rate of COVID-19 depends on age.

*Corresponding Author: Department of Microbiology, Faculty of Medicine, Abadan University of Medical Sciences, Abadan, Iran. Tel: +989123738603; Email: s_abbasi80@yahoo.com

Introduction

In December 2019, the first Coronavirus Disease 2019 (COVID-19) case was reported in Wuhan, China. COVID-19 has quickly spread throughout China to around the world. On March 11, 2020, World Health Organization (WHO) declared Coronavirus Disease 2019 as a global pandemic [1]. As of November 10, 2020, according to a report of the WHO, COVID-19 has affected 49.7 million patients in more than 200 countries and has caused 1.2 million deaths globally [2].

SARS-CoV-2 is an enveloped, positive-sense, and single-strand RNA virus classified in the Coronaviridae family. According to genetic properties, there are four genera of Coronaviridae, including alpha (α), beta (β), gamma (γ), and delta (δ) coronavirus. Some beta coronaviruses, including SARS-CoV, MERS-CoV, and SARS-CoV-2, can cause respiratory infections and pose public health challenges [3].

Coronaviruses genome size is in the range of 27-32 kb, and genome organization is conserved in 5'-leader-UTR-replicase-S (Spike), E(Envelope), M(Membrane), N(Nucleocapsid)-3'UTR-poly(A)tail. Coronaviruses genome comprises two large open reading frames encoding polyproteins, which are processed into 16 nonstructural proteins by viral-encoded enzymes, including chymotrypsin-like protease (3CLpro) or main protease (Mpro) and one or two papain-like proteases [4].

Structural proteins of coronaviruses are necessary for the initiation of infection and assembly: surface spike glycoprotein (S)

belongs to class I viral fusion protein that has a major role in binding to cellular receptors and the viral entry into the host cell. It consists of S1 and S2 subunits. The S1 subunit contains the receptor-binding domain (RBD) responsible for binding to the cellular receptor, and the S2 subunit mediates the fusion and entrance process. Membrane protein facilitates the assembly process via increasing the membrane curvature. Envelope protein plays a key role in releasing viral particles. Nucleocapsid protein is crucial as interferon antagonistic and can support viral replication [5]. The average incubation period for SARS-CoV-2 is 5.1 days [6]; however, one study reported up to 19 days in a person with asymptomatic infection [7]. Studies showed that the main symptoms of COVID-19 are fever, cough, shortness of breath, muscle ache, confusion, and headache [8]. Laboratory tests and chest computed tomography scans were used to diagnose COVID-19. However, results presented in severe cases laboratory parameters such as low lymphocyte counts and bilateral pneumonia were common clinical features [9, 10].

Coronavirus disease 2019 in children

SARS-CoV-2 infects people of all ages [11]. Initial reports indicated that most COVID-19 cases occurred in older people than 45 years compared to adults [12]. In the early of the outbreak prevalence of COVID-19 disease in children was not clear due to low diagnostic tests in the children population. There was no involvement of children under 15 years old. However, the total number of COVID-19 cases

in children was increased [13,14]. In the early epidemic, some studies showed that children could be affected by SARS-CoV-2. A few studies have investigated the COVID-19 disease in children; researchers in a study reported that 0.9% and 1.2% of the total confirmed COVID-19 cases were in the range of 0–9 and 10–19 year age groups, respectively [15].

Some studies showed that most children with COVID-19 were mild or to be asymptomatic. Children as asymptomatic carriers can have a key role in transmitting SARS-CoV-2 in the community [16]. However, the prevalence of asymptomatic SARS-CoV-2 infection in children has been reported at 4.4%, while 17.4% in adults COVID-19 cases. The clinical symptoms of COVID-19 disease are generally mild in children, but most severe or critical illness cases in children are less than one year old [12]. Common symptoms of COVID-19 in children include fever, cough, and fatigue, along with nasal stuffiness, rhinorrhea, sputum, diarrhea, and headache [17]. The mortality rate of COVID-19 in children is lower than in adult infection [18]. According to studies, some features of COVID-19 vary in children from adults; for example, vomiting and diarrhea are more prominent. However, low-grade fever and cough also have been seen in children [19]. Laboratory findings such as biochemical, hematological, and radiological results in children with COVID-19 have no diagnostic value [20]. It is estimated that some factors can decrease COVID-19 severity in children, such as angiotensin-converting enzyme 2 (ACE2) as the cellular receptor of SARS-CoV-2. Besides, ACE2 expression increases in the nasopharynx

with age. However, more researches are required to work on this hypothesis [21]. In addition, the low maturity of children's immune system can be considered as another factor for mild symptoms in the children population [22]. Researches in some studies have found that race may affect the susceptibility of children to COVID-19 as a risk factor [23].

Given that children are considered a ring of transmission of COVID-19, managing this group with COVID-19 is important. According to reports, mainly children contract the COVID-19 via household exposure, and 56%–90% of children with COVID-19 had an infected family member [24]. So, developing awareness-raising tools for children and self-care practice training can effectively manage children in the COVID-19 pandemic.

Coronavirus disease 2019 in adults

Commonly, several conditions increase the susceptibility of individuals to SARS-CoV-2 infection, such as aging [25]. Both men and women at any age are susceptible to COVID-19 illness. Due to pathophysiological changes in the respiratory system of the older group, they may experience a severe form of the COVID-19 [26]. Aging plays a vital factor in severe COVID-19. In most cases, aging causes an increased disease severity, hospitalization, and even death. It has been reported that the mortality rate of COVID-19 increases via aging [27]. Studying 16035 patients referred to Tehran hospitals shows that the highest mortality was observed in people over 65 [28]. Recently, Svartengren et al. reported that clearance of inhaled particles in the airway region is decreased by increasing age [29]. In

addition, smoking is considered a risk factor in lung damage and increased severity of COVID-19 in adults [30]. A study conducted by Nikpouraghdam et al. showed that older age, male gender, and having comorbidities were significantly related to the risk of death among patients with COVID-19 [31]. Fever, cough, dyspnea, and myalgia are common clinical presentations in older adults. Some forms of organ damage have been reported in adult cases with COVID-19, such as acute respiratory distress syndrome, acute respiratory failure, cardiac injury, and liver damage, and required vasopressor support for treatment [32].

Researchers calculated the probability of infection in various groups under different conditions by using a computational model. The rate of person-to-person transmission and the degree of prevention in outdoor activities were measured in this method. As a result of this simulation, the rate of death and the severity of symptoms are associated with the age of patients, but patients' age cannot affect their risk of developing the disease [33].

The current pipeline of vaccines for SARS-CoV-2 infection

Several licensed vaccines, including inactivated, nucleic acid-based, and vector vaccines, are produced to fight COVID-19. Moderna, Pfizer, and BioNTech are mRNA-based vaccines encapsulated in lipid

nanoparticles and focus on the S protein. These vaccines can elicit neutralization and Th1-biased CD4⁺ T-cell responses. The viral-vector-based vaccine against SARS-CoV-2, including Sputnik V, Oxford-AstraZeneca, Johnson & Johnson, are constructed from recombination Adenoviruses (rAd) such as rAd 5,26 or chimpanzee adenovirus (ChAdOx1) that carry the S gene of SARS-CoV-2 and induce the humoral and cellular immune. Sinovac, Sinopharm, Bharat Biotech are inactivated vaccines produced by growing SARS-CoV-2 in Vero cells containing the whole virus and can protect the immune response [34, 35].

Conclusion

The susceptibility to SARS-CoV-2 infection is independent of age, even though the mortality rate of COVID-19 is dependent on age. After the prevalence of B.1.1.7 variant, evidence reported high hospital admissions and more severe illness in children and adolescents, leading to the general confusion about B.1.1.7 variant. On the other hand, the population of young children can be a target group for immunization against SARS-CoV-2 infection.

Conflict of Interest

The authors declare no conflict of interest.

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References

- [1]. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol.* 2021; 19(3): 141-54.
- [2]. World Health Organization (WHO). Coronavirus disease (COVID-19) weekly epidemiological update and weekly operational update [Internet]. Geneva: WHO; 2020 [cited

- 2020 November 10]. Available from: <https://www.who.int/publications/m/item/weekl-y-epidemiological-update---10-november-2020>.
- [3]. Fani M, Zandi M, Soltani S, Abbasi S. Future developments in biosensors for field-ready SARS-CoV-2 virus diagnostics. *Biotechnol Appl Biochem*. 2021; 68(4): 695-99.
- [4]. Denison MR, Graham RL, Donaldson EF, Eckerle LD, Baric RS. Coronaviruses: an RNA proofreading machine regulates replication fidelity and diversity. *RNA Biol*. 2011; 8(2): 270-79.
- [5]. Sanami S, Zandi M, Pourhossein B, Mobini GR, Safaei M, Abed A, et al. Design of a multi-epitope vaccine against SARS-CoV-2 using immunoinformatics approach. *Int J Biol Macromol*. 2020; 164: 871-83.
- [6]. Kesheh MM, Hosseini P, Soltani S, Zandi M. An overview on the seven pathogenic human coronaviruses. *Rev Med Virol*. 2021: 2282.
- [7]. Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020; 323(14): 1406-407.
- [8]. Hosseini P, Dehghan A, Navand AH, Moghadami M, Soltani S, Zandi M. Coronavirus disease 2019 (COVID-19): Immune responses, transmission and clinical features: An update. *Journal of Cellular & Molecular Anesthesia* 2020; 5(4): 266-68.
- [9]. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Y, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. *Int J Infect Dis*. 2020; 96: 131-135.
- [10]. Davarpanah AH, Asgari R, Moharamzad Y, Mahdavi A, Abrishami A, Nekooghadam S, et al. Risk factors for poor outcome in patients with severe viral pneumonia on chest CT during the COVID-19 outbreak: a perspective from Iran. *SN Compr Clin Med*. 2020; 2(9): 1366-76.
- [11]. Kalantari H, Tabrizi AHH, Foroohi F. Determination of COVID-19 prevalence with regards to age range of patients referring to the hospitals located in western Tehran, Iran. *Gene Rep*. 2020; 21: 100910.
- [12]. Soltani J, Sedighi I, Shalchi Z, Sami G, Moradveisi B, Nahidi S. Pediatric coronavirus disease 2019 (COVID-19): An insight from west of Iran. *North Clin Istanb*. 2020; 7(3): 284-91.
- [13]. Kim L, Whitaker M, O'Halloran A, Kambhampati A, Chai SJ, Reingold A, et al. COVID-NET surveillance team. hospitalization rates and characteristics of children aged <18 years hospitalized with laboratory-confirmed COVID-19 - COVID-NET, 14 States, March 1-July 25, 2020. *MMWR Morb Mortal Wkly Rep*. 2020; 69(32): 1081-1088.
- [14]. CDC COVID-19 Response Team. Coronavirus disease 2019 in children - United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep*. 2020; 69(14): 422-26.
- [15]. Surveillances V. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)-China, 2020. *China CDC weekly* 2020; 2(8): 113-22.
- [16]. Li X, Xu W, Dozier M, He Y, Kirolos A, Theodoratou E. The role of children in transmission of SARS-CoV-2: A rapid review. *J Glob Health* 2020; 10(1): 11101.
- [17]. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, et al. COVID-19 task force of YO-IFOS. clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. *J Intern Med*. 2020; 288(3): 335-44.
- [18]. Dhochak N, Singhal T, Kabra SK, Lodha R. Pathophysiology of COVID-19: Why children fare better than adults? *Indian J Pediatr*. 2020; 87(7): 537-46.
- [19]. Hoang A, Chorath K, Moreira A, Evans M, Burmeister-Morton F, Burmeister F, et al. COVID-19 in 7780 pediatric patients: A systematic review. *Eclinical Medicine* 2020; 24: 100433.
- [20]. Frater JL, Zini G, d'Onofrio G, Rogers HJ. COVID-19 and the clinical hematology laboratory. *Int J Lab Hematol*. 2020; 42(S 1): 11-8.
- [21]. Steinman JB, Lum FM, Ho PP, Kaminski N, Steinman L. Reduced development of COVID-19 in children reveals molecular checkpoints gating pathogenesis illuminating potential therapeutics. *Proc Natl Acad Sci USA*. 2020; 117(40): 24620-4626.
- [22]. Maggini S, Pierre A, Calder PC. Immune function and micronutrient requirements change over the life course. *Nutrients* 2018; 10(10): 1531.
- [23]. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. PIMS-TS study group and EUCLIDS and PERFORM consortia. clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *JAMA* 2020; 324(3): 259-69.
- [24]. Choi SH, Kim HW, Kang JM, Kim DH, Cho EY. Epidemiology and clinical features of coronavirus disease 2019 in children. *Clin Exp Pediatr*. 2020; 63(4): 125-32.
- [25]. Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? *Aging (Albany NY)*. 2020; 12(10): 9959-981.
- [26]. Perrotta F, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. *Aging Clin Exp Res*. 2020; 32(8): 1599-608.

- [27]. Santesmasses D, Castro JP, Zenin AA, Shindyapina AV, Gerashchenko MV, Zhang B, et al. COVID-19 is an emergent disease of aging. *Aging Cell* 2020; 19(10): 13230.
- [28]. Zali A, Gholamzadeh S, Mohammadi G, Azizmohammad Looha M, Akrami F, Zarean E, et al. Baseline characteristics and associated factors of mortality in COVID-19 patients; an analysis of 16000 cases in Tehran, Iran. *Arch Acad Emerg Med*. 2020; 8(1): 70-9.
- [29]. Svartengren M, Falk R, Philipson K. Long-term clearance from small airways decreases with age. *Eur Respir J*. 2005; 26(4): 609-15.
- [30]. Reddy RK, Charles WN, Sklavounos A, Dutt A, Seed PT, Khajuria A. The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. *J Med Virol*. 2021; 93(2): 1045-1056.
- [31]. Nikpouraghdam M, Jalali Farahani A, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. *J Clin Virol*. 2020; 127: 104378.
- [32]. Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and multiorgan response. *Curr Probl Cardiol*. 2020; 45(8): 100618.
- [33]. Omori R, Matsuyama R, Nakata Y. The age distribution of mortality from novel coronavirus disease (COVID-19) suggests no large difference of susceptibility by age. *Sci Rep*. 2020; 10(1): 16642.
- [34]. Amanat F, Krammer F. SARS-CoV-2 vaccines: status report. *Immunity* 2020; 52(4): 583-89.
- [35]. Zandi M, Rashid S, Nasimzadeh S, Pourhossein B, Fazeli M. A snapshot of different types of under research vaccines against COVID-19: A review. *Archives of Medical Laboratory Sciences* 2020; 6(1): 1-7.