

## **Epidemiology and Clinical Features of Coronavirus disease 2019 in Children**

(Running title: COVID-19 in Children)

Soo-Han Choi<sup>1</sup>, Han Wool Kim<sup>2</sup>, Ji-Man Kang<sup>3,4</sup>, Dong Hyun Kim<sup>5</sup>, Eun Young Cho<sup>6</sup>

<sup>1</sup>Department of Pediatrics, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea

<sup>2</sup>Department of Pediatrics, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea

<sup>3</sup>Department of Pediatrics, Severance Children's Hospital, Yonsei University College of Medicine, Seoul, Korea

<sup>4</sup>Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Seoul, Korea

<sup>5</sup>Department of Pediatrics, Inha University Hospital, Inha University School of Medicine, Incheon, Korea

<sup>6</sup>Department of Pediatrics, Chungnam National University Hospital, Daejeon, Korea

### **Correspondence to:**

Eun Young Cho, MD

Clinical Associate Professor of Pediatric Infectious Diseases

Department of Pediatrics, Chungnam National University Hospital

282 Munhwa-ro, Jung-gu, Daejeon, 35015, Korea

Office: +82-42-280-7265, Mobile: +82-10-9215-0210

E-mail: eycho@cnuh.co.kr, pedeyc@gmail.com

<https://orcid.org/0000-0002-2286-4593>

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## **Abstract**

Coronavirus disease-2019 (COVID-19), which started in Wuhan, China, in December 2019 and has been declared a worldwide pandemic in March 11, 2020, is a novel infectious disease that causes respiratory illness and death. Pediatric COVID-19 accounts for a small percentage of patients with outbreaks and is often milder than adults, but can progress to severe disease in some cases. Even neonates can suffer from COVID-19, and children may play a role as a spreader in the community. In this review, we summarize what is known about COVID-19 in children and adolescents until now.

## **Keywords**

Coronavirus, COVID-19, child, infant, newborn

## Introduction

In December 2019, the first cases of pneumonia of unknown etiology were identified in Wuhan, China. A previously unknown betacoronavirus was detected in respiratory samples of the patients<sup>1</sup>. The virus was named SARS-CoV-2 (severe acute coronavirus 2), and the disease caused by it was named Coronavirus disease 2019 (COVID-19)<sup>2</sup>. COVID-19 swept the mainland China rapidly and spread around the globe, causing 118,319 confirmed cases and 4,292 deaths in 113 nations as of March 11, 2020. The World Health Organization (WHO) declared COVID-19 a pandemic<sup>3</sup>. In the Republic of Korea, starting with a Chinese traveler from Wuhan in January 19<sup>4</sup>, 7,755 confirmed cases leading to 60 deaths had occurred until March 11, 2020<sup>5</sup>.

COVID-19 is a novel infectious disease that is forecasted to have an enormous effect worldwide. This article reviews what is known about COVID-19 in children and adolescents to help clinicians in managing pediatric patients, as of March 12, 2020.

## Epidemiology in children (Table 1)

Published data on COVID-19 focuses primarily on adults, and the rate of COVID-19 infection in children is relatively low<sup>6</sup>. The first pediatric case was reported on January 20, 2020, in a 10-year-old boy from Shenzhen, China, whose family had visited Wuhan City<sup>7</sup>. However, in a retrospective study that enrolled 366 children ( $\leq 16$  years of age) who were hospitalized for respiratory infections between January 7 and 15, 2020, COVID-19 was confirmed in 6 (1.6%) children whose onset of illness occurred between January 2 and 8, 2020. This study result suggests that COVID-19 infections in children were occurring early in the epidemic<sup>8</sup>.

Limited data is available on prevalence of COVID-19 in pediatric population, because children

were rarely tested for the virus in earlier phase of the outbreak, especially in Hubei province in China where the most patients were confirmed<sup>9)</sup>. Until January 31, 2020, out of 11,791 confirmed COVID-19 cases in mainland China, 74 (0.6%) pediatric patients aged 1.5 months to 18 years were reported, and 56% (34/61) of the pediatric patients had a history of household contact<sup>10)</sup>. Until February 7, 2020, though the data was incomplete, 285 children (0.8%) out of 34,546 confirmed cases were documented, and 71.2% (183/257) of infected children reported having a household contact<sup>11)</sup>. The youngest was a 36-hour-old newborn and is currently the youngest COVID-19 patient in the world<sup>12)</sup>. As of February 11, 2020, the Chinese Center for Disease Control and Prevention reported 44,672 laboratory-confirmed cases; 416 cases (0.9%) were aged 0-9 years, and 549 (1.2%) were aged 10-19 years; 1 death occurred in age group 10-19 years, and fatality rate in this group was 0.18%<sup>13)</sup>. According to a report from the WHO-China Joint Mission on COVID-19, the largest-scale report to date, 55,924 cases had been laboratory-confirmed by February 20, 2020. The patient median age was 51 years (ranged 2 days to 100 years; interquartile range, 39 to 63 years), and 2.4% were children under 19 years, out of which 2.5% were severely ill and 0.2% were critical<sup>6)</sup>.

By February 10, 2020, a total of 10,924 adult cases and 398 pediatric cases were confirmed in mainland China, excluding the Hubei Province. The rate of pediatric case was 3.5% (398/11,322)<sup>9)</sup>. In 6 northern Chinese provinces, 31 children were diagnosed with COVID-19 from January 15 to February 21, 2020. The median age was 7.1 years (ranged 6 months to 17 years); 21 children (68%) had a history of contact with a confirmed adult patient; 28 children (90%) had an infected family member<sup>14)</sup>.

Pediatric COVID-19 cases outside of China have been sporadically reported, but limited data is available. Two Malaysian boys with age of 2 years and 11 years on January 25<sup>15)</sup>, a German boy on

January 31<sup>16)</sup>, a Singaporean 6-month-old boy on February 5<sup>17, 18)</sup>, and a Vietnamese 3-month-old infant on February 11<sup>19)</sup> have been reported. All these cases were related to an exposure to an infected family member.

In Singapore, after an index case from China was first diagnosed with COVID-19 on January 23, 2020, the infection spread through community transmission. By March 11, 2020, 167 patients were confirmed, 6 (3.6%) of which were children whose ages were 6 months, 1 year, 2 years, 5 years, 12 and 17 years. Three children were residents of Wuhan; 2 children had an infected family member, and 1 reported an exposure to an adult patient<sup>17)</sup>. In Italy, where a rapid rise of COVID-19 confirmed cases ensued after the cluster cases on February 21, 2020, a total of 8,342 cases had been reported by March 9, 2020; 1.4% of cases were children under aged 0-18 years and there was no fatality in this age group<sup>20)</sup>. In Australia, a total of 71 COVID-19 cases were confirmed by March 7, 2020; 2 cases in 0-9 years and 2 in 10-19 years were reported, therefore 5.6% of the confirmed cases were in age group of 0-19 years<sup>21)</sup>.

In Korea, a 10-year-old girl whose mother and uncle had been diagnosed with COVID-19 was the first pediatric case, reported on February 19, 2020<sup>22)</sup>. Thereafter, the youngest record has been updated and reported by newspapers: a 4-year-old on February 23<sup>23)</sup>, a 45-day-old infant on February 29<sup>24)</sup>, and a 4-week old newborn on March 8<sup>25)</sup>. The 4-year-old had contacted an infected daycare teacher, while the 45-day-old and the 4-week-old had an infected family member.

As of midnight March 11, 2020, a total of 7,755 patients had been confirmed, of which 75 (1.0%) were children aged 0-9 years and 405 (5.2%) were aged 10-19 years. No fatality has been reported in these age groups. COVID-19 incidence rate in Korea is calculated: 15.0 per 100,000 in all ages, 1.8 per 100,000 in ages 0-9 years, and 8.2 per 100,000 in ages 10-19 years, according to national population data in February 2020 (51,844,627 in total population, 4,134,824 in aged 0-9

years, and 4,920,794 in aged 10-19 years)<sup>5, 26)</sup>. As of March 11, 2020, according to the pediatric age group analysis by school years performed by Korea Centers for Disease Control, 23 children were between 0-2 years, 26 in 3-6 years, 82 in 7-12 years, 78 in 13-15 years, and 123 in 16-18 years (Fig. 1)<sup>27)</sup>.

### **Clinical features in children (Table 2)**

It is known that children with COVID-19 show milder symptoms than adults<sup>11)</sup>, but limited data exists on the burden of COVID-19 in children. A 10-year-old boy from Shenzhen, the first pediatric COVID-19 patient, was asymptomatic but displayed ground-glass opacity on his initial computed tomography (CT)<sup>7)</sup>. In a study analyzed 10 laboratory-confirmed Chinese children in Shanghai, Hainan, Hefei, and Quindao between January 19 and February 3, 2020, the median age of patients was 74 months (range, 3-131 months). Fever was noted in 8 children, cough in 6, sore throat in 4, stuffy nose in 3, and rhinorrhea in 2 children. Fever ranged from 37.7-39.2°C and resolved within 24 hours. Patchy infiltrations on chest CT were observed in 4 patients. None of the 10 patients required oxygen therapy<sup>28)</sup>. Another study described 9 infants (age range, 1-11 months) in China outside of Hubei Province. Out of 7 infants who reported symptoms, 4 had fever, 2 had mild respiratory symptoms, and 1 was asymptomatic; no severe complication was noted<sup>29)</sup>.

In a study that enrolled 31 pediatric patients from 6 northern Chinese provinces from January 25 to February 21, 2020, there were 4 (12.9%) asymptomatic cases, 13 (41.9%) mild symptomatic with normal radiographic studies, 14 (45.2%) pneumonia, and no severe illness. Ten (32.3%) of the 31 patients complained of fever over 38°C, and 10 (32.3%) had a mild fever of 37.3-38°C. The fever lasted from 1 to 9 days and subsided within 3 days in 15 patients (75%). Fourteen (45.2%) had dry cough, 3 had fatigue, 3 had headache or dizziness, 2 had rhinorrhea, and 2 had sore throat. One of

the patients reported having sore throat only, and 3 patients initially presented with diarrhea without vomiting<sup>14</sup>).

So far, two studies have described chest CT findings of pediatric patients in detail<sup>30, 31</sup>. A study analyzed 15 pediatric COVID-19 cases admitted to a hospital in Shenzhen, China, between January 16 and February 6, 2020. The median age of patients was 7 years (range, 4 to 14 years). At diagnosis, 5 patients complained of fever, 1 had cough, 1 had nasal congestion, and 8 (53.3%) was asymptomatic. Leukocyte count was decreased in 8 (53.3%) and was in normal range in 7 children. At the time of diagnosis, the chest CT displayed ground-glass opacity in 9 (60%) and appeared normal in 6 patients. A follow-up CT after 3-5 days showed development of new inflammatory lesions with ground-glass opacity in 3 out of 9 patients whose SARS-CoV-2 polymerase chain reaction (PCR) continued to be positive. Of the 6 patients whose PCR converted negative, 2 patients showed improvement in chest CT findings<sup>30</sup>.

A study was conducted in 20 pediatric COVID-19 patients admitted to Wuhan Children's Hospital in China, from January 23 to February 8, 2020. The median age of the patients was 2.1 years (range, 1 day to 14.6 years) including 3 neonates. Thirteen patients complained of cough, 12 had fever over 37.3 °C, 3 had diarrhea, 3 had rhinorrhea, and 2 had tachypnea. Respiratory crackles were auscultated in 3 patients, chest retraction was observed in 1, and cyanosis was observed in 1 patient. Most of the patients presented with signs of pneumonia. Leukocyte count was within normal range in 14 (70%), decreased in 4 (20%), increased in 2 (10%) patients. Lymphocyte fraction was decreased in 7 (35%) and increased in 3 patients (15%). C-reactive protein was increased in 9 (45%), and procalcitonin was increased in 16 (80%) patients. Eight patients (40%) were coinfecting with influenza A or B virus, *Mycoplasma pneumoniae*, respiratory syncytial virus, or cytomegalovirus. The initial chest CT showed unilateral pulmonary lesions in 6 (30%), bilateral

pulmonary lesions in 10 (50%), and no abnormality in 3 neonates and 1 child (4/20, 20%). All 20 children displayed subpleural lesions with localized inflammatory infiltration; 10 (50%) cases showed consolidation with surrounding halo sign; 12 (60%) showed ground-glass opacity; 4 (20%) showed fine mesh shadow; 3 (15%) showed tiny nodules<sup>31</sup>).

The first severe pediatric case reported was a 13-month-old boy admitted to Wuhan Children's Hospital in January 27, 2020. He presented with pneumonia, shock, acute respiratory distress and renal failure at the time of admission. The patient did not have known medical comorbidity; he reported having been treated at local clinic for the past 6 days because of intermittent diarrhea and vomiting but denied having any respiratory symptoms. He showed fever, dyspnea, and oliguria at the time of admission and received intensive care including intubation and mechanical ventilation. After treatment, he recovered gradually<sup>32</sup>).

The largest-scale report on COVID-19 in children was on 134 patients whose clinical data was available out of 285 pediatric cases diagnosed in China by February 7, 2020. The most common symptoms were fever and cough; other clinical features included fatigue, myalgia, rhinorrhea, nasal congestion, sore throat, headache, dizziness, nausea, vomiting, abdominal pain, and diarrhea. Symptoms mostly resolved within a week. Among 117 children whose body temperatures were recorded, 89 (76.1%) patients had fever which lasted 1-2 days, up to 8 days. Complete blood counts were within normal range in most patients; 2 showed decreased leukocyte count; 1 showed slight decrease in lymphocyte count. C-reactive protein was normal or temporarily increased (>20mg/L in 3 patients). When classified by symptoms and chest radiologic findings in 134 cases, 9 (6.7%) patients were asymptomatic with normal chest radiograph, 87 (64.9%) had mild symptoms with normal chest radiograph, 36 (26.9%, including 7 subclinical patients) had pneumonia, and 2 (1.5%) were critically ill, both of whom were mechanically ventilated. One of the critically ill was

moderately malnourished and had a history of a cardiac surgery due to congenital heart disease, while the other had hydronephrosis and left renal stone. Out of 54 patients whose chest radiologic data was available, 38 displayed ground-glass opacity or exudative/infiltrative lesion—7 of whom were subclinical, 4 displayed increased pulmonary markings, and 12 showed no abnormality<sup>11)</sup>.

Aside to studies of clinical manifestations of COVID-19, there is a study analyzed pathogens retrieved from hospitalized children with respiratory infections during early COVID-19 outbreak in Wuhan, China. Among the 366 children ( $\leq 16$  years of age) admitted to three hospitals in Wuhan between January 7 and 15, 2020, 43 (11.7%) children were infected with influenza A or B, while 6 (1.6%) were infected with COVID-19. COVID-19 infected children were aged between 1 to 7 years. All 6 children had fever over  $39^{\circ}\text{C}$  (duration range, 3 to 11 days; median 6 days) and cough, and 4 of them had vomiting. Four of the patients showed pneumonia on chest CT. One patient, a 3-year-old who showed ground-glass opacity on chest CT, received intensive care including oxygen therapy. The median length of stay was 7.5 days (range, 5 to 13 days), and all patients recovered<sup>8)</sup>.

In summary, COVID-19 infected children most commonly present with fever, cough, and fatigue, along with nasal stuffiness, rhinorrhea, sputum, diarrhea, and headache. Patients may be afebrile or present with a mild fever; fever subsides within 1-2 weeks in most cases. Dyspnea and cyanosis can occur as the condition progresses usually after 1 week of the disease, accompanied by systemic symptoms, such as malaise or restlessness, poor feeding, bad appetite and decreased activity. Pneumonia may develop, and some cases rapidly progress and may fall into respiratory failure that cannot be corrected by conventional oxygen within 1–3 days. In severe cases, septic shock, metabolic acidosis and irreversible bleeding and coagulation dysfunction may occur<sup>33, 34)</sup>. Ground-glass opacity and subpleural lesions were commonly observed on chest CT<sup>30, 31)</sup>.

In Korea, a case report on the first COVID-19 pediatric patient is the only known academic

publication in children so far. A 10-year-old girl presented with a mild fever of 37.3 °C and scarce amount of sputum. She tested positive for COVID-19. On 4<sup>th</sup> day of symptom onset, her chest CT showed patchy nodular consolidations accompanied with ground-glass opacity. She did not require an antiviral therapy and recovered after supportive care<sup>22)</sup>.

### **Importance of managing COVID-19 infected children**

Numerous family clustering cases of COVID-19 have been reported in China. Of 1,836 cases occurred in Guangdong and Sichuan Province, 1,308 cases related to 344 clusters, most (78-85%) of which occurred in families. According to a preliminary study ongoing in Guangdong, China, the secondary attack rate within a household is estimated to be 3-10%<sup>6)</sup>. Children are primarily transmitted through household exposure, and 56-90% of infected children had an infected family member<sup>10, 11, 14, 28)</sup>.

Children are usually diagnosed with COVID-19 after an exposure to an infected adult within or outside of family circle; however, the source of infection could not be identified in some cases; in others, diagnosis of a child preceded that of an adult. A 3-month-old child confirmed with COVID-19 on January 26, 2020, in Hubei Province was hospitalized due to fever and was found to have a mild pneumonia on chest CT. At the time of diagnosis, his parents were asymptomatic with negative SARS-CoV-2 PCR results. After 7 days of hospitalization of the infant, his father complained of fever and fatigue, while his mother was asymptomatic; both of his parents showed signs of pneumonia on their chest CT and tested positive for SARS-CoV-2 PCR. It was undetermined whether incubation period was shorter in the infant than in the parents or the virus was transmitted from the infant to the parents<sup>9, 35)</sup>. In the first severe case of a 13-month-old who developed pneumonia, shock, acute respiratory distress, and renal failure, the source of infection could not be

identified. His parents had not been tested for COVID-19<sup>32)</sup>.

Influenza surveillance during the first two weeks of January 2020 in Wuhan City, in which COVID-19 outbreak originated, indicated that SARS-CoV-2 was detected in adults but not in children<sup>6)</sup>. In an analysis of 365 COVID-19 cases confirmed until February 5, 2020, in Shenzhen, China, the rate of infected children rapidly increased from 2% (before January 24) to 13% (between January 25 to February 5) ( $P < 0.001$ ). The possible reasons for this might be that exposure to SARS-CoV-2 was lower in children earlier in the course of outbreak. Or, children were less likely to be tested because of mild symptoms and signs especially in the setting of limited resources in the early phase of the outbreak<sup>36)</sup>.

Not much is known about the duration of viral shedding in children, and reported durations have varied widely across patients and samples. A 6-month-old infant diagnosed in Singapore on February 4, 2020, was asymptomatic but tested positive for SARS-CoV-2 PCR on a nasopharyngeal sample; his mother was previously confirmed to have COVID-19 pneumonia. The blood PCR sample turned positive for SARS-CoV-2 on hospital day 2, on which the patient had a fever of 38.5 °C that resolved immediately. A series of daily nasopharyngeal samples for PCR revealed that viral load presented as 1/cycle threshold peaked at the time of diagnosis and decreased over time. Negative conversion was achieved on hospital day 17. Stool PCR on hospital day 2 was negative but turned positive on day 9<sup>18)</sup>.

In a study that enrolled 10 Chinese children in Shanghai, Hainan, Hefei and Qingdao, symptoms appeared in a median of 6.5 days (range, 2 to 10) from the onset of illness in the index case. Patients tested positive for SARS-CoV-2 PCR of nasopharyngeal or throat swab 4-48 hours after the onset of symptoms, and negative conversion was seen in a median of 12 days (range, 6 to 22). Prolonged shedding of virus RNA in feces was observed for 18-30 days in 5 patients<sup>28)</sup>.

In summary, transmission of COVID-19 in children primarily occurs through contact with other adult patients, mainly through household exposure. On the other hand, direct transmission from a child to an adult has not been reported yet. However, it is suggested that children and adolescents may play a role as potential transmitters in community, based on the observation of prolonged detection of viral RNA in nasopharyngeal/throat swabs and feces of pediatric patients.

### **Considerations in pregnant women and newborns (Table 3)**

In the report of the WHO-China Joint Mission on COVID-19 patients diagnosed until February 20, 2020, pregnant women were not at a higher risk for severe COVID-19 infection. Of 147 (64 confirmed, 82 suspected and 1 asymptomatic) pregnant women investigated, 8% were severe with dyspnea and hypoxemia, and 1% was critical requiring intensive care<sup>6)</sup>. However, one of the most common infections during pregnancy except obstetric problem is pneumonia, which may lead to premature rupture of membrane, preterm labor, intrauterine growth retardation, and stillbirth<sup>37-39)</sup>. Sporadic case reports on COVID-19 infection in pregnant women observed obstetrical complications including stillbirth, preterm birth, and premature rupture of membrane<sup>40-43)</sup>. In a study of 9 COVID-19 infected pregnant women diagnosed in Wuhan, China, from January 20 to 31, 2020, all women were infected at gestational age 36 weeks or higher and delivered by caesarean section. Seven women complained of fever at the time of diagnosis, but none of them developed severe pneumonia that led to mechanical ventilation or death. Obstetrical complications included 4 preterm deliveries and 2 premature rupture of membranes; no neonatal asphyxia or stillbirth was observed. From 6 patients, amniotic fluid, cord blood, breast milk, and neonatal throat swab samples were tested for SARS-CoV-2, and all samples tested negative for the virus<sup>40)</sup>. A case report from Suzhou, China, describes a pregnant woman at gestational age 30 weeks. She was confirmed

with COVID-19 pneumonia on February 6, 2020, delivered a 1.83kg-weighted preterm baby with emergency caesarean section due to fetal distress. SARS-CoV-2 PCR was negative in amniotic fluid, placenta, cord blood, neonatal gastric juice, and neonatal throat swab<sup>41</sup>). A study analyzed 13 pregnant women with COVID-19 from December 8, 2019 to February 25, 2020 in mainland China outside of Wuhan, included 2 women in their second trimester. Ten women had fever, 3 had dyspnea, and 1 was asymptomatic. Of 13 women, 3 (23%) recovered and was discharged with uncomplicated ongoing pregnancy; ten delivered by caesarean section. Five women underwent emergency caesarean section due to fetal distress (3 cases), premature rupture of membrane (1 case), and stillbirth (1case). Six women had preterm labor. One of the women was confirmed at gestational age 34 weeks, developed acute respiratory distress syndrome and multiple organ failure requiring extracorporeal membrane oxygenation (ECMO) support, and delivered stillbirth<sup>42</sup>).

In a report of 10 neonates born to 9 COVID-19 infected mothers in Hubei, China, from January 20 to February 5, 2020, intrauterine distress was observed in 6 and premature rupture of membrane was observed in 3 patients. Six infants were born premature, 2 were small for gestational age, and 1 was large for gestational age. Clinical features of the newborns included shortness of breath (6 cases) and fever (2 cases). Two newborns developed thrombocytopenia complicated with abnormal liver function. One of the newborns was delivered at gestational age 34 weeks and 5 days, developed shock and multiple organ failure on day 8, and died on day 9. Nine of the newborns underwent SARS-CoV-2 PCR test on days 1 to 9, all of which turned out negative<sup>44</sup>). To date, there have been no reports of vertical transmission of SARS-CoV-2. However, existing reports are incomprehensive, because they are small in sample size and primarily dealt with COVID-19 infections occurred in third trimester, and not all pregnant women were tested for SARS-CoV-2 PCR. Continuous monitoring is needed to assess the possibility of mother-to-child transmission.

So far, 3 cases of COVID-19 confirmed neonates have been reported in Wuhan, China<sup>11, 12, 31, 45)</sup>. A neonate was diagnosed with COVID-19 at 36 hours after birth. His mother was at gestational age 40 weeks and developed a fever on February 1, 2020. Her chest CT displayed ground-glass opacities suggesting viral pneumonia. Emergency caesarean section was performed on the same day and the newborn did not have contact with the mother after birth. The mother's SARS-CoV-2 PCR report came out positive the next day. A pharyngeal swab was collected from the newborn at 36 hours after birth, which was later confirmed positive for SARS-CoV-2. However, cord blood, placenta, and breast milk were negative for SARS-CoV-2. The newborn was afebrile with no cough or vomiting, but his chest CT showed nodular shadow under the pleura on day 6. His chest CT showed small pieces of patchy shadows on day 12 and was improved on day 17. SARS-CoV-2 PCRs taken from pharyngeal and anal swabs on day 17 were negative and he was discharged on day 18<sup>12)</sup>. Another 5-day-old neonate with a fever was diagnosed with COVID-19, and his mother was confirmed as COVID-19<sup>11)</sup>. A 17-day-old newborn was hospitalized on February 5, 2020, complaining of sneezing and vomiting for one week. His parents had been confirmed with COVID-19 three days ago. His chest CT showed increased pulmonary markings and all symptoms resolved by hospital day 7<sup>45)</sup>. There are only a small number of neonatal COVID-19 infections reported, and infected neonates had mild or no symptoms. However, current data supports that neonates are susceptible to COVID-19, therefore special precautions including hand hygiene are required in having close contact with newborns.

## **Conclusion**

COVID-19 is a novel infectious disease that has been declared a pandemic. It is rapidly spreading throughout the globe, infecting and killing thousands of people. Limited information is

available on this previously unknown coronavirus that has been around less than 3 months. It is known that children take up a small fraction of COVID-19 cases, and symptoms in pediatric patients are often mild. However, some pediatric cases may progress to severe disease, and initial atypical presentations may delay the diagnosis of COVID-19, leading to unfavorable outcome. It is worth mentioning that newborns are susceptible to this disease and viruses are detected from them for a prolonged period, therefore newborns might play a role in community transmission. As of now, there is no standard of management or prevention. More investigation is needed to assess the reason for differences in clinical features of COVID-19 by age, to evaluate the role of children in community transmission, and to develop treatment and vaccines for the disease. We hope that current and future research on COVID-19 can answer the questions and we look forward to wisely coping with this crisis of all mankind.

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## **Conflict of Interest**

The authors have nothing to declare.

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## References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727-33.
2. World\_Health\_Organization. Situation Report 22 2020 [Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf>].
3. World\_Health\_Organization. Situation Report 51 2020 [Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf>].
4. Kim JY, Choe PG, Oh Y, Oh KJ, Kim J, Park SJ, et al. The First Case of 2019 Novel Coronavirus Pneumonia Imported into Korea from Wuhan, China: Implication for Infection Prevention and Control Measures. *J Korean Med Sci.* 2020;35(5):e61.
5. The Updates of COVID-19 in Republic of Korea, as of 11 March, 2020 [press release]. 2020.
6. WHO-China\_Joint\_Mission. Report of the WHO-China joint Mission on COVID-19. 2020 16-24 Feb 2020.
7. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395(10223):514-23.
8. Liu W, Zhang Q, Chen J, Xiang R, Song H, Shu S, et al. Detection of Covid-19 in Children in Early January 2020 in Wuhan, China. *N Engl J Med.* 2020.

9. Cao Q, Chen YC, Chen CL, Chiu CH. SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics. *J Formos Med Assoc.* 2020.
10. Fang F, Luo XP. Facing the pandemic of 2019 novel coronavirus infections: the pediatric perspectives. *Zhonghua Er Ke Za Zhi.* 2020;58(2):81-5.
11. Society\_of\_Pediatrics\_Chinese\_Medical\_Association, Editorial\_Board\_Chinese\_Journal\_of\_Pediatrics. Recommendations for the diagnosis, prevention and control of the 2019 novel coronavirus infection in children (first interim edition). *Zhonghua Er Ke Za Zhi.* 2020;58(3):169-74.
12. Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A case report of neonatal COVID-19 infection in China. *Clin Infect Dis.* 2020.
13. Novel\_Coronavirus\_Pneumonia\_Emergency\_Response\_Epidemiology\_Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2020;41(2):145-51.
14. Wang D, Ju XL, Xie F, Lu Y, Li FY, Huang HH, et al. Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China. *Zhonghua Er Ke Za Zhi.* 2020;58(4):E011.
15. New\_Straits\_Times. 3 coronavirus cases in Malaysia include 2-year-old boy [Available from: <https://www.nst.com.my/news/nation/2020/01/559584/3-coronavirus-cases-malaysia-include-2-year-old-boy>]. *New Straits Times.* 25 Jan 2020.
16. Current information on the corona virus situation in Bavaria - Bavarian Ministry of Health: 8th case confirmed - 33-year-old man from Munich [Available from: <https://www.stmgp.bayern.de/presse/aktuelle-informationen-zur-coronavirus-lage-in-bayern->

bayerisches-gesundheitsministerium-8/] [press release]. Feb 01 2020.

17. Singapore\_Government\_Agency. Coronavirus disease 2019: Cases in Singapore: A Singapore Government Agency Website; 2020 [Available from: <https://www.gov.sg/article/covid-19-cases-in-singapore>].

18. Kam KQ, Yung CF, Cui L, Lin Tzer Pin R, Mak TM, Maiwald M, et al. A Well Infant with Coronavirus Disease 2019 (COVID-19) with High Viral Load. *Clin Infect Dis*. 2020.

19. Ministry\_of\_Health\_Vietnam. Situation of diseases, COVID-19, 11 Feb 2020 2020 [Available from: <https://ncov.moh.gov.vn/web/guest/dong-thoi-gian>].

20. Italian\_National\_Institute\_of\_Health. COVID-19 Integrated Surveillance in Italy. 09 Mar 2020.

21. Covid-19\_National\_Incident\_Room\_Surveillance\_Team. COVID-19, Australia: Epidemiology Report 6 (Reporting week ending 19:00 AEDT 7 March 2020). *Commun Dis Intell* (2018). 2020;44.

22. Park JY, Han MS, Park KU, Kim JY, Choi EH. First Pediatric Case of Coronavirus Disease 2019 in Korea. *J Korean Med Sci*. 2020;35(11):e124.

23. Kim BG. 4-year-old becomes youngest COVID-19 patient [Available from: <http://www.koreaherald.com/view.php?ud=20200223000222>]. *The Korea Herald*. 2020 Feb 23.

24. Yonhap\_News\_Agency. 45-day-old baby infected with new coronavirus in S. Korea: authorities [Available from: <https://en.yna.co.kr/view/AEN20200301001500320>]. *Yonhap News Agency*. 2020 Mar 01.

25. Yonhap\_News\_Agency. 4 week old newborn baby was confirmed in Dongdaemun-gu,

Seoul: Probably the nation's youngest [Available at:

<https://www.yna.co.kr/view/AKR20200308073500004>]. Yonhap News Agency. 2020 Mar 08.

26. Korean\_Statistical\_Information\_Service. Registered population by administrative district / year-old, Feb 2020 2020 [Available from:

[http://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT\\_1B04006&conn\\_path=I2](http://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT_1B04006&conn_path=I2).

27. Korea\_Centers\_for\_Disease\_Control\_and\_Prevention. Pediatric COVID-19 patients in Korea [unpublished data]. 2020.

28. Cai J, Xu J, Lin D, Yang Z, Xu L, Qu Z, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clin Infect Dis*. 2020.

29. 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. *JAMA*. 2020.

30. Feng K, Yun YX, Wang XF, Yang GD, Zheng YJ, Lin CM, et al. Analysis of CT features of 15 Children with 2019 novel coronavirus infection. *Zhonghua Er Ke Za Zhi*. 2020;58(0):E007.

31. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. *Pediatr Pulmonol*. 2020.

32. Chen F, Liu ZS, Zhang FR, Xiong RH, Chen Y, Cheng XF, et al. First case of severe childhood novel coronavirus pneumonia in China. *Zhonghua Er Ke Za Zhi*. 2020;58(3):179-82.

33. Chen ZM, Fu JF, Shu Q, Chen YH, Hua CZ, Li FB, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. *World J Pediatr*. 2020.

34. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, et al. Diagnosis, treatment, and

prevention of 2019 novel coronavirus infection in children: experts' consensus statement. *World J Pediatr.* 2020.

35. Zhang YH, Lin DJ, Xiao MF, Wang JC, Wei Y, Lei ZX, et al. 2019-novel coronavirus infection in a three-month-old baby. *Zhonghua Er Ke Za Zhi.* 2020;58(0):E006.

36. Liu J, Liao X, Qian S, Yuan J, Wang F, Liu Y, et al. Community Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, Shenzhen, China, 2020. *Emerg Infect Dis.* 2020;26(6).

37. Benedetti TJ, Valle R, Ledger WJ. Antepartum pneumonia in pregnancy. *Am J Obstet Gynecol.* 1982;144(4):413-7.

38. Berkowitz K, LaSala A. Risk factors associated with the increasing prevalence of pneumonia during pregnancy. *Am J Obstet Gynecol.* 1990;163(3):981-5.

39. Madinger NE, Greenspoon JS, Ellrodt AG. Pneumonia during pregnancy: has modern technology improved maternal and fetal outcome? *Am J Obstet Gynecol.* 1989;161(3):657-62.

40. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.* 2020;395(10226):809-15.

41. Wang X, Zhou Z, Zhang J, Zhu F, Tang Y, Shen X. A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. *Clin Infect Dis.* 2020.

42. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect.* 2020.

43. Li Y, Zhao R, Zheng S, Chen X, Wang J, Sheng X, et al. Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China. *Emerg Infect Dis.* 2020;26(6).

44. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr.* 2020;9(1):51-60.

45. Zeng LK, Tao XW, Yuan WH, Wang J, Liu X, Liu ZS. First case of neonate infected with novel coronavirus pneumonia in China. *Zhonghua Er Ke Za Zhi.* 2020;58(0):E009.

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1 Figure legend

2 Fig. 1. Cumulative numbers of pediatric coronavirus disease 2019 in Korea, according to age groups.

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3 Table 1. Summary of studies on epidemiology of pediatric coronavirus disease 2019

Study area	China <sup>(10)</sup>	China <sup>(11)</sup>	China <sup>(13)</sup>	China <sup>(6)</sup>	Singapore <sup>(17)</sup>	Italy <sup>(20)</sup>	Australia <sup>(21)</sup>	Republic of Korea <sup>(5)</sup>
Study period	~ 31 Jan, 2020	~ 7 Feb, 2020	~ 11 Feb, 2020	~ 20 Feb, 2020	~ 11 Mar, 2020	~ 9 Mar, 2020	~ 7 Mar, 2020	~ 11 Mar, 2020
Total confirmed patients	11,791	34,546	44,672	55,924	167	8,342	71	7,755
Age and numbers (proportion) of children	1.5 months - 18 years, 74 (0.6%)	Pediatric (youngest: 36-hour-old), 285 (0.8%)	0-9 years, 416 (0.9%) 10-19 years, 549 (1.2%)	0-18 years, (2.4%)	6 months - 17 years, 6 (3.6%)	0-18 years, (1.4%)	0-9 years, 2 (2.8%) 10-19 years, 2 (2.8%)	0-9 years, 75 (1.0%) 10-19 years, 405 (5.2%)

4

5 Table 2. Summary of studies on clinical manifestations of pediatric coronavirus disease 2019

	Liu et al. <sup>(8)</sup> (n=6)	Cai et al. <sup>(28)</sup> (n=10)	Wei et al. <sup>(29)</sup> (n=9)	Wang et al. <sup>(14)</sup> (n=31)	Feng et al. <sup>(30)</sup> (n=15)	Xia et al. <sup>(31)</sup> (n=20)	Society of Pediatrics, Chinese Medical Association <sup>(11)</sup> (n=134)
Characteristics of the study and study area	Hospitalized children with acute respiratory infections in Wuhan, China	Outside Hubei in China: Shanghai, Hainan, Hefei, Qingdao	Infants outside Hubei in China: Beijing, Hainan, Guangdong, Anhui, Shanghai, Zhejiang, Guizhou	Outside Hubei in China: Shaanxi, Gansu, Ningxia, Hebei, Henan, and Shandong provinces	Shenzen, China	Wuhan, China (* includes 8 co-infections)	China (nationwide)
Study period	7 Jan - 15 Jan, 2020	19 Jan - 3 Feb, 2020	8 Dec 2019 - 6 Feb 2020	25 Jan - 21 Feb, 2020	16 Jan - 6 Feb, 2020	23 Jan - 8 Feb, 2020	- 7 Feb, 2020
Sex, male (%)	2 (33.3%)	4 (40.0%)	2 (22.2%)	15 (48.4%)	5 (33.3%)	13 (65.0%)	
Age, median (range)	3 years (1-7)	6.2 years (0.3-10.9)	0.6 years (0.2-0.9)	7.1 years (0.5-17)	7 years (4-14)	2.1 years (1 day-14.6 years)	Youngest: 36-hour-old
Clinical classifications			NA			NA	
1) Asymptomatic	0 (0.0%)	0 (0.0%)		4 (12.9%)	0 (0.0%)		9 (6.7%)
2) Acute upper respiratory tract infection	2 (33.3%)	6 (60.0%)		13 (41.9%)	3 (20.0%)		87 (64.9%)
3) Mild pneumonia	3 (50.0%)	4 (40.0%)		14 (45.2%)	12 (80.0%)		36 (26.9%)
4) Severe pneumonia	1 (16.7%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)
5) Critical case	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		2 (1.5%)

Clinical symptoms			7 available				117 available
Fever	6 (100.0%)	8 (80.0%)	4 (57.1%)	20 (64.5%)	5 (33.3%)	12 (60.0%)	89 (76.1%)
Cough	6 (100.0%)	6 (60.0%)	2 (28.6%)	14 (45.2%)	1 (6.7%)	13 (65.0%)	NA
Rhinorrhea/Sneezing	1 (16.7%)	2 (20.0%)	1 (14.3%)	2 (6.5%)	NA	3 (15.0%)	NA
Sore throat	NA	4 (40.0%)	NA	2 (6.5%)	NA	1 (5.0%)	NA
Headache/Dizziness	NA	NA	NA	3 (9.7%)	NA	NA	NA
Diarrhea	NA	0 (0.0%)	NA	3 (9.7%)	NA	3 (15.0%)	NA
Dyspnea/Tachypnea	1 (16.7%)	0 (0.0%)	NA	0 (0.0%)	NA	2 (10.0%)	NA
Laboratory findings			NA		NA		NA
Lymphopenia	6 (100.0%)	0 (0.0%)		2 (6.5%, 2/31)		7 (35.0%)	
Elevated C-reactive protein	5 (83.3%) (>10 mg/L)	3 (30.0%) (>8.0 mg/L)		3 (10.0%, 3/30)		(<45%)	
Abnormal liver enzymes	4 (66.7%)	2 (10.0%) (AST >40 U/L)		6 (22.2%, 6/27)		7 (35.0%) (>3 mg/L)	
						5 (25.0%) (ALT >40 IU/L)	
Chest computed tomography finding	5 available	NA	NA	30 available			54 available
Normal	1 (20.0%)			16 (53.3%)	6 (40.0%)	4 (20.0%)	12 (22.2%)
Abnormal	4 (80.0%)			14 (46.7%)	9 (60.0%)	16 (80.0%)	42 (77.8%)
	- 3 patchy shadows in both lungs			- 9 patchy ground glass shadows and nodules	- 9 ground glass opacities	- 10 consolidation with surrounding halo sign	- 38 ground-glass or exudative/invasive lesions
	- 1 patchy ground-glass opacities in both lungs					- 12 ground-glass opacities	- 4 increased pulmonary markings
						- 4 fine mesh shadow	
						- 3 tiny nodules	

6 Abbreviation: ALT, alanine transaminase; AST, aspartate transaminase; NA, not available

7 Table 3. Summary of studies on perinatal coronavirus disease 2019

	Chen et al. <sup>(40)</sup>	Liu et al. <sup>(42)</sup>	Zhu et al. <sup>(44)</sup>
Study area	Wuhan, China	Outside Wuhan, China	Hubei province, China
Number of pregnant women cases (laboratory-confirmed SARS-CoV-2)	9	13	9
Number of births	9	10	10
Study period	20 Jan ~ 31 Jan, 2020	8 Dec 2019 ~ 25 Feb, 2020	20 Jan ~ 5 Feb, 2020
Maternal age (median years with range)	28 (26-40)	30 (22-36)	30 (25-35)
Gaestational age (median weeks, with range)	37w 2d (36w – 39w 4d)	35w (25w – 38w 3d)	34w 6d (31w – 39w)
Maternal severe pneumonia	0 (0.0%)	1* (7.7%)	NA
Discharge without complication before delivery	0 (0.0%)	3 (23.1%)	0 (0.0%)
Delivery related information			
Caesarean section	9 (100.0%)	10 (100.0%)	7 (77.8%)
Preterm labour/delivery	4 (44.4%)	6 (60.0%)	6 (66.7%)
Fetal distress	2 (22.2%)	3 (30.0%)	6 (66.7%)
Premature rupture of the membrane	2 (22.2%)	1 (10.0%)	3 (33.3%)
Stillbirth	0 (0.0%)	1* (10.0%)	0 (0.0%)
Neonatal asphyxia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Postnatal death	0 (0.0%)	0 (0.0%)	1† (10.0%)

8 Abbreviations: NA, not available

9 \*The mother's condition deteriorated during hospitalization, requiring mechanical ventilation with extracorporeal membrane oxygenation (ECMO)

10 support.

11 †The neonate died of refractory shock and gastric bleeding.

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