

Coronavirus disease 2019 in children: Current status

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Abstract: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged from China in December 2019. The outbreak further exploded in Europe and America in mid-March 2020 to become a global health emergency. We reviewed recent published articles and on-line open messages on SARS-CoV-2-positive infants and children younger than 20 years of age. Symptoms are usually less severe in children than in adults. Twelve critically or mortally ill children were found in the published or news reports before April 6, 2020. Vertical transmission from the mother to her fetus or neonate has not been proven definitively. However, six early-onset (<7 days) and 3 late-onset neonatal SARS-CoV-2 infections were found in the literature. We also summarized the presentations and contact information of 24 SARS-CoV-2-positive children announced by the Taiwan Centers for Disease Control. Early identification and isolation, adequate management, prevention, and vaccine development are the keys to controlling the disease spread. Clinical physicians should be alert to asymptomatic children with COVID-19. Multidirectional investigations are crucial in the global fight against COVID-19.

Keywords: Adult; Coronavirus; COVID-19; Global health; Infant; Taiwan

1. COVID-19 PANDEMIC

Acute respiratory dysfunction caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially noted by alert physicians in Wuhan, China. It then turned out to cause serious endemic and epidemic pneumonia with rapid deterioration to acute respiratory distress syndrome (ARDS) with high mortality in complicated patients. The first case was identified on December 8, 2019, and this disease was initially reported by China to the World Health Organization (WHO) on December 31, 2019.^{1,2} On March 11, 2020, the WHO characterized this coronavirus disease 2019 (COVID-19) as a global pandemic because of the rapidly increasing numbers of infected cases throughout countries in Europe and America, and the confirmed case numbers reached more than 125 000 cases.³

From December 2019 to February 2020, the highest confirmed case number was in Hubei, China, followed by a gradually increasing number in Asia. In the beginning of February, an outbreak on the cruise ship Diamond Princess off the coast of Japan occurred. A total of 619 of 3700 passengers and crew (17%) tested SARS-CoV-2-positive by February 20, 2020.⁴ Subsequently, an explosive outbreak started from a religious group in the end of February 2020, and the Republic of Korea

temporarily became into the second largest confirmed COVID-19 country after China on March 2, 2020.⁵

Since early March 2020, the confirmed case number has increased rapidly in Italy and Iran, and subsequently in many other countries of Europe and America. Importantly and disconcertingly, the pattern of confirmed cases and deaths has shown a terrible and exponential increase since the middle of March (Fig. 1) around the world.³ At 16:56 (Taipei time) on April 7, 2020, the report of the confirmed COVID-19 case number in the world reached to 1 350 841 with 74 870 deaths in 184 countries/regions. The overall case fatality rate (CFR) reached to 5.5%.³ The United States became the country with the highest number of confirmed COVID-19 cases (n = 368 449; deaths = 10 993; CFR = 3.0%), followed by Spain (n = 136 675; deaths = 13 341; CFR = 9.8%).⁶ The highest CFR remained at 12.5% in Italy (n = 132 547; deaths = 16 523).⁶ China remained with the highest number of confirmed cases in Asia during the past 3 months (n = 82 697; deaths = 3335; CFR = 4.0%). Fighting COVID-19 has become a true war of saving human lives all over the world.

2. INITIAL PRESENTATIONS OF COVID-19

Fever and cough seem to be the most common initial symptoms in SARS-CoV-2-positive patients, followed by dyspnea and fatigue in cases with severe pneumonia. In a recent systematic review by Rodriguez-Morales et al,⁷ a total of 19 original articles and 39 separate case reports from January and February, including 656 confirmed COVID-19 patients, were analyzed. These cases were reported from 39 countries/regions, and most of the cases were from China in that period of time. The top three symptoms of these confirmed COVID-19 cases were fever (88.7%), cough (57.6%), and dyspnea (45.6%). Among them, 20.3% required intensive care, and the CFR of these hospitalized COVID-19 patients was 13.9%.⁷ In another meta-analysis by Yang et al⁸ on the cases of China, they analyzed eight studies with a total of 46 248 infected patients and demonstrated that the most prevalent clinical symptoms were fever (91% ± 3%,

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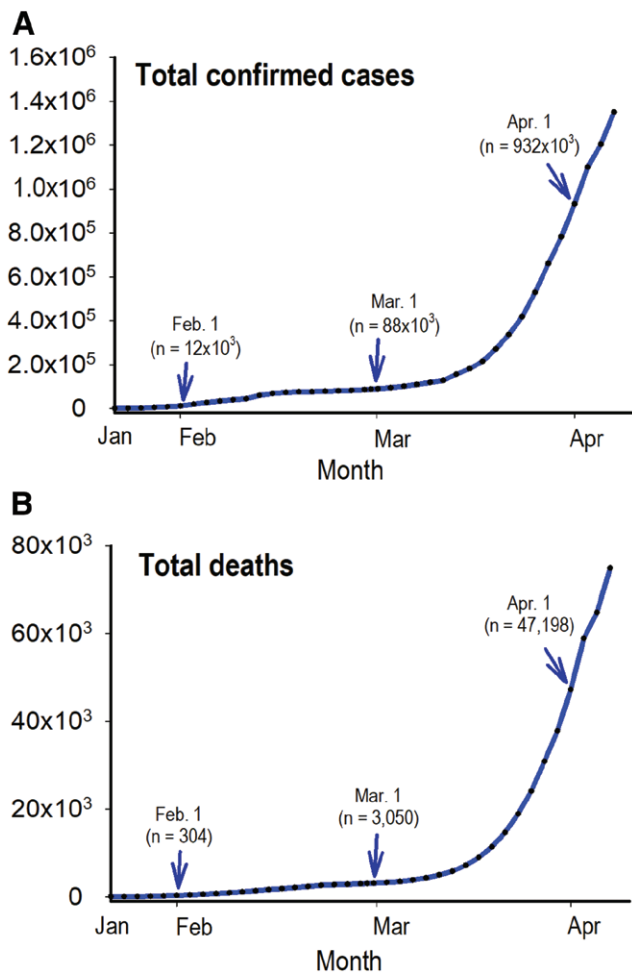


Fig. 1 Cumulative numbers of confirmed COVID-19 cases and deaths. The numbers of confirmed COVID-19 cases (A) and deaths (B) are from 181 countries or regions in the world from January 22 to April 5, 2020. Data for drawing graphs are retrieved from the website of Coronavirus Resource Center of Johns Hopkins University (<https://coronavirus.jhu.edu/map.html>). COVID-19, coronavirus disease 2019.

95% CI, 86%–97%), cough (67% ± 7%, 95% CI, 59%–76%), fatigue (51% ± 0%, 95% CI, 34%–68%), and dyspnea (30% ± 4, 95% CI, 21%–40%).⁸ The findings were similar in these two studies.

Other symptoms, including sore throat, rhinorrhea, stuffy nose, muscle aches, muscle soreness, headache, vomiting, and diarrhea, are also observed in the beginning of the disease.^{2,7,8} Additionally, loss of smell (anosmia) and/or taste (ageusia) has been noted in younger patients since March 2020.⁹ These symptoms were rarely mentioned in the early cases in China, but they were frequently mentioned in young people living in or traveling back to their countries from Europe or America.¹⁰

A proportion of SARS-CoV-2–infected people are completely asymptomatic. According to the report based on the passengers on board the Diamond Princess cruise ship, the estimated asymptomatic proportion was as high as 17.9%.¹¹ In one report of childhood cases, 94/731 (12.9%) SARS-CoV-2–positive children had no symptoms according to nucleic acid tests, and more than 70% of them were between the ages of 6 and 15 years.¹² The proportion of asymptomatic subjects may be underestimated because many potentially infected people do not receive a SARS-CoV-2 test when they have no symptoms. However, asymptomatic carriers have the potential to transmit the coronavirus that causes COVID-19.¹³ It has been proposed that up

to 80% of infected people are asymptomatic carriers.¹⁴ Further investigations should be carried out to clarify this issue regarding the prevalence of asymptomatic carriers.

3. COMMON PRESENTATIONS OF COVID-19 IN CHILDREN

Regarding children, they were relatively rarely diagnosed at the beginning of COVID-19's presence in the world. It was initially thought that children may be less susceptible to COVID-19.¹⁵ In one report by Wu and McGoogan² enrolling cases from December 8 to February 20, 2020, only 1% of teenagers and 1% of children younger than 10 years old in China were affected.² In a recent report from United States up to March 16, 2020, no intensive care unit (ICU) admissions or deaths among persons aged ≤19 years were reported among a total of 4226 confirmed COVID-19 cases. The authors summarized that the risk for serious disease and death from COVID-19 is higher in older age groups, in close agreement with other reports.¹⁶

However, more and more young people have been diagnosed along with the pandemic progression of the disease and the development of rapid COVID-19 testing techniques. Currently, we know that young people also can be seriously affected by SARS-CoV-2.^{5,17}

Most children became infected after close contact with confirmed COVID-19 patients, either family or other members of the public. Some of them had travel histories to epidemic regions. The published reports in children with COVID-19 are summarized in Table 1, and most of the publications analyzed cases from China before April 2020.^{12,18–23} In Vietnam, one 3-month-old infant was reported.²¹

As shown, fever is the most common initial symptom in children, followed by dry cough.^{12,18–23} Other symptoms of the respiratory tract, gastrointestinal tract, muscle and nervous system, and fatigue were all reported, but some infected children are completely symptom free.^{12,18,20,23}

In moderate to severe cases, dyspnea and hypoxia could occur and require various types of respiratory support. ARDS and life-threatening multiple organ failure had been reported in a few critical cases.¹²

4. CRITICAL CASES AND MORTALITY IN CHILDREN AND INFANTS WITH COVID-19

Even though most infected children have mild symptoms, SARS-CoV-2–infected children might still become severely ill.²⁵ The recent published and unpublished reports of critical children and infants are summarized in Table 2. As shown, most of current published cases are from China, and infants and teenagers are common subjects in all published and unpublished critical cases.^{12,20,22,23,26–30}

In the published reports from 10 hospitals across Hubei province of China, two of 25 (8%) SARS-CoV-2–positive children were critical and required intubation.²² In the report of the Wuhan Children's Hospital, 3 of 171 (1.8%) SARS-CoV-2–positive children required intubation.²⁰ These three children were described in detail together with five other severe cases aged 2 months to 15 years.²³ Septic shock and multiorgan dysfunctions were found in these critically ill children and infants, including the nervous, blood, urinary, and cardiac systems.²³ All of above-mentioned children or infants had underlying diseases. Among them, one 10-month-old female infant died of multiorgan failure.²³ Additionally in China, one 14-year-old boy with COVID-19 who died on February 7, 2020, was mentioned among 731 confirmed children (CFR = 0.14%), but there was no detail description.¹² To summarize this information, severe or critical cases occurred more often in small children, and the

Table 1**Published reports on SARS-CoV-2-positive children and infants up to April 6, 2020**

Country	First Author	Journal	Case no.	Age, y	Major initial symptoms	Critical/mortality
China ¹²	Dong	<i>Pediatrics</i>	731	0–17	Various (fever, cough, etc)	3 ^a /1
China ²⁰	Lu	<i>N Engl J Med</i>	171	0–15	Cough, fever	3 ^a /0
China ¹⁹	Qiu	<i>Lancet Infect Dis</i>	36	0–16	Fever, cough, hypoxia	0/0
China ²²	Zheng	<i>Curr Med Sci</i>	25	0–14	Fever, cough	2/0
China ¹⁸	Feng	<i>Chin J Pediatr</i> ^b	15	4–14	Fever	0/0
China ²³	Sun	<i>World J Pediatr</i>	8 ^c	0–15	Fever, cough	3 ^a /1
Vietnam ²¹	Le	<i>Lancet Child Adolesc Health</i>	1	0 ^d	Fever, rhinorrhea, stuffy nose	0/0
Korea ⁵	KSID ^e	<i>J Korean Med Sci</i>	201	0–19	NM	NM
United States ²⁴	f	<i>MMWR Morb Mortal Wkly Rep</i>	2572 ^g	0–17	Fever, cough, shortness of breath	15/3

NM = not mentioned; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

^aThese three critical cases are the same cases.

^bSame as "Zhonghua Er Ke Za Zhi."

^cIncluded severe and critical cases.

^d3 mo old.

^eKorean Society of Infectious Disease.

^fUS CDC COVID-19 Response Team.

^gThe total COVID-19 children number is 2572, but only 745 cases had records of information on hospitalization status.

Table 2**Published and unpublished critical or mortality cases in children and infants before April 6, 2020**

Country	Journal	Age, y	Gender	Underlying disease	Condition
China ²²	<i>Curr Med Sci</i>	0 (8 mo)	M	CHD and suspected metabolic disease	C
China ²²	<i>Curr Med Sci</i>	1	M	CHD	C
China ^{20,23}	<i>N Engl J Med</i> <i>World J Pediatr</i>	1	M	Hydronephrosis	C
China ^{20,23}	<i>N Engl J Med</i> <i>World J Pediatr</i>	8	M	Leukemia	C
China ^{20,23}	<i>N Engl J Med</i> <i>World J Pediatr</i>	0 (10 mo)	F	Intussusception	M
China ¹²	<i>Pediatrics</i>	14	M	NM	M
Belgium ²⁶	<i>News</i> ^a	12	F	NM	M
United Kingdom ²⁶	<i>News</i> ^a	13	M	NM	M
France ²⁷	<i>News</i> ^a	16	F	NM	M
United States ²⁸	<i>News</i> ^a	0 (6 wk)	?	NM	M
Japan ²⁹	<i>News</i> ^a	0 (8 mo)	F	NM	C
United Kingdom ³⁰	<i>News</i> ^a	5	?	NM	M

C = critical and requiring intubation; CHD = congenital heart disease; M = mortality; NM = not mentioned.

^aUnpublished data, only reported on the web site as a news.

prevalence seemed to be less than 10% among infected children. The CFR was less than 1% in SARS-CoV-2-positive children and infants according to current reports.

In the end of March and the beginning of April 2020, there was a little unpublished data regarding the death or critical condition of a few children and infants (Table 2).^{26–30} In the United States, one 6-week-old infant was brought unresponsive to a hospital and died after resuscitation.²⁸ On April 2, 2020, in Japan, one 8-month-old female infant was brought to hospital in out-of-hospital cardiac arrest (OHCA) status.²⁹ Both of them were thereafter identified as SARS-CoV-2-positive cases according to the news. These cases remind first-line physicians to take strong precautions while resuscitating any children, especially those with sudden collapse or OCHA. Additionally, four other SARS-CoV-2-positive children's deaths appeared on the news, including those of three teenagers (Table 2).^{26,27,30} Official reports should be obtained soon to confirm this information.

5. SARS-COV-2-POSITIVE CHILDREN IN CHINA

The Chinese Center for Disease Control and Prevention (China CDC) recently published the largest case series of COVID-19

up to February 11, 2020, in mainland China.² Of the confirmed 44 672 SARS-CoV-2-positive cases, 549 (1.2%) cases were aged 0–19 years (549 cases), and 416 (0.9%) cases were younger than 10 years of age.² Thus, the overall proportion of children among SARS-CoV-2-positive cases was 2.2%.

Dong et al¹² reported 2143 suspected COVID-19 children younger than 18 years of age by analyzing data from the China CDC by February 8, 2020. One third (n = 731) of them were SARS-CoV-2 positive, and all ages could be susceptible to COVID-19. The median age of confirmed case was 10 years, and the interval from symptom onset to diagnosis was 3 days.¹² The authors mentioned that the clinical manifestations of pediatric patients were relatively less severe than those of adult patients. Infants accounted for 11.8% of confirmed children.¹² Among these 731 confirmed cases, three kids progressed critical condition, and one 14-year-old boy died.¹² The proportion of critical deterioration or mortality in SARS-CoV-2-positive case was 0.5%.

Lu et al²⁰ summarized 171 SARS-CoV-2-positive children (0–15 years old) who were identified in Wuhan Children's Hospital up to February 26, 2020. Among them, the median age of confirmed diagnosis was 6.7 years old. Among them, 111

cases (64.9%) got image-detectable pneumonia, and 27 (15.8%) children were free from any symptoms. Specifically, 31 (18.1%) infants were identified as COVID-19–confirmed cases. The most common radiographic findings on chest computed tomography were bilateral ground glass opacity (32.7%), and some cases only had patchy or interstitial infiltration.

Some other reports described 8–36 children from different views (Table 1).^{18,19,22,23} Summarizing these reports, the top common initial symptoms of SARS-CoV-2–positive children were fever and cough, especially dry cough. None of these publications mentioned the symptom of loss of smell or taste.

6. SARS-COV-2-POSITIVE CHILDREN IN THE REPUBLIC OF KOREA

According to the official report of the Korean Society of Infectious Diseases, the Republic of Korea reported their first SARS-CoV-2–positive case on January 19, 2020. After the explosive outbreak in the city of Daegu and Gyeongsangbuk-do, the Republic of Korea became the country with the second largest number of confirmed cases ($n = 4212$) after China ($n = 80026$) on March 2, 2020.⁵ Among these reported cases, there were 32 (0.8%) children aged 0–9 years and 169 (4.0%) cases aged 10–19 years, accounting for 4.8% of all SARS-CoV-2–positive cases.⁵

Their first SARS-CoV-2–positive child was announced on February 19, 2020. The 10-year-old girl had close contact history with her mother and uncle, who were SARS-CoV-2–positive cases. The girl only had mild pneumonia without the need for specific management.^{5,31} A 45-day-old male infant, the youngest case in Korea, was identified on March 2. He had close contact with his SARS-CoV-2–positive father.⁵

Up to March 10, 2020, based on published reports, no critical complications or mortality in pediatric patients was reported in the Republic of Korea.³²

7. SARS-COV-2-POSITIVE CHILDREN IN THE UNITED STATES

The first pediatric COVID-19 case was reported to US CDC on March 2, 2020.²⁴ According to the early published report enrolling data from February 12 to March 16, 2020 in the United States, a total of 4226 COVID-19–confirmed cases were reported. Among 2449 hospitalized patients with known age, only 5% of them aged 0–19 years, and no ICU admissions or deaths were reported in this aged group during that period of time.¹⁶

Since the number of confirmed COVID-19 cases in the United States has risen rapidly since mid-March 2020, the “CDC COVID-19 Response Team” recently further reported 2572 (1.7%) laboratory positive children (<18 years old) among 149080 confirmed cases from February 12 to April 2, 2020, in the United States.²⁴ Their median age was 11 years. The proportions at age of 15–17, 10–14, 5–9, 1–4, and < 1 years are 32%, 27%, 15%, 11%, and 15%, respectively. Among them, more than 90% had an exposure history to other confirmed COVID-19 cases.²⁴ Characteristic COVID-19 symptoms of fever, cough, or shortness of breath were observed in 73% of infected children. The hospitalization rate was 19.7% (147/745), and ICU admission rate was 2% (15/745) among COVID-19 children in the United States. Infants (<1 year old) accounted for the highest percentage (59/95, 62%) of hospitalizations and ICU (5/59, 8.5%) admissions. Additionally, 77% (28/37) hospitalized COVID-19 children had underlying conditions, and there was a total of three deaths (0.4%) in COVID-19 children in the United States up to April 2, 2020.²⁴

8. SARS-COV-2-POSITIVE CHILDREN IN TAIWAN

In Taiwan, the first case was confirmed and announced on January 17, 2020.³³ Up to April 7, a total of 376 cases were confirmed by Taiwan Centers for Disease Control (TCDC), and five adult cases died (1.3%). Among confirmed cases, 24 (6.4%) cases are younger than 20 years old, and only four cases (1.7%) were younger than 10 years of age. Most of the children and teenagers (20, 83.3% of infected children) had travel history to European or American locations (Table 3). Four other children all had definite direct or indirect contact histories with someone who had travelled back from other countries.

Among the 24 children and teenagers, only one 11-year-old boy (4.2%) was completely asymptomatic (Table 3). Fever ($n = 17$, 70.8%), cough ($n = 9$, 37.5%), and headache ($n = 6$, 25.0%) were the top three symptoms, especially in teenagers. Loss of smell and/or taste were found in three (12.5%) teenagers. One of them just travelled back from Spain, and the other two cases had travelled back from the United Kingdom. In the four reported preschool children, fever was the only presentation when they were diagnosed. According to the statement of the TCDC, there was no mortality among these children and teenagers.

All information on these SARS-CoV-2–positive children listed in Table 3 were obtained from the daily announcement of the TCDC.^{10,34} Until April 7, 2020, no infants or neonates had been identified in Taiwan.

9. SARS-COV-2-POSITIVE NEWBORNS

During infectious disease outbreaks, fetuses and newborn infants are the most susceptible. Perinatal SARS-CoV-2 infection may induce fetal distress, premature labor, and neonatal illness, such as respiratory distress, viral sepsis, multiorgan involvement, and even death. However, there is still no definite evidence of vertical transmission from a SARS-CoV-2–infected pregnant mother to her fetus or newborn infants to date.

Some investigators have reported on their experiences with SARS-CoV-2–positive pregnant mothers and their newborn infants.^{35–39} According to these publications, cesarean sections are usually the delivery method of choice when the mother has symptomatic COVID-19. Most of the reports regarding specimens collected from amniotic fluid, cord blood, neonatal throat swabs, or breastmilk samples revealed that nearly all were negative for SARS-CoV-2.^{36–40}

However, early-onset (<7 days) neonatal COVID-19 was found in a few neonates born to SARS-CoV-2–positive mothers (Table 4). Zeng et al³⁵ reported three SARS-CoV-2–positive neonates born to mothers with confirmed COVID-19 (Table 4).³⁴ All three of these confirmed babies were symptomatic, including fever, lethargy, respiratory distress, and pneumonia on chest images. Their nasopharyngeal and anal swabs were positive for SARS-CoV-2 on days 2 and 4 and negative on day 6 or 7. Additionally, both Lu and Shi¹⁷ and Yu et al⁴¹ also reported a total of three infected neonates born from infected mothers, and they were positive for SARS-CoV-2 tests at the ages of 30 hours, 36 hours, and 5 days after birth. Therefore, the possibility of vertical transmission from an infected mother cannot be completely excluded. Additionally, late-onset (≥ 7 days) neonatal COVID-19 was reported in three neonates between the ages of 15 and 19 days. The infectious sources included their infected mothers ($n = 2$) and a housemaid (Table 4).^{42–44} Close contact with infected persons after birth is the most probable transmission route of these late-onset neonatal COVID-19 cases. All of these reported SARS-CoV-2–positive neonates recovered after management.

Table 3

SARS-CoV-2-positive children and teenagers younger than 20 years old in Taiwan from January 10 to April 7, 2020^{10,34}

Case	TCDC case no	Onset date	Confirmed date	Age, y	Gender	Symptom	Travel	Contact source (country)
1	31	NA	2/25	11	M	None	N	Taiwan ^a
2	59	3/12	3/15	10–19	M	Cough, sorethroat, rhinorrhea, headache	Y	Greece
3	103	3/15	3/19	10–19	M	Fever, sorethroat	N	Taiwan ^b
4	114	3/17	3/20	10–19	M	Headache, stuffy nose, painful eyes	Y	Spain, United Kingdom, Germany
5	130	3/17	3/20	10–19	F	Cough	N	Taiwan ^b
6	133	3/18	3/20	10–19	F	Fever, rhinorrhea, headache	Y	United Kingdom
7	156	3/12	3/22	10–19	F	Fever, cough, headache, muscle soreness	Y	United States
8	167	3/19	3/22	10–19	M	Fever, cough, fatigue	Y	United Kingdom
9	175	3/10	3/23	4	M	Fever	Y	The Netherlands
10	205	3/21	3/24	5	F	Fever	Y	Turkey
11	215	3/23	3/24	10–19	F	Fever, cough, muscle soreness	Y	United States
12	217	3/20	3/25	10–19	M	Rhinorrhea	Y	United Kingdom
13	230	3/22	3/25	10–19	F	Fever	Y	United States
14	231	3/22	3/25	10–19	F	Fever, sorethroat, headache	Y	United States
15	265	3/12	3/27	10–19	F	Fever	Y	United States
16	276	3/18	3/28	10–19	F	Stuffy nose, rhinorrhea, loss of smell	Y	Spain
17	279	3/20	3/28	10–19	F	Fever, cough	Y	Spain
18	281	3/20	3/28	10–19	F	Fever, cough	Y	Spain
19	292	3/22	3/29	10–19	F	Fever, cough, headache, cold sweating	Y	United States
20	297	3/23	3/29	10–19	M	Fever, cough, sorethroat, fatigue, muscle ache, muscle soreness, stuffy nose, rhinorrhea, headache	Y	France
21	299	3/26	3/30	5	M	Fever	N	Taiwan ^c
22	332	3/25	4/2	10–19	M	Fever, loss of smell and taste	Y	United Kingdom
23	337	3/26	4/2	10–19	M	Sorethroat, diarrhea, loss of smell and taste	Y	United Kingdom
24	365	3/25	4/6	4	M	Fever	N	Taiwan ^d

Data are retrieved from the daily report of TCDC. The total confirmed case number reported by TCDC was 376 on April 7, 2020.

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TCDC = Taiwan Centers for Disease Control.

^aClose contact to SARS-CoV-2-positive family members (TCDC case numbers: 27–30), and someone traveled back from China.

^bClassmate of a SARS-CoV-2-positive teenager (TCDC case number: 59) who traveled back from Greece.

^cClose contact to a SARS-CoV-2-positive family member who contacted to another SARS-CoV-2-positive case (back from Philippine) (TCDC case number: 277).

^dClose contact to SARS-CoV-2-positive family members (TCDC case numbers: 343, 356), and one of them traveled back from the United States.

Table 4

Published reports on SARS-CoV-2-positive newborns before April 2020

Country	First author	Journal	Diagnostic time after birth	Gestations, wk	Birth weight, g	Major symptoms	Contacted COVID-19 patient ^a
Early-onset (<7 d)							
China ³⁵	Zeng	<i>JAMA Pediatr</i>	1 d	40	3250	Fever, lethargy, pneumonia	Mother
			1 d	40	3360	Fever, lethargy, vomiting, pneumonia	Mother
			1 d	31	1580 ^b	RDS, pneumonia, bacteremia	Mother
China ⁴¹	Yu	<i>Lancet Infect Dis</i>	1 d (36 h)	39	3250	Respiratory distress	Mother
China ¹⁷	Lu	<i>J Med Virol</i>	1 d (30 h)	NM	NM	Asymptomatic	Mother
			5 d	NM	NM	Fever	Mother
Late-onset (≥7 d)							
China ⁴²	Zeng	<i>Chin J Pediatr^c</i>	17 d	39	4070	Fever, cough, vomiting	Housemaid
China ⁴³	Wang	<i>Chin J Contemp Pediatr^d</i>	19 d	38	3030	Vomiting and milk refusal	Mother
Iran ⁴⁴	Kamali Aghdam	<i>Infect Dis (Lond)</i>	15 d	Full-term	3460	Fever, lethargy, cutaneous mottling, and respiratory distress	Mother

COVID-19 = coronavirus disease 2019; NM = not mentioned; RDS = xxx; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

^aContacted SARS-CoV-2-positive case.

^bRequired endotracheal intubation and ventilation.

^cSame as "Zhonghua Er Ke Za Zhi."

^dSame as "Zhongguo Dang Dai Er Ke Za Zhi."

10. FUTURE PROSPECTS TO FIGHT COVID-19 IN CHILDREN AND INFANTS

Children are not free from COVID-19. Everybody has the

possibility of getting the illness after coming into contact with someone carrying SARS-CoV-2, including children of any age. Although current published reports reveal that children develop

less severe cases of COVID-19 than adults, critical deterioration or death did occur. Asymptomatic children are not tested usually for SARS-CoV-2 in many countries, so the prevalence of infected children is underestimated in the current reported data.

Usually, younger children take part in fewer daily social activities than teenagers, and their contact opportunities with carriers or patients should thus be lower, resulting in a lower risk of getting the COVID-19 illness. Although not as prevalent as those of 20- to 30-year-old adults, the social activities of teenagers, including international travelling, are still eventful. That may partly explain why the number of confirmed COVID-19 cases in teenagers is much higher than that in small children, according to data from the TCDC. In infancy and toddlerhood, the major contacts of small children are further narrowed to their family and caregivers, and thus their COVID-19 incidence seems to be the lowest. Nevertheless, we still need to monitor all children carefully when the COVID-19 pandemic is under today's explosive outbreak in many countries.

In comparison with adults, children with COVID-19 were deemed to have milder illness and a better prognosis.⁴⁵ Although most of the originally healthy children with COVID-19 are mild, critical cases did occur. When children had a chronic underlying disease, the risk of critical illness, or even mortality, rose. Investigations into the susceptibility of children of different ages and the mechanisms of disease severity are necessary for future care of pediatric patients and disease prevention.

Smell and/or taste disturbance is a specific symptom in some COVID-19 patients, and that require further investigations. In a multicenter European study among 417 mild-to-moderate COVID-19 patients, 85.6% and 88.0% of patients had olfactory and/or gustatory dysfunctions, respectively.⁴⁶ The authors suggest that olfactory and gustatory disorders are prevalent symptoms in European COVID-19 patients, and the sudden anosmia or ageusia need to be recognized as important symptoms of the COVID-19 infection.⁴⁶ As shown in Table 3, all three teenagers who lost smell and/or taste were diagnosed during late March 2020, and they all had a recent history of travel to Europe (Spain or the United Kingdom) in late March. Therefore, further researches on European COVID-19 for its special presentation and suspected higher CFR should be done.

Isolation of confirmed or suspected cases with mild illness is also an important way to block viral transmission. Therefore, developing accurate and rapid diagnostic techniques to identify SARS-CoV-2 patients or carriers is crucial. Although real-time reverse transcription polymerase chain reaction assays remain the molecular test of choice for COVID-19 etiologic diagnosis, many new antibody-based techniques are being investigated and tried.⁴⁷ We hope and believe that new diagnostic ways to promote the diagnostic speed and accuracy and monitor SARS-CoV-2 viral viability will be applied in clinical situations soon and that they will help control the outbreak of COVID-19.

Prevention is always more important than treatment in infectious diseases, especially for such a very contagious virus as COVID-19. Histories of travelling to COVID-19 epidemic regions or contact with infected subjects are more important than age when judging whether or not to perform further assessments. The well-known transmission routes of COVID-19 are droplet and contact transmission. Air-borne transmission is possible, but more evidence still required to prove it. Therefore, the precautionary measures for recommended for the general population should include hand washing; not touching the mouth, nose, and eyes; maintaining social distance; and wearing masks to cover the mouth and nose in public spaces. For medical personnel, different grades of advanced protective gowns and hats, N95 or surgical masks, goggles, and gloves should be employed liberally to protect these first-line medical providers and save more people from COVID-19.

Vaccine development for COVID-19 is the most important measure for future and long-term prevention. An effective vaccine to rapidly induce potent and long-lasting virus-specific immune responses

against SARS-CoV-2 is one of the most urgently needed weapons to fight COVID-19. The characteristic structural component of the viral envelope, the virus spike (S) protein, is considered a good target for developing vaccines for COVID.^{48,49} There have been many investigators on the way to vaccine development; some have started their phase 1 trials.^{49,50} Evidence of their efficacy and safety in the near future to help save people's lives is eagerly awaited.

In conclusion, COVID-19, caused by SARS-CoV-2, has become a global health emergency since December 2019 and has increased explosively since March 2020. Although the proportion of children infected by SARS-CoV-2 seems relatively lower, and their symptoms are relatively less severe than those of adults, a few infected children could progress to critical illness. Vertical transmission from the mother to her fetus or neonate has yet to be proven, but case reports of sick neonates exist. Early identification and isolation, adequate management, prevention, and vaccine development are the keys to controlling disease spread. Further studies on the different faces of COVID-19 are required to fight this viral pandemic.

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