

Epidemiology of COVID-19 Among Children in China

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abstract

OBJECTIVE: To identify the epidemiological characteristics and transmission patterns of pediatric patients with the 2019 novel coronavirus disease (COVID-19) in China.

METHODS: Nationwide case series of 2135 pediatric patients with COVID-19 reported to the Chinese Center for Disease Control and Prevention from January 16, 2020, to February 8, 2020, were included. The epidemic curves were constructed by key dates of disease onset and case diagnosis. Onset-to-diagnosis curves were constructed by fitting a log-normal distribution to data on both onset and diagnosis dates.

RESULTS: There were 728 (34.1%) laboratory-confirmed cases and 1407 (65.9%) suspected cases. The median age of all patients was 7 years (interquartile range: 2–13 years), and 1208 case patients (56.6%) were boys. More than 90% of all patients had asymptomatic, mild, or moderate cases. The median time from illness onset to diagnoses was 2 days (range: 0–42 days). There was a rapid increase of disease at the early stage of the epidemic, and then there was a gradual and steady decrease. The disease rapidly spread from Hubei province to surrounding provinces over time. More children were infected in Hubei province than any other province.

CONCLUSIONS: Children of all ages appeared susceptible to COVID-19, and there was no significant sex difference. Although clinical manifestations of children's COVID-19 cases were generally less severe than those of adult patients, young children, particularly infants, were vulnerable to infection. The distribution of children's COVID-19 cases varied with time and space, and most of the cases were concentrated in Hubei province and surrounding areas. Furthermore, this study provides strong evidence of human-to-human transmission.

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WHAT'S KNOWN ON THIS SUBJECT: A growing number of studies have focused on the 2019 novel coronavirus disease (COVID-19) since its outbreak, but few data are available on epidemiological features and transmission patterns in children with COVID-19.

WHAT THIS STUDY ADDS: Children of all ages were susceptible to COVID-19, but no significant sex difference was found. Clinical manifestations of pediatric patients were generally less severe than those of adult patients. However, young children, particularly infants, were vulnerable to 2019 novel coronavirus infection.

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In early December 2019, a number of pneumonia cases of unknown origin emerged in Wuhan, Hubei province, China.^{1,2} Most of these patients reported exposure to the Huanan Seafood Wholesale Market selling many species of live animals. The disease rapidly spread, domestically, to other parts of China, and globally to many countries across 6 continents. On January 3, 2020, a novel member of enveloped RNA coronavirus was identified in samples of bronchoalveolar lavage fluid from a patient in Wuhan and subsequently confirmed as the cause of this disease by the Chinese Center for Disease Control and Prevention (CDC).³⁻⁵ On January 7, 2020, the World Health Organization (WHO) named it the 2019 novel coronavirus (2019-nCoV). On February 11, 2020, the WHO named the illness associated with 2019-nCoV the 2019 novel coronavirus disease (COVID-19).

Emergence of 2019-nCoV has attracted global attention, and the WHO has declared the COVID-19 a public health emergency of international concern (PHEIC).⁶ Since the outbreak of severe acute respiratory syndrome in Guangdong, China, in 2003, the WHO has declared 5 PHEICs: H1N1 (2009), polio (2014), Ebola in West Africa (2014), Zika (2016), and Ebola in the Democratic Republic of the Congo (2019). Declaring a PHEIC is an urgent call, at the highest level, for the international community to launch a global coordinated effort to stop the outbreak, which requires a strong public health response, high-level political commitment, and sufficient funding. As of March 2, 2020, a total of 80 174 COVID-19 cases in China and 8774 cases in 64 countries (and regions) have been confirmed.⁷ Despite the worldwide spread, the epidemiological and clinical patterns of COVID-19 remain largely unclear, particularly among children. In this study, we explored the

epidemiological characteristics and transmission patterns of 2135 pediatric patients with COVID-19 in mainland China.

METHODS

Data Sources

We conducted a retrospective study on the epidemiological characteristics of 2135 pediatric patients with COVID-19. Children were defined as being <18 years old.

The cases were initially diagnosed on the basis of clinical manifestations and exposure history.^{8,9} Within the last 2 weeks, if a child was exposed to a COVID-19 case patient or lived in an epidemic area (ie, Hubei province), a community where a COVID-19 case (or cases) was reported, or a nonepidemic area where no COVID-19 case(s) was reported, she or he was defined as having high, medium, or low risk, respectively, on the basis

of the possibility of contracting the disease. Suspected cases were identified if a child at high risk had 2 of the following conditions: (1) fever, respiratory, digestive symptoms (eg, vomiting, nausea, and diarrhea), or fatigue; (2) laboratory test white blood cell count was normal, decreased, or had a lymphocyte count or increased level of C-reactive protein; or (3) abnormal chest radiograph imaging result. For a child at medium or low risk, similar diagnostic criteria were applied after excluding influenza and other common respiratory infections. Suspected cases that met any one of the following criteria were defined as confirmed cases:

1. Nasal and pharyngeal swab specimens or blood samples tested positive for 2019-nCoV nucleic acid by using real-time reverse-transcriptase polymerase chain reaction assay.

TABLE 1 Characteristics of Children's COVID-19 Cases in China

Characteristics	All Cases	Category		P
		Confirmed	Suspected	
Age, median (interquartile range)	7 (2–13)	10 (4–15)	6 (2–12)	<.001
Age group, n (%)				
<1	379 (17.6)	85 (11.7)	291 (20.7)	<.001
1–5	491 (23.0)	137 (18.8)	354 (25.2)	
6–10	522 (24.5)	170 (23.4)	352 (25.0)	
11–15	412 (19.3)	180 (24.7)	232 (16.5)	
>15	334 (15.6)	156 (21.4)	178 (12.6)	
Sex, n (%)				
Male	1208 (56.6)	418 (57.4)	790 (56.1)	.575
Female	927 (43.4)	310 (42.6)	617 (43.9)	
Severity of illness, n (%)				
Asymptomatic	94 (4.4)	94 (12.9)	0 (0.0)	—
Mild	1088 (51.0)	314 (43.1)	774 (55.0)	<.001
Moderate	826 (38.7)	298 (40.9)	528 (37.5)	
Severe	112 (5.2)	18 (2.5)	94 (6.7)	
Critical	13 (0.6)	3 (0.4)	10 (0.7)	
Missing	2 (0.1)	1 (0.2)	1 (0.1)	
Days from symptom onset to diagnosis				
Median (interquartile range)	2 (1–5)	3 (1–5)	2 (0–4)	<.001
Range	0–42	0–42	0–36	—
Province, n (%)				
Hubei	981 (46.0)	229 (31.5)	752 (53.4)	<.001
Surrounding areas ^a	396 (18.5)	154 (21.1)	242 (17.2)	
Other	758 (35.5)	345 (47.4)	413 (29.4)	
Total	2135	728 (34.1)	1407 (65.9)	—

—, not applicable.

^a Surrounding areas are the provinces and municipality bordering Hubei; they are Anhui, Henan, Hunan, Jiangxi, Shaanxi, and Chongqing.

TABLE 2 Different Severity of Illness by Age Group

Age Group, y ^a	Asymptomatic, n (%)	Mild, n (%)	Moderate, n (%)	Severe, n (%)	Critical, n (%)	Total, n
<1	7 (1.9)	204 (54.2)	125 (33.2)	33 (8.8)	7 (1.9)	376
1–5	15 (3.1)	245 (49.9)	195 (39.7)	34 (6.9)	2 (0.4)	491
6–10	30 (5.8)	277 (53.3)	191 (36.7)	22 (4.2)	0 (0.0)	520
11–15	27 (6.5)	198 (48.1)	170 (41.3)	14 (3.4)	3 (0.7)	412
>15	15 (4.5)	164 (49.1)	145 (43.4)	9 (2.7)	1 (0.3)	334
Total	94 (4.4)	1088 (51.0)	826 (38.7)	112 (5.3)	13 (0.6)	2133

See also Supplemental Table 3.

^a Two cases had missing values.

2. Genetic sequencing of respiratory tract or blood samples is highly homologous with 2019-nCoV.

The severity of COVID-19 was defined on the basis of the clinical features, laboratory testing, and chest radiograph imaging, including asymptomatic infection, as mild, moderate, severe, or critical. The diagnostic criteria were as follows.⁸

1. Asymptomatic infection: without any clinical symptoms and signs, and the chest imaging results

normal, whereas the 2019-nCoV nucleic acid test result is positive.

2. Mild: symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. Physical examination shows congestion of the pharynx and no auscultatory abnormalities. Some cases may have no fever or have only digestive symptoms, such as nausea, vomiting, abdominal pain, and diarrhea.

3. Moderate: with pneumonia, frequent fever, and cough (mostly dry cough, followed by productive cough); some may have wheezing, but no obvious hypoxemia such as shortness of breath, and lungs can hear sputum or dry and/or wet snoring. Some cases may have no clinical signs and symptoms, but chest computed tomography shows lung lesions, which are subclinical.

4. Severe: early respiratory symptoms, such as fever and

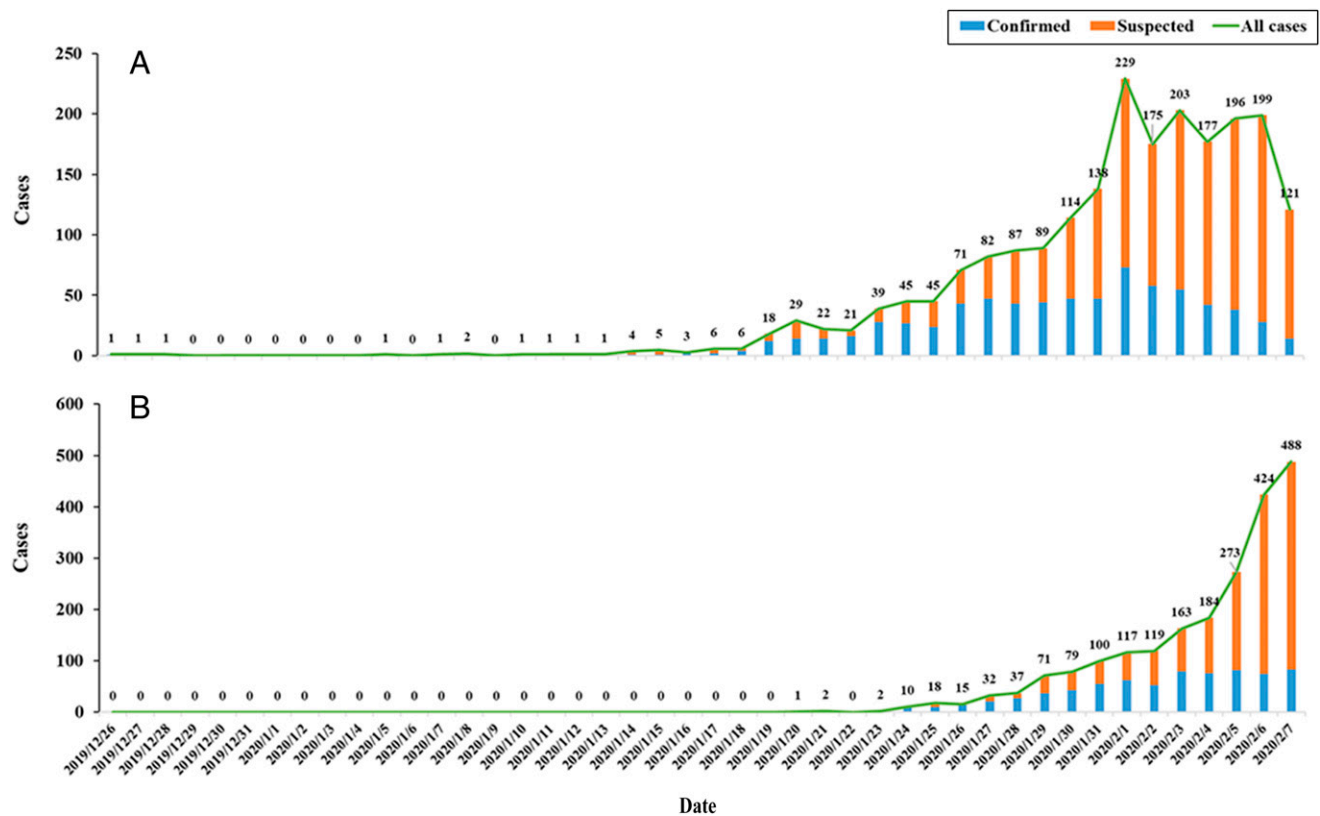


FIGURE 1 Onset and diagnosis dates of 2135 children's COVID-19 cases in China. A, Onset date. B, Diagnosis date.

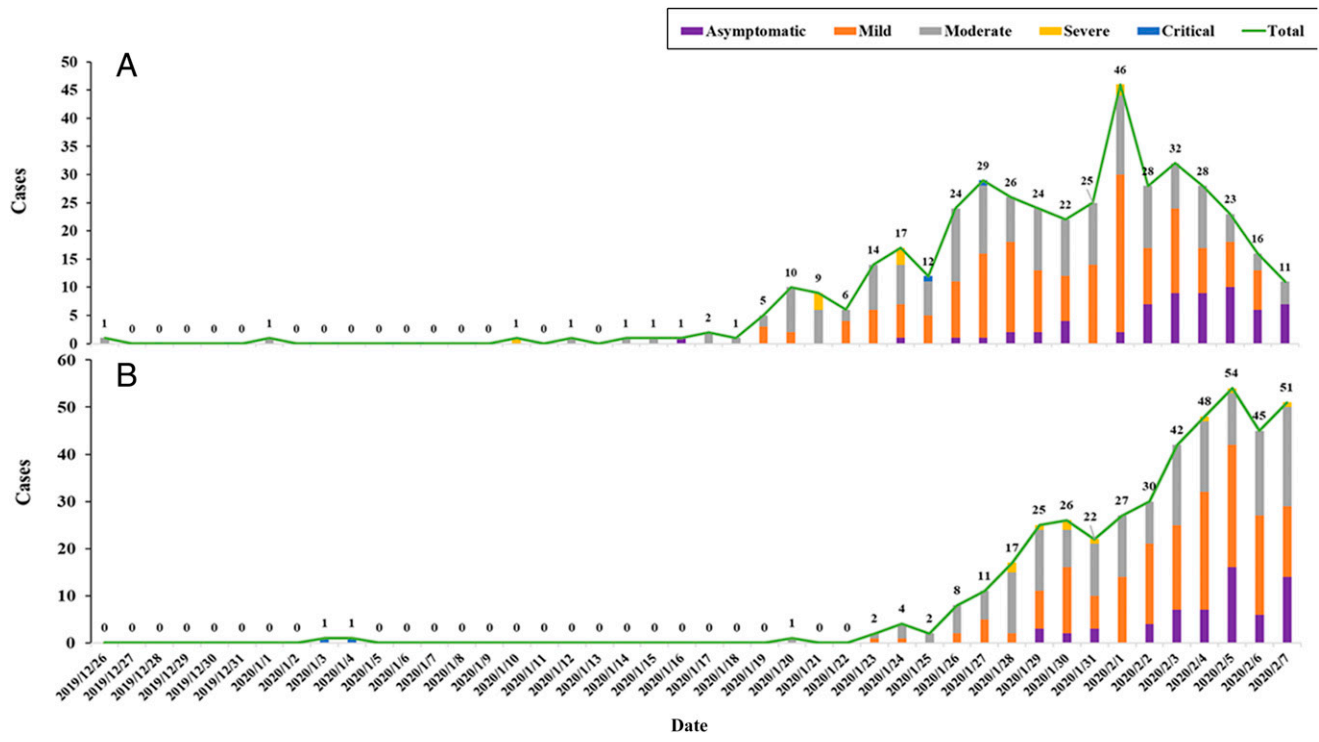


FIGURE 2 Onset and diagnosis dates of 418 confirmed male children's COVID-19 cases in China. A, Onset date. B, Diagnosis date.

cough, may be accompanied by gastrointestinal symptoms, such as diarrhea. The disease usually progresses at ~1 week, and dyspnea occurs with central cyanosis. Oxygen saturation is <92% with other hypoxia manifestations.

5. Critical: children can quickly progress to acute respiratory distress syndrome or respiratory failure and may also have shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute kidney injury. Organ dysfunction can be life-threatening.

Both the laboratory-confirmed and suspected cases were included in the analysis. The data sets were extracted from the National Notifiable Infectious Disease Surveillance System at the Chinese CDC. Data were entered into a computer and secured with a password at Shanghai Children's Medical Center.

Cross-check and data cleaning were performed before the data analysis.

Statistical Analysis

We first described case characteristics, including age, sex, dates of disease onset and diagnosis, and location where the case was notified. χ^2 tests and Fisher's exact tests were used for categorical variables as appropriate, and the Mann-Whitney *U* test was used for comparing median values of nonnormally distributed variables. The epidemic curves were constructed by key dates of disease onset and case diagnosis. Because of the data unavailability (ie, no detailed exposure data), we were unable to estimate the incubation period. Onset-to-diagnosis curves were constructed by fitting a log-normal distribution to data on both the onset and diagnosis dates. All analyses were conducted with the use of SPSS 22.0 software (IBM SPSS Statistics, IBM Corporation), and distribution maps

were plotted by using ArcGIS version 10.2.

Ethics

Because of the nature of aggregated data and the ongoing public health response to control the outbreak, as well as the importance of sharing the research findings and bridging the knowledge gaps, an ethical approval was waived by institutional review board.

RESULTS

By February 8, 2020, 2135 pediatric patients with COVID-19 were reported to the Chinese CDC (Table 1). Of the patients, 728 (34.1%) were identified as laboratory-confirmed cases, and 1407 (65.9%) were suspected cases. The median age of all patients was 7 years (interquartile range: 2–13 years). Among those patients, 1208 cases (56.6%) were boys, and there was no statistically significant difference in the number of pediatric patients

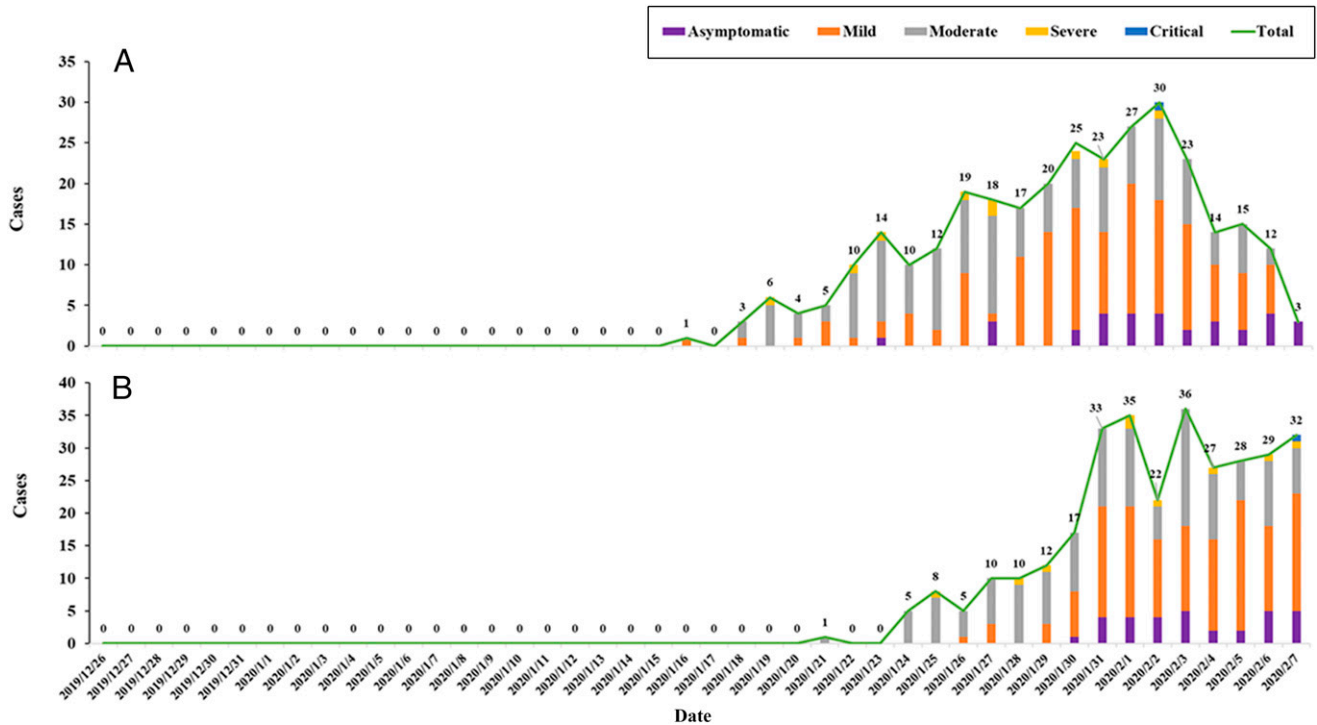


FIGURE 3 Onset and diagnosis dates of 310 confirmed female children's COVID-19 cases in China. A, Onset date. B, Diagnosis date.

between boys and girls. Regarding the severity (including both confirmed and suspected cases), 94 (4.4%), 1088 (51.0%), and 826 (38.7%) cases were diagnosed as asymptomatic, mild, or moderate, respectively; and totally accounted for 94.1% of all cases. Approximately half of the patients were from Hubei province (981; 46.0%), whereas 396 (18.5%) case patients were from Anhui, Henan, Hunan, Jiangxi, Shanxi and

Chongqing, which border Hubei province.

Table 2 shows the severity of illness by age and reveals that young children, particularly infants, were vulnerable to 2019-nCoV infection. The proportions of severe and critical cases were 10.6%, 7.3%, 4.2%, 4.1%, and 3.0% for the age groups <1, 1 to 5, 6 to 10, 11 to 15, and ≥16 years, respectively. A 14-year-old boy from

Hubei province died on February 7, 2020.

In the temporal distribution, among the 2135 pediatric patients, there was a trend of rapid increase of disease onset in the early stage of the epidemic and then a gradual and steady decrease (Fig 1). The total number of pediatric patients increased remarkably between mid-January and early February, peaked around February 1, and then has declined since early February 2020. The number of diagnoses had been rising every day from January 20, when the first case was diagnosed. Similar trends of onset and diagnoses were found in confirmed cases (Figs 2 and 3) and suspected cases (Supplemental Figs 6 and 7). The earliest date of illness onset was December 26, 2019, whereas the earliest date of diagnosis was January 20, 2020. The median number of days from illness onset to diagnosis was 2 days (range: 0–42 days). Figure 4 shows that most cases were

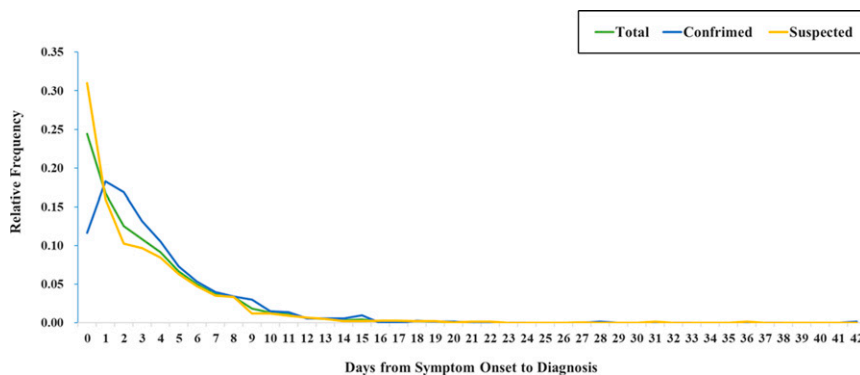


FIGURE 4 Relative frequency of days from symptom onset to diagnosis.

diagnosed in the first week after illness onset occurred.

In the spatial distribution, there was a clear trend that disease spread rapidly from Hubei province to surrounding provinces and cities over time. There were more children infected in the areas around Hubei province than in areas farther away except for Heilongjiang province (Fig 5).

DISCUSSION

To the best of our knowledge, this is the first retrospective study on the epidemiological characteristics and transmission dynamics of children's COVID-19 in China. Because most of these children were likely to expose themselves to family members and/or other children with COVID-19, it clearly indicates person-to-person transmission. Supportive evidence of such a transmission pathway has also been reported from studies on adult

patients.¹⁰⁻¹² As of February 8, 2020, of the 2135 pediatric patients included in this study, only 1 child died and most cases were mild, with much fewer being severe and critical cases (5.8%) than in adult patients (18.5%).¹³ The evidence suggests that, compared with adult patients, clinical manifestations of children's COVID-19 may be less severe.

Coronaviruses are large, enveloped, positive-strand RNA viruses that can be divided into 4 genera, α , β , δ , and γ , of which α and β coronaviruses are known to infect humans, which are called human coronaviruses (HCoVs).¹⁴ Four HCoVs (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10% to 30% of upper respiratory tract infections in adults.¹⁵ Although HCoVs have long been regarded as inconsequential pathogens because of their mild phenotypes in humans, in the early 21st century, 2 large-scale epidemics with alarming morbidity and

mortality (ie, severe acute respiratory syndrome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus), have changed that view. From December 2019 to March 25, 2020, 2019-nCoV, another highly pathogenic HCoV, caused 81285 confirmed cases of illnesses and 3287 deaths.¹⁶ The epidemic is ongoing and rapidly evolving, and the ultimate scope and impact of this event is still unclear.

Genomic analyses suggest that the 2019-nCoV may originally come from bats because of the similarity of its genetic sequence to those of other known coronaviruses, but the pathogen was probably transmitted to humans by other animals that may serve as intermediate hosts, facilitating recombination and mutation events with the expansion of genetic diversity.³⁻⁵ On February 7, 2020, researchers in Guangzhou, China, identified the pangolin as one of the potential sources of 2019-nCoV



FIGURE 5

Spatial distribution of children's COVID-19 cases diagnosed in different time periods. A, January 20, 2020, to January 24, 2020. B, January 25, 2020, to January 31, 2020. C, February 1, 2020, February 7, 2020. D, January 20, 2020, to February 7, 2020.

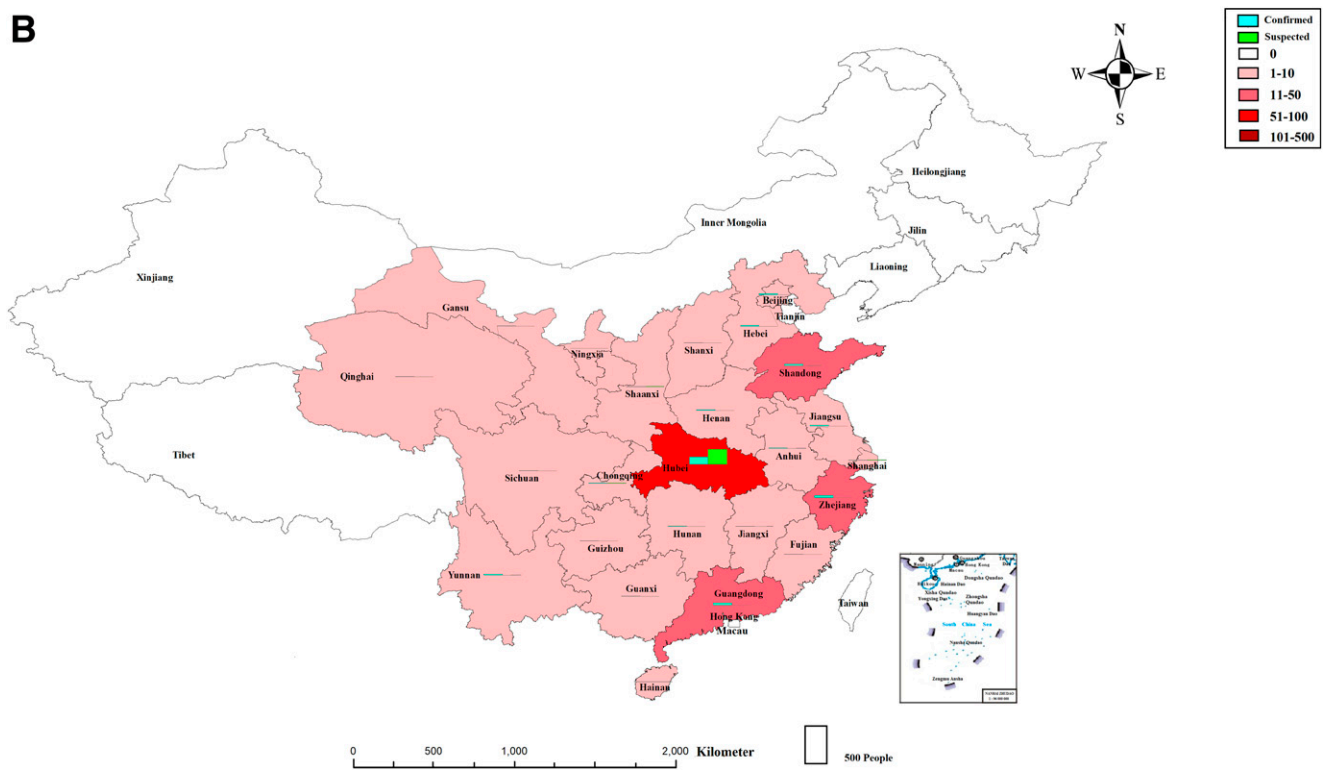


FIGURE 5
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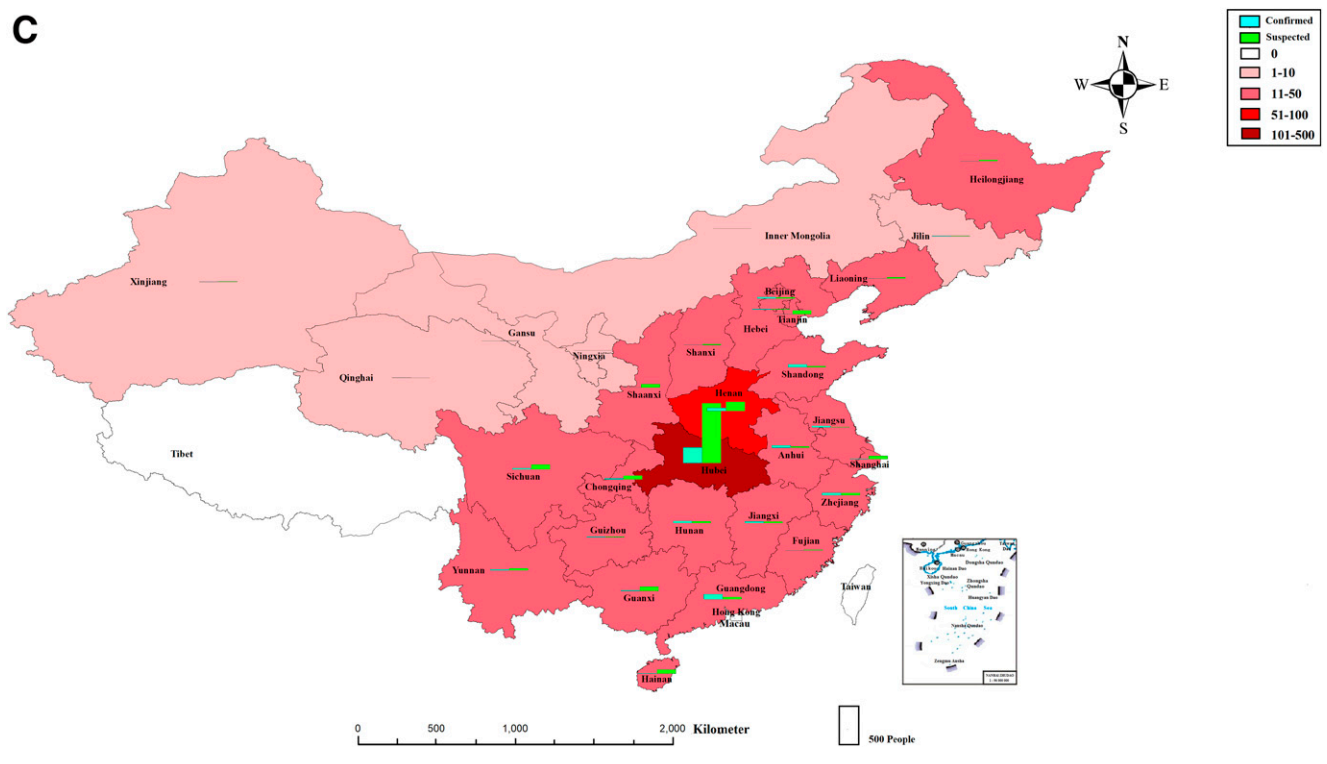


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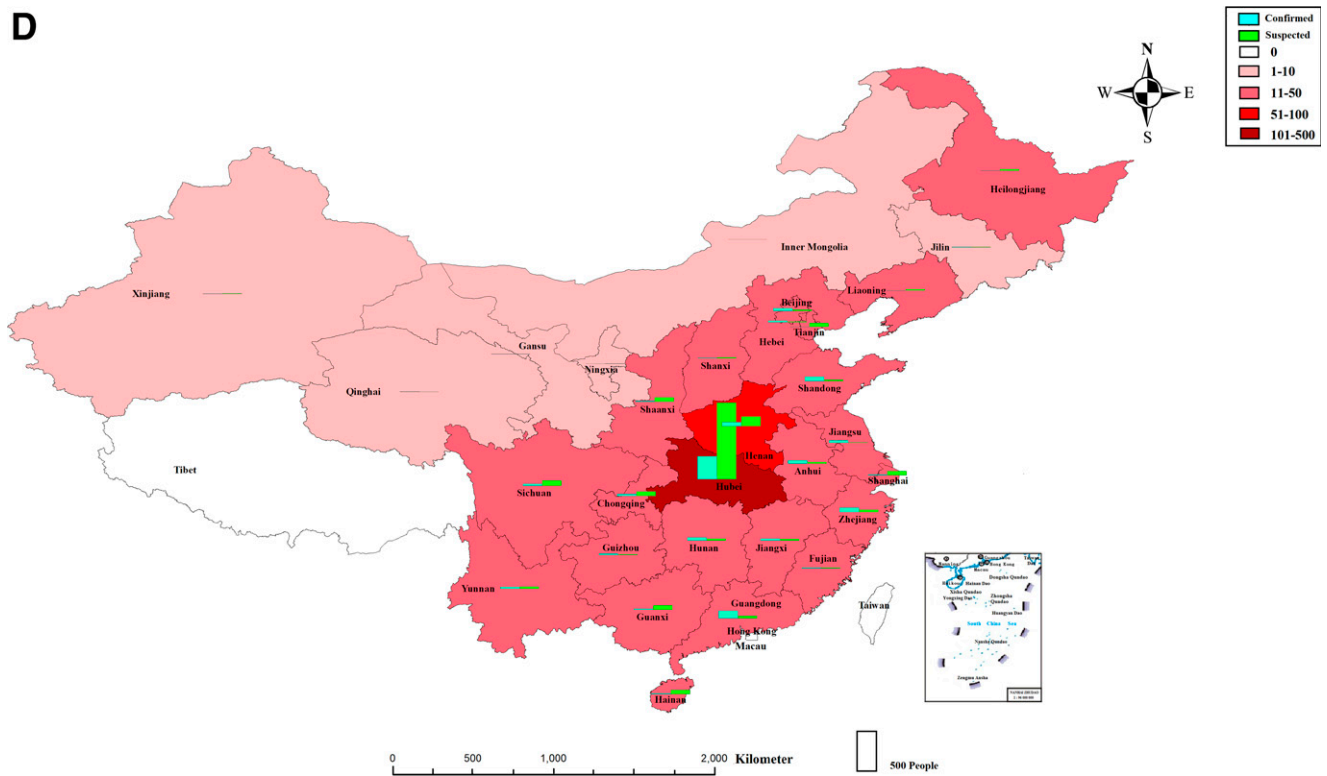


FIGURE 5

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on the basis of a genetic comparison of CoVs in the samples taken from the animals and from humans who were infected in the outbreak and other findings.^{17,18} Genetic sequences of viruses that were isolated from the scaly animals are 99% similar to that of the circulating virus.

Why most of the children's COVID-19 cases were less severe than adult cases is puzzling. This may be related to both exposure and host factors. Children were usually well cared for at home and might have relatively fewer opportunities to expose themselves to pathogens and/or patients who are sick. Angiotensin-converting enzyme II (ACE2) was known as a cell receptor for SARS-CoV.¹⁹ 2019-nCoV has some amino acid homology to SARS-CoV and may be able to use ACE2 as a receptor. Recent evidence indicates that ACE2 is also likely the cell receptor of 2019-nCoV.^{20,21} It is speculated that children were less sensitive to

2019-nCoV because the maturity and function (eg, binding ability) of ACE2 in children may be lower than in adults.²² Additionally, children often experience respiratory infections (eg, respiratory syncytial virus [RSV]) in winter and may have higher levels of antibody against virus than adults. Furthermore, children's immune systems are still developing and may respond to pathogens differently from adult immune systems. However, we found that the proportion of severe and critical cases was 10.6%, 7.3%, 4.2%, 4.1%, and 3.0% for the age groups <1, 1 to 5, 6 to 10, 11 to 15, and >15 years, respectively. These results suggest that young children, particularly infants, were vulnerable to 2019-nCoV infection. Therefore, the mechanisms for the difference in clinical manifestations between children and adults remains to be determined.

There were more severe and critical cases in the suspected than confirmed

category in this study. However, it remains to be determined if these severe and critical cases in the suspected group were caused by 2019-nCoV or other pathogens (eg, RSV). It may become clearer because the epidemic is quickly unfolding.

We observed slightly more boys than girls (56.6% vs 43.4%) being affected in the COVID-19 outbreak, which is similar to the 2 recent epidemiological studies.^{13,23} However, no significant sex difference was observed in this study. The median age of all children's COVID-19 cases was 7 years (interquartile range: 2–13), but ages ranged from 1 day to 18 years. This finding suggests that all ages of childhood were susceptible to 2019-nCoV.

Temporal distribution of children's COVID-19 cases shows that, in the early stage of the epidemic (ie, between December 2019 and early February 2020), there was a trend of rapid increase of disease onset. Since

early February 2020, the number of children's COVID-19 cases has been declining. This finding indicates that the disease control measures implemented by the government were effective, and it is likely that this epidemic will continue to decline and finally stop in the near future unless sustained human-to-human transmissions occur. Most of the children's COVID-19 cases were concentrated in Wuhan but spread to other areas of Hubei province and farther to other areas of China. It seems that the closer to Wuhan, the more cases in that area, which suggests that population mobility is an important factor of the spread of 2019-nCoV. Heilongjiang province is an exception, which may be because many visitors went there, including those from Wuhan, because of the Ice and Snow Sculpture Festival in Harbin, the provincial capital.

This study has several strengths. First, this is the first nationwide study, to date, with a major focus on the epidemiological characteristics and transmission dynamics of children's COVID-19 in China. It shows that, compared with the adult cases, the severity of children's COVID-19 cases was milder, and the case fatality rate was much lower.^{13,23} Second, the large number of children's COVID-19 cases enabled us to conduct detailed stratified analyses on sex, age, and spatiotemporal distribution. Finally, we included both

confirmed and suspected COVID-19 cases, and it may reveal a comprehensive picture of pediatric patients with COVID-19 in China.

This study also has a number of limitations. First, we were unable to assess clinical characteristics of children's COVID-19 because these data were unavailable at the time of analysis. As an important and urgent issue, clinical features of children's COVID-19 need to be analyzed in further research. It appeared to have more severe and critical cases in the suspected than in the confirmed group (Table 1), which suggests that some suspected cases might be caused by other respiratory infections (eg, RSV). Second, we did not have information on children's exposure history, and thus, the incubation period was not examined in this study. Finally, because the epidemic of COVID-19 is ongoing and rapidly evolving, many children who are affected still remain hospitalized. To gain a better understanding of children's COVID-19, more detailed patient information, particularly clinical outcomes (eg, discharge, transfer to ICU, or death), should be collected in future studies.

CONCLUSIONS

Children of all ages were sensitive to COVID-19, and there was no significant sex difference. Clinical manifestations of children's COVID-19 cases were less severe than those of

adult patients. However, young children, particularly infants, were vulnerable to 2019-nCoV infection. The distribution of children's COVID-19 cases varied with time and space, and most of the cases were concentrated in Wuhan and surrounding areas. Furthermore, the results of this study provide strong evidence for human-to-human transmission because children were unlikely to visit the Huanan Seafood Wholesale Market, where the early adult patients were reported to have obtained 2019-nCoV.

ACKNOWLEDGMENT

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ABBREVIATIONS

2019-nCoV:	2019 novel coronavirus
ACE2:	angiotensin-converting enzyme II
CDC:	Center for Disease Control and Prevention
COVID-19:	2019 novel coronavirus disease
HCoV:	human coronavirus
PHEIC:	public health emergency of international concern
RSV:	respiratory syncytial virus
SARS-CoV:	severe acute respiratory syndrome coronavirus
WHO:	World Health Organization

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