

Clinical Implications of 37 Childhood Cases with SARS-COV-2 Infection in Shenzhen, China

Yanrong Wang (✉ 123rong@sohu.com)

the Third People's Hospital of Shenzhen

Yingxia LIU

The Third People's Hospital of Shenzhen

Yang Yang

The Third People's Hospital of Shenzhen

Xianfeng WANG

The Third People's Hospital of Shenzhen

Lei LIU

The Third People's Hospital of Shenzhen

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Abstract

Background SARS-CoV-2 was first identified in December 2019 in samples obtained from a 61 years old man who died of acute respiratory failure in the city of Wuhan, China with a subsequent outbreak in China. Till now, there were rare reports about childhood patients with SARS-CoV-2 infection.

Methods We report 37 children diagnosed with SARS-CoV-2 infection admitted in the Third People's hospital of Shenzhen from December 11, 2019 to February 11, 2020.

Results There were 9 mild cases, 20 ordinary cases and 1 severe case and 7 cases with asymptomatic infection. The age ranged from 7 months to 17 years old and the median age was 7 years old. The median length of hospital stay is about 14 days. The time from illness onset to diagnosis ranged from 0.5 to 10 days (median time: 2 days). The common clinical features were fever (29.7%, 11/37) and cough (32.4%, 12/37). No death occurred among our patients. 86.5% (32/37) children were infected with SARS-CoV-2 after their family members (parents or grandparents). 1 child was identified with SARS-CoV-2 infection after 3 times testing. The majority (78.4%) of cases occurred in those children who travelled to Hubei Province.

Conclusions The majority of childhood cases with SARS-CoV-2 infection was mild or ordinary COVID-19 and had travelled to Hubei Province. Family cluster transmission of SARS-CoV-2 was suspected in 86.5% of patients. Timely continuous SARS-CoV-2 pathogen testing is recommended. Key words: SARS-CoV-2; infection; children

Background

In December 2019, SARS-CoV-2 infection was first reported in Wuhan, China in a 61 years old man with severe pneumonia¹. The virus causes worldwide infections², as well as family cluster and health-care-associated infections³. As of July 15, 2020, 85677 people have been identified as COVID-19 (Corona Virus Disease 2019), and 4649 have died since the first reported case was detected in China. Till now, there were rare reports about childhood patients. Here we report 37 pediatric cases of SARS-CoV-2 infections. Data was collected including the epidemiological and clinical features, laboratory findings and treatment outcomes in a China outbreak.

Methods

Ethical consideration

This study was approved by the Ethics Committee of the Third People's Hospital of Shenzhen, China, on January 23, 2020. Informed consent was obtained from the patients' guardians.

Clinical classification and epidemic findings: We obtained clinical data and possible exposures to COVID-19 by direct interviewing with their guardians. All symptoms, physical examination, laboratory, and image

data were obtained from medical records. The patients' inclusion criteria were: (1) below 18 years old, (2) laboratory-confirmed SARS-CoV-2 infection with PCR (polymerase chain reaction) test of the virus in samples taken from the respiratory tract of the patient, and (3) patients admitted to the Third People's Hospital of Shenzhen from January 11, 2020 to February 11, 2020. Cases were classified as follows: (1) Asymptomatic, positive SARS-CoV-2 RNA without symptom ; (2) mild, mild clinical symptoms without pneumonia seen at chest computed tomography; (3) ordinary, fever and other respiratory symptoms with pneumonia seen at imaging; (4) severe, respiratory distress, hypoxia (oxygen saturation, $\leq 93\%$), or abnormal results of blood gas analysis ($\text{PaO}_2 < 0 \text{ mm Hg}$ or $\text{PaCO}_2 > 50 \text{ mm Hg}$); and (4) critical, respiratory failure requiring mechanical ventilation, shock, or other organ failure requiring intensive care unit monitoring and treatment. The exclusion criteria were suspected cases of COVID-19 without a confirmed diagnosis. All acquired data were crosschecked by two physicians to ensure that there was no duplicated data. Clinical classification was recommended according to the diagnostic criteria⁴.

Specimen collection: Nasopharyngeal swabs, sputum, blood and/or tracheal aspiration samples were tested for nucleic acid from each patient at various times. Two sets of nasopharyngeal swab samples were collected at initial diagnosis (sampling interval of at least 1 day). Follow-up sets of specimens were collected after symptoms had disappeared. SARS-CoV-2 laboratory testing: Specimens were tested using a SARS-CoV-2 real-time reverse transcription PCR (RT-qPCR) method. A licensed kit (GeneoDX Co. Ltd. Shanghai) was recommended by National microbiology Data Center of China for detection of SARS-CoV-2, (http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html?from=timeline&isappinstalled=0). All PCR procedures were done at Center for Disease Control and Prevention of Shenzhen and the results were reported within 48 hours of collection.

Treatment: According to the guideline⁵, Lopinavir/Ritonavir (200mg/50mg), the recommended doses: weight 7-15kg, 12mg/3mg/kg; weight 15-40 kg, 10 mg/2.5 mg/kg; weight >40 kg, 400 mg/100 mg as adult each time⁶, twice a day for 1-2 weeks. Interferon- $\alpha 2b$ nebulization, 100,000-200,000 IU/kg, twice a day for 5-7 days. No patients received intravenous immunoglobulin (IVIG) and methyl-prednisone. During the course of hospitalization, pay attention to the changes in asymptomatic children's conditions, regularly monitor vital signs, SpO₂, etc.

Data analysis: Basic descriptive analyses were carried out in all patients. A result of p value < 0.05 indicated statistically significant. IBM SPSS statistics was used for statistical analyses.

Results

Gender and age distribution of 2019-nCoV infection

A total of 37 patients, including 19 boys and 18 girls, met the eligible criteria. There were 9 mild cases, 20 ordinary cases, 1 severe case and 7 cases with asymptomatic infection. The male had relatively higher opportunity to be infected by COVID-19 than female, but the difference did not show significantly

($P > 0.05$) (table 1). The age ranged from 7 months to 17 years old and the median age was 7 years old. The percentage of cases in preschool and in schools was 48.6 % and 51.4 % respectively ($P > 0.05$) (table 2).

Clinical manifestations, radiological and laboratory findings of the cases

The onset clinical characteristics included fever (29.7%, 11/37) and cough (32.4%, 12/37). The temperature ranged from 38.0°C to 39.0°C. Family cluster occurred in 32 cases (86.5%, 32/37). Table 3 showed the clinical manifestations, radiological and laboratory findings of the cases. The majority of thoracic physical examination was normal but thoracic Computed Tomography (CT) showed multiple small ground-glass appearance on lower lobe of both lungs (figure 1). Only 1 case had wheezes and hypoxia and there was no critical case. 29 cases (78.4%) had travelled to Hubei Province and 32 (86.5%) were infected with SARS-CoV-2 after their family members (parents or grandparents). 1 child's specimen was tested SARS-CoV-2 RT-qPCR for three times within two weeks and was identified with SARS-CoV-2 infection eventually.

Discussion

In this report, family cluster occurred in 86.5% people. The finding indicated that family cluster transmission of SARS-CoV-2 was the main mode of transmission among children. The median length of hospital stay is about 14 days. Only one patient had no epidemiologic exposure history. The median time from illness onset to diagnosis was 2 days.

7 patients had asymptomatic infection but showed pneumonia upon thoracic CT. The lack of prominent symptoms often delayed diagnosis. The thoracic CT findings of SARS-CoV-2 infection may present bilateral patchy densities, interstitial infiltrates, or opacities, consolidation, and pleural effusions in adults^{7,8}. However, our pediatric pneumonia typically infected the lower lobes⁹. So those cases of lower-lobe pneumonia that occur during COVID-19 outbreak and had epidemiology history of exposure should be considered the possibility of SARS-CoV-2 infection.

It was reported that fever, sore throat, cough, myalgia, lymphopenia usually occurred among adult patients¹⁰. However, only one third of our patients presented fever. The respiratory symptoms such as cough and sputum were not prominent during the onset of the disease. Mildly increased C-reactive protein (CRP), Lactate dehydrogenase (LDH) and white blood cells (WBC) level occurred in 5 patients respectively. Only 1 patient presented neutropenia which was frequently observed in adult patients. Previous study indicated¹¹ that age, viral load and blood biochemistry indexes such as, CRP and LDH may

be predictors of disease severity. It was evident that childhood patients' laboratory features were not similar to adults'.

We noticed that the median time from illness onset to diagnosis was 2 days. Those children were not isolated and might be the latent source of infection before diagnosis. So early diagnosis and promptly medical isolation are needed to suspected cases.

In this report, the positive rate of SARS-CoV-2 was 89.2% at admission. 3 patients were identified with SARS-CoV-2 infection two days later and 1 child was confirmed infected case the third time ten days later. So those children who had a history of exposure to COVID-19 are recommended for timely continuous SARS-CoV-2 pathogen testing in order to effectively diagnose the patients and promptly to isolate the source of infection. An extensive public awareness campaign may play an important role in preventing the spread of infection.

Previously Lopinavir/Ritonavir and INF-a2b nebulization were used during the SARS¹² epidemic of 2003 and MERS of 2014^{13,14}. These drugs kill viruses at high doses individually, whereas a combination of Lopinavir/ritonavir and IFN-a2b had a synergistic affection at much lower doses with possible lower toxicity¹⁵. SARS-CoV-2 is similar to the 2 CoVs, so therapy with Lopinavir/ritonavir and IFN-a2b may be a potential treatment for 2019-nCoV. Further study should be carried out to better understand the therapeutic effect of antiviral treatment.

Conclusions

This report suggests that family cluster transmission of COVID-19 was suspected in 86.5% of patients. The majority of childhood cases with SARS-CoV-2 infection was mild or ordinary COVID-19 and had travelled to Hubei Province. Timely continuous SARS-CoV-2 pathogen testing is recommended.

Abbreviations

Corona Virus Disease 2019 (COVID-19)

Interferon-α2b (IFN-α2b)

Center for Disease Control and Prevention (CDC)

PCR (polymerase chain reaction)

Real-time reverse transcription PCR (RT-qPCR)

Computed Tomography (CT)

C-reactive protein (CRP)

Lactate dehydrogenase (LDH)

White blood cell (WBC)

Declarations

Ethics approval and consent to participate: The study was approved by the Ethics Committees of the Third People' Hospital of Shenzhen. Informed consent was obtained from parents or guardian for participants under 16 years old.

Consent for publication

Consent for publication obtained from guardians

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests. **Funding:** This work is supported by grants from the Science and Technology Innovation Committee of Shenzhen Municipality (202002073000001) National Key Research and Development Program (2020YFC0841700)

Authors' contributions Y Y and XW: data collection and clinical diagnosis of patients; Y L and LL: Study design; YW: data analysis and writing. All authors read and approved the final manuscript.

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Tables

Table 1 Gender-Specific proportion of cases infected with 2019-nCov

Gender	Asymptomatic infection	Mild patients	Common patients	Severe patients
Male	2(28.6)	5(55.6)	13(65.0)	0(0)
Female	5(71.4)	4(44.4)	7(35)	1(100.0)
Total	7(100.0)	9(100.0)	20(100.0)	1(100.0)

Data in brackets refer to percentage of total cases in the corresponding clinical type. (Fisher's exact test =3.839 P value=0.223)

Table 2 Age distribution of 2019-nCov cases

Age (y)	Asymptomatic infection	Mild patients	Common patients	Severe patients	Total patients
<6	3(42.9%)	6(66.7)	9(45.0)	0(0.0)	18(48.6)
>6	4(57.1%)	3(33.3)	11(55.0)	1(100.0)	19(51.4)
Total	7(100.0%)	9(100.0)	20(100.0)	1(100.0)	37(100.0)

Data in brackets refer to percentage of total cases in the corresponding clinical type (Fisher's exact test =2.275 P value=0.632)

Table 3. Clinical manifestations, radiological and laboratory findings of the patients

Item	Result
Median age	7y(7m-17y)
Median length of hospital stay	14d(1-20d)
Median time from illness onset to diagnosis	2d(0.5-10 d)
Family cluster	
Yes	32
No	5
Fever	
Yes	11
No	26
Cough	
Yes	12
No	25
diarrhea/vomit	
Yes	1
No	36
CT/DR	
Positive	20
Negative	17
Leukocyte	
<4*10 ⁹ /L	1
4-10*10 ⁹ /L	31
>10*10 ⁹ /L	5
Lymphocyte	
<1.5*10 ⁹ /L	1
Normal	36
CRP	
<10mg/L	32
>10mg/L	5
LDH	
Normal	32

CT: Computed Tomography; CRP: C-reactive protein; LDH: Lactate dehydrogenase

Figures

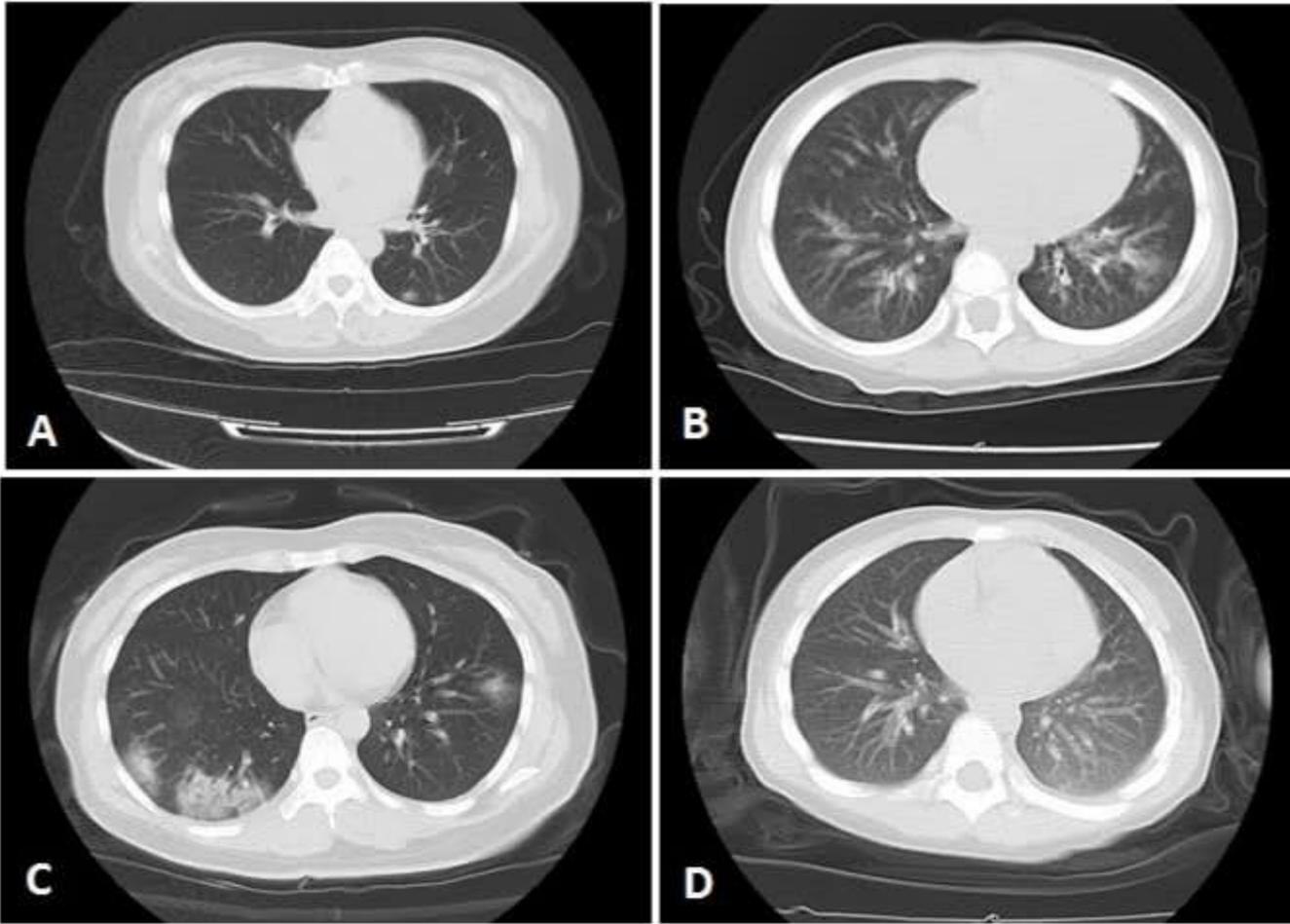


Figure 1

Representative images of the thoracic CT scans in the lungs of patients, A: mild case; B and D: ordinary case; C: severe case