A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features

Cai Jiehao†, Xu Jing†, Lin Daojiong†, Yang zhi‡, Xu Lei§, Qu Zhenghai§, Zhang Yuehua¶, Zhang Hua†, Jia Ran‡, Liu pengcheng‡, Wang Xiangshi‡, Ge Yanling‡, Xia Aimei‡, Tian He‡, Chang Hailing‡, Wang Chuning‡, Li Jingjing‡, Wang Jianshe‡, Zeng Mei*†

1 Department of infectious diseases, Children’s Hospital of Fudan University, National Children’s Medical Center

2 Division of virology, Department of clinical laboratory, Children’s Hospital of Fudan University, National Children’s Medical Center

3 Department of infectious diseases, Hainan Women and Children’s Medical Center

4 Department of infectious diseases, Anhui Provincial Children’s Hospital

5 Children’s medical center, The Affiliated Hospital of Qingdao University

6 Department of pediatric infectious diseases, Haikou People’s Hospital

7 Department of pediatrics, Sanya Central Hospital

† Equally contributed to this paper.

Corresponding Author:

Mei Zeng, MD, PhD

Department of Infectious Diseases, Children’s Hospital of Fudan University, 399 Wanyuan Road, Shanghai 201102, China.

E-mail: zengmeigao@aliyun.com
Abstract

We first described the 2019 novel coronavirus infection in 10 children occurring in areas other than Wuhan. The coronavirus diseases in children are usually mild and epidemiological exposure is a key clue to recognize pediatric case. Prolonged virus shedding is observed in respiratory tract and feces at the convalescent stage.

Key word: 2019 novel coronavirus; coronavirus diseases; children
Introduction

A novel coronavirus (2019-nCoV) was identified as the causative agent associated with a cluster of cases of pneumonia detected in Wuhan City by Chinese authorities on 7 January [1]. Since the discovery of 2019-nCoV, the virus has been diagnosed quickly [2,3]. With the number of people confirmed with 2019-nCoV rising rapidly in Wuhan and increasing outside of Wuhan and China, WHO declared that the outbreak of 2019-nCoV constitutes a Public Health Emergency of International Concern on 30 January 2020 [4]. By 11 February 2020, 44,672 confirmed cases were reported in China with 8,255 (18.5%) severe cases and 1023 (2.3%) deaths, and 395 confirmed cases with 1 death were reported in 24 countries outside of China [5,6]. Thus far, the notifiable cases were mostly among adults, with pediatric cases rarely reported [7,8]. The clinical profiles of 2019-nCoV infection in children is unknown. Herein, we reported the clinical and epidemiological features in children with coronavirus diseases (COVID) in China.

Method

Between 19 January and 3 February, 2020, a total of ten children with confirmed 2019-nCoV infection were admitted to the Children’s Hospital in Shanghai, Hainan, Hefei in Anhui province, and Qingdao in Shandong province. According to China CDC protocol for detection 2019-nCoV, a duplex one-step real-time RT-PCR was performed to confirm 2019-nCoV infection at the local CDC reference laboratory. If respiratory samples obtained from patients were successfully tested positive by both open reading frame 1ab gene and nucleocapsid protein gene, the specimens were considered as positive and the case was considered to be laboratory-confirmed. A cycle threshold value less than 35 was defined as a positive test. All pediatric cases were hospitalized for the screening of 2019-nCoV infection when
they were considered as suspected cases based on the following two criteria: having an epidemiological link to adult cases or an exposure to Wuhan or other epidemic areas in Hubei province and presenting with acute fever and or respiratory symptoms. All patients were admitted to the isolation ward within 2 days after illness onset and nasopharyngeal and throat swabs were collected immediately for the detection of 2019-nCoV. At the meantime, influenza virus A and B were routinely tested on respiratory swab by colloidal gold assay for all patients.

Results

The detailed information on patients was shown in Table. Seven (70%) children were local residents, 2 (20%) were from Wuhan and 1 (10%) was from Xiaogan (an endemic area 50 kilometers far away from Wuhan). Eight (80%) children had direct contact with adult patients with 2019-nCoV infection who had a history of travel to Wuhan or contact with persons from Wuhan. Exposure setting included household exposure in 7 patients (70%), endemic area exposure in 2 patients (20%), and bus travelling exposure in 1 (10%) patient who had contact with 2 adult travellers from Wuhan who already had mild respiratory symptoms during the bus travelling and were confirmed with COVID after returning to Wuhan. Among seven children exposed to household adult cases, the number of secondary symptomatic cases including the child ranged from 1 to 4 (mean: 2.43). For the 3-month-old infant (patient 7 in Table), her parents developed symptomatic COVID 7 days after they looked after the sick baby without protection measures. The interval between symptom onset and exposure to index symptomatic case ranged from 2 to 10 days (mean: 6.5 days) and the interval between symptom onset and departure from endemic areas was 1 day and 9 days.
The 10 patients were aged 3-131 months (mean: 74 months) and the ratio of male to female was 1:1.5. Eight (80%) patients had fever, 6 (60%) had cough, 4 (40%) had sore throat, 3 (30%) had stuffy nose and 2 (20%) had sneezing and rhinorrhea. None of patients had diarrhea or dyspnea during the course of illness. Fever resolved 24 hours after fever onset with the peak of fever ranging from 37.7°C to 39.2°C. Chest radiograph revealed unilateral patchy infiltrate in 4 (40%) of 10 patients. The laboratory findings showed (median): white blood cell count $7.35 \times 10^9$/L, C-reactive protein 7.5 mg/L, procalcitonin 0.07 ng/dL, creatine kinase-MB 23 U/L, alanine aminotransferase 18.5 U/L, aspartate aminotransferase 27.7 U/L, urea 3.1 mmol/L, creatinine 35.5 µmol/L, lactate dehydrogenase 25 U/L and D-dimer 0.45 µg/mL; influenza virus A and B were all negative. All patients received symptomatic treatment with no need of oxygen therapy and a few of patients with pneumonia received empirical antibiotic therapy. As of 19 February, all patients had been discharged when they recovered uneventfully with 2 consecutive respiratory samples tested negative for 2019-nCoV RNA.

2019-nCoV RNA was detected in nasopharyngeal and throat swabs from all patients within 4-48 hours after symptom onset. 2019-nCoV RNA in nasopharyngeal/throat swabs was undetectable within 6-22 days (mean: 12 days) after illness onset. Six patients had fecal samples tested for 2019-nCoV RNA within 3-13 days after illness onset and 5 (83.3%) showed positivity (Of note, fecal sample from patient 2 was obtained on day 10 after illness onset and showed negativity). As of 19 February, these 5 patients still have 2019-nCoV RNA detected in feces within 18-30 days after illness onset and are under close follow-up. Five patients had urine and serum samples tested for 2019-nCoV RNA within 2-3 days after illness onset and all showed negativity.
Discussion

This is the first case series report on 2019-nCoV infection in children. Our preliminary clinical findings showed that children with COVID usually presented with mild respiratory infections, as compared with adult cases [9]. For pediatric patients, fever and mild cough are common symptoms at disease onset. For mild case, fever is brief and resolved rapidly. A few of patients presenting with/without cough also showed radiographic evidence of patchy infiltrate at symptom onset. In one study of a family cluster, an asymptomatic 10-year-old child infected with 2019-nCoV due to household exposure had radiological ground-glass lung opacities [7]. Radiographic evidence of pneumonia was a characteristics of 2019-nCoV infection at the earliest stage of infection, thus, close observation is very necessary for a child with either mild symptomatic or asymptomatic infection. We don’t recommend use of antiviral agents for the treatment of self-limited non-severe COVID because no evidence has shown the effectiveness of antiviral agents currently available. Influenza virus screening is necessary to rule out the possible coinfection considering the seasonal overlap between influenza and COVID. Empirical antibiotic initiation is not recommended for treatment of non-severe 2019-nCoV-associated pneumonia without evidence of superbacterial infection. By 22 January 2020, all notifiable COVID cases and severe cases were aged $\geq 15$ years old in Wuhan [9, 10]. In theory, children are also susceptible to 2019-nCoV and mild or atypical cases were largely underdiagnosed according to the initial screening criteria which focused on suspected pneumonia case [2].

The epidemiological evidence has demonstrated that COVID can be transmitted from person to person and the basic reproductive number was estimated to be 2.2 [10]. We observed the mean number of secondary symptomatic cases in household exposure setting was 2.43. Our findings highly support the evidence of human-to-human transmission of COVID. All pediatric patients had an epidemiological
link directly or indirectly to Wuhan or other endemic area of Hubei, where the outbreak of COVID originated and is ongoing. Most of pediatric cases occurring outside of Wuhan were secondary cases after exposure to adult cases through household contact or travel contact. However, we can not neglect the potential risk of transmission from the infected child to adult contacts, as shown in patient 7. Thus, personal medical protection is crucial when care providers look after the infected child. The major pattern of transmission was intrafamily transmission. The general transmission pattern of COVID is similar to that of SARS and MERS in children [11, 12]. Based on our field investigation, the mean incubation period between household exposure to a symptomatic adult case and symptom onset was 6.5 days, longer than 5.4 days observed in adult cases [10]. This difference could be suggestive of longer incubation period for 2019-nCoV infection in children. Currently, these epidemiological features are a key clue to help early recognition of 2019-nCoV infection in children outside of Wuhan and take infection prevention control interventions in time.

Virus shedding in respiratory specimens is longer in children with mild COVID, which will impose a challenge for infection control. 2019-nCoV RNA was not detected in serum samples in our study. Viremia could be related to the severity of disease because 2019-nCoV RNA was detected in blood samples obtained from 15% of adult patients with pneumonia [9]. Surprisingly, we also noted a high frequency (83.3%) of 2019-nCoV RNA detection in feces in mild patients and prolonged virus RNA shedding in feces for at least 2 weeks and even more than 1 month, which raises a question concerning whether the gastrointestinal tract may be another site of viral replication. The impact on 2019-nCoV shedding in feces on transmission model and infection prevention and control should be further assessed.
The COVID epidemic is now spreading globally. Further research and surveillance are crucial to help us understand the clinical characteristics and natural history of 2019-nCoV infection in children.
Notes

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Potential conflicts of interest.

The authors declare that they have no conflicts of interests, financial or otherwise, related to the publication of this study.
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| Patient | Admission date | City      | Age (month) | Sex   | Exposure setting | Index case | The interval between symptom onset and exposure to index case (days) | Number of secondary |
|---------|----------------|-----------|-------------|-------|------------------|------------|-------------------------------------------------------------------|---------------------|
| 1       | 19 Jan         | Shanghai  | 84          | Male  | Household        | Father     | 8                                                                 | Unknown             |
| 2       | 25 Jan         | Shanghai  | 131         | Female| Household        | Adult sister| 7                                                                 | Unknown             |
| 3       | 31 Jan         | Shanghai  | 131         | Female| Epidemic area    | Unknown    | 7                                                                 | Unknown             |
| 4       | 1 Feb          | Shanghai  | 108         | Male  | Household        | Wuhan Travellers | 3                                                                 | Unknown             |
| 5       | 3 Feb          | Shanghai  | 7           | Female| Household        | Grandfather | 10                                                                |                     |
| 6       | 30 Jan         | Qingdao   | 72          | Female| Household        | Grandmother | 2                                                                 |                     |
| 7       | 26 Jan         | Haikou    | 3           | Female| Epidemic area    | Friends    | 7                                                                 |                     |
| 8       | 1 Feb          | Sanya     | 48          | Female| Household        | Mother     | 10                                                                |                     |
| 9       | 27 Jan         | Sanya     | 96          | Female| Household        | Grandmother | 2                                                                 |                     |
| 10      | 27 Jan         | Hefei     | 60          | Male  | Household        |            | 7                                                                 |                     |
symptomatic cases including the child &

| Clinical characteristics |  |  |  |  |  |  |  |  |  |  |  |
|--------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Peak of fever (°C)       | 38.0 | 38.4 | 37.7 | 39.2 | afebrile | 38.5 | 38.2 | afebrile | 38.6 | 38.5 |  
| Duration of fever (days) | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   |  
| Cough                    | Yes | Yes | Yes | Yes | Yes | Yes |  | Yes | Yes | Yes |  
| Sneezing                 | Yes | Yes |  |  |  |  |  |  |  |  |  
| Stuffy nose              | Yes | Yes | Yes |  |  |  |  |  |  |  |  
| Rhinorrhea               | Yes | Yes |  |  |  |  |  |  |  |  |  
| Sore throat              | Yes | Yes | Yes |  |  |  |  |  |  |  |  
| Dyspnea                  |  |  |  |  |  |  |  |  |  |  |  
| Diarrhea                 |  |  |  |  |  |  |  |  |  |  |  

Treatment

| Treatment | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |  

Radiographic findings
| Chest X-ray | Normal | Normal | Retremonic Opacity on the left | Opacities in the right lung | Opacities in the right lung | Normal | Normal | Opacities in the right lung | Normal | Normal |
|-------------|--------|--------|-------------------------------|-----------------------------|-----------------------------|--------|--------|----------------------------|--------|--------|

**Laboratory findings**

| White blood cell count (×10⁹ /L) : | 16.0↑ | 5.9 | 6.7 | 3.2↓ | 8.0 | 6.0 | 9.7 | 5.4 | 11.9↑ | 12.5↑ |
| (normal range 3.9-9.9) | |

| Hemoglobin (g/dL) : | 12.8 | 14.2 | 13 | 15.2 | 11.3 | 13 | 12.3 | 13.1 | 12.1 | 14.4 |
| (normal range 11–16) | |

| Neutrophil count (×10⁹ /L) : | 11.2↑ | 3.4 | 3.2 | 1.1↓ | 2.0 | 1.6↓ | 4.2 | 1.3↓ | 8.07 | 7.4 |
| (normal range 2.0–7.0) | |

| Lymphocyte count (×10⁹ /L) : | 3.2 | 1.7 | 1.2 | 1.7 | 5.1 | 3.7 | 4.2↑ | 3.6 | 2.1 | 3.3 |
| (normal range 1.2–4.0) | |
| Test                        | Normal Range            | Result     | % Change |
|-----------------------------|-------------------------|------------|----------|
| Platelet count (×10⁹ /L)    | 162–341                 | 138 184 211 312 188 186 494↑ 311 357↑ 266 |          |
| C-reactive protein (mg/L)   | 0.0–8.0                 | 15.0↑ 8.0 16.0↑ 35.0↑ 8.0 7.0 5.6 0.5 3.1 4.8 |          |
| Procalcitonin (ng/dL)       | 0.0–0.5                 | 0.07 0.03 0.08 0.07 0.12 0.03 0.07 0.02 0.05 0.09 |          |
| Creatine kinase-MB (U/L)    | <25                     | 29.0↑ 14.9 42.3↑ 12.3 33.0↑ 13 12 27.0↑ 31.0↑ 19 |          |
| Alanine aminotransferase (U/L) | 9.0–50.0           | 17.0 7.7 19.8 26.2 100↑ 13.6 40.0 19.0 18.0 14.0 |          |
| Aspartate aminotransferase (U/L) | 15.0–40.0         | 33.0 21.4 27.5 19.7 142↑ 24.5 51.0↑ 28.0 20.0 34.0 |          |
| Urea (mmol/L)               | 3.7–4.1                 | 3.7 4.1 3.2 3.2 1.9↓ 3.8 0.5↓ 2.6↓ 3.0 3.0 |          |
Creatinine (µmol/L); (normal range 21–65)

|          | 29.0 | 54.0 | 54.0 | 48.0 | 13.0↓ | 58.9 | 16.0↓ | 23.0 | 38.0 | 33.0 |
|----------|------|------|------|------|-------|------|-------|------|------|------|

Lactate dehydrogenase (U/L); (normal range 110–290)

|          | 394↑ | 161  | 228  | 189  | 368↑  | 194  | 280   | Normal| Normal| 304↑ |
|----------|------|------|------|------|-------|------|-------|-------|-------|------|

D-dimer (µg/mL); (normal range 0·0–0·5)

|          | 0.6↑  | 0.3   | 0.6↑  | 0.2   | Normal |
|----------|-------|-------|-------|-------|--------|

Detection of 2019-nCoV RNA

| Nasopharyngeal/throat swabs | Positive | Positive | Positive | Positive | Positive | Positive | Positive | Positive | Positive | Positive |
|-----------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| Duration of virus shedding in respiratory swabs (days) | 12 | 22 | 8 | 8 | 6 | 15 | 8 | 12 | 14 | 15 |

| Stool | Positive | Negative | Positive | Positive | Positive | Not tested⁺ | Positive | Not tested⁺ | Not tested⁺ | Not tested⁺ | Not tested⁺ |
|-------|----------|----------|----------|----------|----------|-------------|----------|-------------|-------------|-------------|-------------|
| Duration of virus shedding in stool (days) | >30 | 10 | >20 | >19 | >18 | Not tested⁺ | >23 | Not tested⁺ | Not tested⁺ | Not tested⁺ | Not tested⁺ |
| Urine     | Negative | Negative | Negative | Negative | Negative | Negative | Not tested# | Negative | Not tested# | Not tested# | Not tested# |
|-----------|----------|----------|----------|----------|----------|----------|-------------|----------|-------------|-------------|-------------|
| Serum     | Negative | Negative | Negative | Negative | Negative | Negative | Not tested# | Negative | Not tested# | Not tested# | Not tested# |

*Patient 4 contacted 2 adult travellers from Wuhan who already had mild respiratory symptoms during the bus travelling and were confirmed with COVID after returning to Wuhan.

*The number of symptomatic secondary cases included the sum of the affected child in this case series and his/her family members who were exposed a common index case and developed symptoms.

*Not tested means the patient’s sample not being tested for 2019-nCoV RNA.