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Epidemiological and clinical characteristics of 35 children with COVID-19 in Beijing, China

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ABSTRACT

Importance: Within the coronavirus disease 2019 (COVID-19) global pandemic, more attention is warranted for whether this new infectious disease has unique manifestations in children.

Objective: To retrospectively determine the epidemiological and clinical characteristics of 35 children with COVID-19 in Beijing, China.

Methods: We collected data for 35 children diagnosed with COVID-19 who were admitted to Beijing Ditan Hospital from January 2020 to June 2020, and analyzed their epidemiological characteristics, clinical manifestations, laboratory examinations, chest imaging findings, treatments, and outcomes.

Results: The children comprised 18 boys (51.4%) and 17 girls (48.6%) aged 6 months to 15 years. All patients had clear epidemiological history, with family clusters accounting for 28 cases (80.0%) and clear tracing of exposure to high epidemic areas in the remaining 7 cases (20.0%). Four (11.4%) patients were classified as asymptomatic, 17 (48.6%) as acute upper respiratory infection, and 14 (40.0%) as mild pneumonia, with no severe or critical cases. Clinical manifestations were mild, including fever in 18 (51.4%), cough in 14 (40.0%), and nausea and diarrhea in 7 (20.0%) patients. White blood cell count was mostly normal (26 cases, 74.3%) or decreased (7 cases, 20.0%); lymphocyte percentage was increased in 24 (68.7%); neutrophil percentage was decreased in 25 (71.4%); alanine aminotransferase was increased in 3 (8.6%); and serum potassium was decreased in 4 (11.4%). Time to negative viral nucleic acid testing was 2–42 days (mean: 14.0 ± 9.4 days). Chest imaging examination revealed that 20 patients (57.1%) had different forms of lung inflammation. Treatment was mainly isolation and nutritional support. Eleven patients were treated with interferon atomization inhalation. No patients required oxygen therapy. All 35 children were cured and discharged. Length of hospital stay was 9–54 days (mean: 25.4 ± 13.8 days). During regular follow-up after discharge, 5 children showed positivity again in the viral nucleic acid test and were re-hospitalized for observation and treatment. The mean length of re-hospitalization stay was 10.8 days.

Interpretation: Children with COVID-19 mainly become infected within their family, and children of all ages are generally susceptible. The disease in children is mostly mild and the prognosis is good. Nucleic acid tests in some patients become positive again after discharge, suggesting that it is of great significance to carry out centralized isolation medical observations and active nucleic acid tests in close contacts for early detection of patients and routine epidemic prevention and control.

KEYWORDS
COVID-19, Children, Epidemiology, Family cluster

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INTRODUCTION

In December 2019, Wuhan of China reported an unexplained pneumonia, which was confirmed by whole-genome sequencing to be caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1,2] The World Health Organization finally named the disease as coronavirus disease 2019 (COVID-19).[3] Subsequently, COVID-19 epidemics of varying degrees appeared in many parts of the country. Although the epidemic in China has been relatively well controlled,[4] the global epidemic situation remains very severe, and prevention and control are very important. In the early stage of the epidemic, the confirmed cases were mainly middle-aged and elderly patients and those with underlying diseases. With increasing prevalence of the epidemic, reports of pediatric patients have gradually increased.[2,3] We need to pay close attention to whether this new infectious disease has unique manifestations in children, and determine how to achieve success in routine prevention and control of the COVID-19 pandemic in children. In the present study, we retrospectively analyzed the epidemiological and clinical characteristics of 35 children with confirmed COVID-19 in Beijing who were admitted to Beijing Ditan Hospital from January 2020 to June 2020, with the aim of providing more evidence for the diagnosis, treatment, prevention, and control of COVID-19 in children.

METHODS

Ethical approval

The study was approved by the Ethics Committee of Beijing Ditan Hospital (2020-009-01). Written informed consent was obtained from all patients or from a legal guardian.

Subjects

From January 2020 to June 2020, 35 children (age: < 16 years) with confirmed COVID-19 were admitted to Beijing Ditan Hospital. As a designated hospital for admission, our hospital has experienced three stages in admission of children with COVID-19. The first stage was January 2020 to February 2020, in which the domestic epidemic growth stage had Hubei Province as the main epidemic area, and all children admitted with COVID-19 were Hubei-related cases (n = 12) and Beijing-local cases (n = 3). The second stage was March 2020 to April 2020, with mainly imported COVID-19 cases, and all children admitted were from other countries or regions with high epidemics in the world (Europe, n = 11; United States, n = 1). The third stage was June 2020, in which all children were related to the Xinfadi market outbreak in Beijing (n = 8). All patients tested positive for SARS-COV-2 using nasal swabs, throat swabs, or sputum samples. Diagnosis and treatment followed the guidelines issued by the National Health Commission of the People's Republic of China (Trial version 8)[5] and recommendations for children with COVID-19 issued by the Pediatric Society of the Chinese Medical Association.[6]

Data collection

We collected demographic, epidemiological, clinical, laboratory, chest imaging, treatment, and outcome data for all children. Severity of COVID-19 was defined as asymptomatic, acute upper respiratory infection, and mild, severe, and critical pneumonia in accordance with the criteria described in the recommendations.[6] The epidemiological investigation included history of exposure to epidemic areas or close contact with a suspected COVID-19 patient within 2 weeks or cluster cases.[5]

Patients with normal body temperature for >3 days, significantly improved respiratory symptoms and lung infiltrates, and two consecutive negative SARS-CoV-2 nucleic acid tests from respiratory tract samples (sample interval: at least 24 h) were allowed to be discharged.

Statistical analysis

SPSS 22.0 was used for data analyses. Normally distributed measurement data were expressed as mean ± SD, and non-normally distributed measurement data are expressed as median and interquartile range.

RESULTS

Characteristics of the patients

The 35 patients with confirmed COVID-19 comprised 18 boys (48.6%) and 17 girls (51.4%). The age range was 6 months to 15 years and the mean age was 7.1 ± 4.2 years. Three patients were aged <1 year, 5 patients were aged between 1 and 3 years, 5 were preschool children aged 3–5 years, and 22 were aged >6 years (Table 1). Four patients had co-infections including two cases of bacterial infection and one each of mycoplasma infection and influenza A. Two patients had underlying diseases including one case of acute leukemia (stage of maintenance chemotherapy) and one of fatty liver disease. Twenty-five patients were permanent residents in Beijing and 10 were permanent residents in other cities.

Epidemiological history

All 35 patients had clear epidemiological history, including 28 (80.0%) with clear history of close contact with a confirmed COVID-19 patient and clear correlation with a high epidemic area who were all within family clusters. Parents, siblings, or other family members were diagnosed successively or jointly. The other 7 patients (20.0%) could be traced to clear history of travel or life in a high epidemic area, but no clear history of contact with a confirmed COVID-19 patient.

Of the 15 patients admitted in the first stage, 12 had clear history of family residence in Hubei and/or contact with confirmed patients, and 3 had history of close contact with confirmed patients in Beijing. The incubation period from exposure to symptom onset was relatively clear, with a range of 5–19 days (mean: 12 days).

For the imported cases admitted in the second stage and the cases related to the Xinfadi market outbreak in Beijing admitted in the third stage, the exact time of exposure was unknown, and most of them were confirmed by active nucleic acid test screening.

Clinical manifestations

The clinical manifestation data are shown in Table 1. Seven patients (20.0%) had no symptoms. Among the remaining patients with symptoms, 18 (51.4%) mainly showed fever, with peak body temperature of 37.5°C–40.0°C (mean peak: 38.6°C ± 0.7°C) and fever duration of 1–11 days (mean: 3.6 ± 3.2 days); 14 (40.0%) had cough or expectoration; and 7 (20.0%) had abdominal pain, vomiting, or diarrhea. Physical examination revealed 3 patients (8.6%) with pharyngeal hyperemia, and 32 patients (91.4%) without any other signs.

TABLE 1 Demographic and clinical data of 35 children with COVID-19

Characteristics	Number of patients, *n* (%)
Age (years)	
<1	3 (8.6)
1–<3	5 (14.3)
3–<5	5 (14.3)
≥5	22 (62.8)
No symptoms	7 (20.0)
Fever	18 (51.4)
Cough, expectoration	14 (40.0)
Abdominal pain, vomiting, or diarrhea	7 (20.0)
Sore throat, throat discomfort	6 (17.1)
Nasal congestion, runny nose	5 (14.3)
Headache, dizziness	2 (5.7)
Eye discomfort	1 (2.9)
Reduced sense of smell and taste	1 (2.9)
Fatigue	1 (2.9)
Rash	1 (2.9)
Pharyngeal congestion	3 (8.6)

COVID-19, coronavirus disease 2019.

Laboratory and radiologic findings

White blood cell count ranged from 3.55×10^9/L–12.1×10^9/L (mean: 6.56×10^9/L ± 2.27×10^9/L). White blood cell count was decreased in 7 (20.0%) and increased in 2 (5.7%) patients. Neutrophil percentage was decreased in 25 (71.4%), lymphocyte percentage was increased in 24 (68.6%), C-reactive protein (CRP) was increased (>5 mg/L) in 4 (11.4%), serum amyloid A was increased in 6 (17.1%), alanine aminotransferase (ALT) was increased in 3 (8.6%), myocardial enzyme CK-MB was increased in 1 (2.9%), serum potassium was decreased in 4 (11.4%), and blood glucose was increased in 1 (2.9%). Procalcitonin (PCT) and blood coagulation function were all normal (Table 2).

Thirty-three patients underwent chest CT examination and 2 patients underwent chest X-ray examination. Fifteen patients showed no abnormalities (42.9%), 8 (22.9%) had patchy/ground-glass opacities, 5 (14.3%) had enhanced lung texture and blurring, 5 (14.3%) had small/micro lung nodules, and 1 (2.9%) each had peribronchitis and lung interstitial changes.

TABLE 2 Laboratory and radiographic findings of 35 children with COVID-19

Items	Patients
Laboratory findings	
White blood Cell count ($\times 10^9$/L)	6.56 ± 2.27
< 4	7 (20.0)
> 10	2 (5.7)
CRP (mg/L)	0.85 (0.20–1.80)
> 5	4 (11.4)
SAA (mg/L)	3.60 (1.65–25.29)
10–100	4 (11.4)
>100	2 (5.7)
ALT > 40 U/L	3 (8.6)
CK-MB > 25 U/L	1 (2.8)
Serum potassium < 3.5 mmol/L	4 (11.4)
Radiologic findings	
Normal	15 (42.9)
Patchy/ground-glass opacities	8 (22.9)
Enhanced lung texture and blurring	5 (14.3)
Small/micro lung nodules	5 (14.3)
Peribronchitis	1 (2.9)
Interstitial abnormalities	1 (2.9)

Data was shown as mean ± standard deviation, median (interquartile range), or *n* (%). CRP, C-reactive protein; SAA, serum amyloid A; ALT, alanine aminotransferase; CK-MB, creatine kinase-muscle and brain type.

Severity of COVID-19

Although 7 patients did not have any clinical symptoms, 3 had radiologic abnormalities, so finally 4 patients (11.4%) were classified as asymptomatic. Seventeen patients (48.6%) were classified as acute upper respiratory infection, and 14 (40.0%) as mild pneumonia. No severe or critical cases were observed.

Treatments

All children received treatment involving isolation, adequate rest, and nutritional support. Antiviral drugs, antibiotics, and other treatment were selected according to the disease condition. Eleven patients (31.4%) were treated with nebulized interferon α2b and the others were not. The time until SARS-CoV-2 nucleic acid test became negative was 11.6 ± 6.2 days in the interferon aerosol treatment group and 8.9 ± 4.9 days in the non-interferon treatment group, with no significant difference ($P > 0.05$). Also there was no significant difference between the two groups in the laboratory test, e.g. white blood cell count and neutrophil count. Twelve patients were treated with traditional Chinese medicine; 5 patients was treated with azithromycin; and 4 was treated with compound glycyrrhizin. None of the children received oxygen therapy.

Outcomes

As of 21 July, 2020, all children had been cured and discharged. Length of hospital stay ranged from 9–54 days (mean: 25.4 ± 13.8 days). Time to first negative viral nucleic acid testing was 2–42 days (mean: 14.0 ± 9.4 days). The large difference between length of hospital stay and time of nucleic acid conversion was because some children had delayed discharge for their parents with COVID-19 did not meet the discharge standards.

Twenty-five patients who were permanent residents in Beijing underwent follow-up in Beijing. After the first discharge, 5 patients were re-hospitalized for positive results in regular nucleic acid testing. Among these patients, 3 had no clinical symptoms, 1 had low fever for 1 day, and 1 had sore throat for 1 day. Chest CT examination was negative. The interval between the positive nucleic acid recheck and the two consecutive negative tests at the secondary hospitalization was 2–10 days (mean: 4 days), and the mean length of re-hospitalization stay was 10.8 days, which was significantly shorter than the first admission. The 10 patients who were permanent residents in other places returned to their local areas for follow-up after discharge from our hospital. The outcomes for these patients remain unknown.

DISCUSSION

COVID-19 has become a major global public health event. Adult cases are more common and children cases are less, which may be due to the relative isolation of children from the outside and fewer exposure opportunities. There are limited data on COVID-19 in children, and it was once considered that children are not susceptible.[2-4] However, with the spread and progression of the epidemic, more children are inevitably exposed to infection by family members, and the number of pediatric patients has increased significantly, especially among younger children. Therefore, early detection, isolation, treatment, and prevention and control measures tailored to the characteristics of the disease in children require great attention.

In China, the epidemic has been characterized by a serious community epidemic in Wuhan and other areas in Hubei province during the early stage of the epidemic, and no subsequent large-scale community epidemics in other provinces and cities.[4] With the effective control of the epidemic in Hubei province and strict prevention and control measures across the country, there were only small-scale outbreaks of clustered cases, sporadic cases, and imported cases during the later stage. Within the epidemic in China, children comprise a special group that has differences from adults. To a large extent, the infections in children arose from cross-infection after contact with close family members. More than 90% of children in Wuhan had clear epidemiological exposure history, almost all of them within their families.[7] Statistics on children diagnosed with COVID-19 in Wuhan and six northern provinces in China found that 70%–90% of cases in children had clear contact with confirmed patients, and up to 90% of children with confirmed COVID-19 had evidence of family clusters.[7-10] The proportion of family clusters in the present study was also high at 80.0%. Therefore, centralized isolation of confirmed cases and active nucleic acid screening in close contacts are very effective methods for protection of susceptible children and early detection of infected children.

The clinical manifestations of COVID-19 in children were usually mild and non-specific. Asymptomatic infections were reported to be common among confirmed cases in children, accounting for up to 50%–70%.[9-13] Symptomatic patients exhibited fever and cough as the main clinical manifestations, accounting for 42%–76% and 48%–54%, respectively.[4] In some cases, diarrhea was the main clinical manifestation, accounting for about 10%.[8,9] A report on 2572 pediatric patients in the United States showed that mild infections were the most common, with few patients requiring hospitalization, hospitalization rate of 6%–20%, and ICU admission necessary in only 0.58%–2%.[10] Other study from China also showed that 90% of cases in children were asymptomatic and mild.[14-16] There were no severe or critical cases in the present study and the overall prognosis was good. One possible reason maybe all the child patients in this study were detected by active screening when their family members were diagnosed with COVID-19, and they were treated or cared in the early stage. However, the occult and contagious characteristics of the asymptomatic and mild features in children make it very difficult to ensure effective isolation and limit secondary transmission,[4] especially now that the epidemics have been effectively controlled in China. Strict epidemiological tracking and nucleic acid screening are particularly important.

There were no significant abnormalities in white blood cell count, lymphocyte count, neutrophil count, and PCT, 3 patients with increased ALT, 1 with increased myocardial enzyme CK-MB, and 4 with increased CRP in the present study. This may be related to the disease being mild.[17,18] In a meta-analysis, Henry et al[19] found that, among children with mild COVID-19, only children aged <1 year had significant increases in white blood cell, lymphocyte, and platelet counts, slight increases in ALT, AST, and LDH, and no changes in CRP, PCT, and CK-MB; among severe cases, lymphocyte counts did not decrease as significantly as those in adult severe cases, but the rising trends in LDH, CRP, and PCT levels were similar to those in adult severe cases. Therefore, continuous monitoring of CRP, PCT, and LDH levels in children with COVID-19 is important to assess the progression of the disease. In particular, elevated CK-MB levels indicate the possibility of heart injury and highlight the importance of monitoring cardiac biomarkers,[20] timely and effective detection of the tendency for mild cases to become severe, and appropriate transfer to the ICU for early treatment.

The chest imaging results were highly consistent with the diversity of chest CT manifestations in children with COVID-19 with increased lung texture and small/micro nodules each in 14.3% of the patients and patchy/ground glass opacities and viral pneumonia changes each in 11.4% of the patients. However, there were also atypical manifestations. Special attention should be paid to discriminate infectious pneumonia from other bacteria, virus, or mycoplasma infections. Some experts recommend that follow-up chest CT examinations are not needed for mild or moderate disease in pediatric patients, with a view to reducing unnecessary radiation exposure in children.[13]

With the global spread of the COVID-19 epidemic, recent studies in Europe and the United States found that some children with SARS-COV-2 infection exhibited similar or atypical Kawasaki disease manifestations, but had significantly more serious disease than Kawasaki disease, often accompanied by multiple system involvement. Cardiovascular system involvement was common. In severe cases, heart failure, shock, and macrophage activation syndrome occurs, and was designated MIS-C by the United States Centers for Disease Control and Prevention.[21-25] However, the etiological relationship between SARS-COV-2 infection and MIS-C has not been clearly determined. There are no reports of MIS-C cases in China,[26] possibly because of the small number of cases, but we still need to be wary of MIS-C.

The prognosis of the children with COVID-19 was good in the present study. We performed interferon α2b treatment in 11 children. Statistical analysis showed that there was no difference in the time to nucleic acid conversion between the groups with and without interferon treatment. Therefore, isolation, nutritional support, and symptom treatment are the main treatment strategies for mild and moderate cases and active antiviral treatment is often unnecessary. However, it remains important to closely observe the progress of the disease in children with mild infection, paying particular attention to the tendency for high-risk cases in children to become more severe.[6]

The nucleic acid results became positive again during regular follow-up in some of the children after discharge. These patients had no or mild clinical symptoms, and the nucleic acid results returned to negative after a short period of observation. However, both confirmed cases and asymptomatic cases were contagious.[1,4,5] Therefore, in the face of the epidemic, we cannot relax prevention and control within the family and in kindergartens, schools, and dormitories after return to work or school. We need to teach children of all ages the concepts and methods for preventing respiratory infectious diseases, especially room ventilation, maintaining safe social distance, wearing masks indoors or in relatively crowded places, and correct hand hygiene methods. It is particularly important for young people to gain scientific hygiene knowledge and habits from an early age. There were some limitations to this study, including the small number of cases and the imperfect data. Further studies are warranted to determine more characteristics of COVID-19 in children.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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