Analysis of 23 Pediatric Patients with SARS-CoV-2 Infection in Anhui Province, China

Lulu Fang

First Affiliated Hospital of Anhui Medical University

Wang Wang

First Affiliated Hospital of Anhui Medical University

Shaohu Huo

First Affiliated Hospital of Anhui Medical University

Jun Liu

The People Hospital of Bozhou

Ming feng Han

The Second People's Hospital of Fuyang

Ming Wei

Maanshan Municipal Hospital for Infectious Diseases

Hui Gao

First Affiliated Hospital of Anhui Medical University

Sheng-Gang Ding (✉ dingsg@ahmu.edu.cn)

First Affiliated Hospital of Anhui Medical University

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Abstract

Background: The global spread of coronavirus disease 2019 (COVID-19) continues to threaten all human health worldwide. Although the symptoms, signs, responses, and outcomes associated with the disease varies for individuals, few studies have reported on pediatric patients with COVID-19.

Methods: This study retrospectively reviewed the medical records from three tertiary hospitals in Anhui province, China, of 23 children with COVID-19. Here, epidemiologic characteristics, clinical features, laboratory test results, and treatment strategies for these pediatric patients are reported and analyzed.

Results: In total, 23 children with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were analyzed. All patients were given a nucleic acid detection test for SARS-CoV-2, and positive results confirmed the diagnosis of COVID-19. Ten patients (43.5%) were female, and 19 patients (82.6%) had defined exposure history and familial clustering. The youngest patient was 16 months of age, the oldest, 17 years. The clinical symptoms of all included pediatric patients with SARS-CoV-2 infection were mild, with cough (12, 52.2%) and fever (10, 43.5%) being the most frequent, making their symptoms indistinguishable from common respiratory infections. There was no difference in clinical manifestation between males and females ($P > 0.05$). Eight patients (34.8%) showed changes on chest computed tomography imaging. The median level of each laboratory test parameter was within the normal reference range. Treatments primarily included antiviral therapies, traditional Chinese medicine therapies, and symptomatic supportive treatment.

Conclusions: The symptoms of all 23 pediatric patients with SARS-CoV-2 infection included in this study were mild. Because the primary presenting symptoms were indistinguishable from common respiratory infections and because most patients had an exposure history and familial clustering, we recommend supporting the diagnosis of mild or atypical COVID-19 in children with detailed epidemiologic information and chest computed tomography imaging as well as with nucleic acid detection tests. Obtaining a correct diagnosis in the early stage of the disease will contribute to controlling the spread of SARS-CoV-2 infection and to providing more immediate relevant treatment for infected children.

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a single-stranded RNA, is a novel lineage betacoronavirus and has a unique genomic character that may be directly related to its pathogenic mechanism^[1,2]. SARS-CoV-2 is responsible for a cluster of acute respiratory illnesses called coronavirus disease 2019 (COVID-19). The main types of COVID-19 include common, mild, and severe types. The clinic symptoms of the common type of COVID-19 includes fever, fatigue, headache, respiratory symptoms such as cough, expectoration, nasal congestion, and runny nose, and gastrointestinal symptoms such as nausea, diarrhea, and vomiting. In the severe COVID-19 type, patients present with coma, septic shock, dyspnea, and even death^[3-6]. The current literature reporting on cases of children with SARS-CoV-2 infection is relatively limited. Therefore, in the present study, we described baseline

characteristics, clinical manifestations, laboratory test results, radiologic imaging results, and treatment strategies from a series of 23 consecutive pediatric patients with COVID-19 reported from three centers in Anhui province, China.

Methods

All included consecutive patients with SARS-CoV-2 infection under 18 years of age were admitted to one of three tertiary hospitals located in Anhui province between January 27, 2020, and February 14, 2020. For the diagnosis of SARS-CoV-2 infection, a throat swab from each patient was collected, and a positive nucleic acid detection test result confirmed the diagnosis.

The following epidemiologic information and sociodemographic characteristics were obtained for each patient: sex, age, body weight, history of exposure, familial clustering, and travel history. Clinical symptoms, laboratory test results, imaging results, and therapeutic strategies were obtained from electronic medical records. All 23 patients had results from routine blood work tests. Only patients from Fuyang City had results of other laboratory tests. Descriptive statistics and other statistical analyses were conducted using SPSS, version 26. Binary variables are presented as No. (%) and were analyzed using Fisher exact tests. Quantitative variables are described by minimum and maximum values, medians, and 25th and 75th percentiles (interquartile ranges). Two-sided values of $P < 0.05$ were considered statistically significant.

Results

In total, 23 children with SARS-CoV-2 infection were included in this analysis. Ten cases (43.5%) were female, and 19 cases (82.6%) had a defined exposure history and familial clustering. The median age was 132 months, and the youngest case was 16 months of age. Cough (12, 52.2%) and fever (10, 43.5%) were the most frequent clinical symptoms. The highest temperature on admission was 39.3 °C. Fatigue and expectoration was observed in only one patient, a female. The lowest blood oxygen saturation was 90%. The highest respiration rate was 24/min. There was no difference in clinical manifestations between males and females ($P > 0.05$). The duration of respiratory symptoms ranged from 3 to 12 days. Of note, eight (34.8%) children had no symptoms but tested positive for SAR-CoV-2. No child had complications. As of February 14, 2020, 10 patients remain hospitalized. For additional demographic and clinical characteristics, see Table 1 and Fig. 1.

Table 1
Demographic and clinical characteristics of the continuous variables for the 23 included pediatric patients

Variable	Minimum	25th Percentile	Median	75th Percentile	Maximum
Age (mo)	16.0	72.0	132.0	168.0	204.0
Body weight (kg)	11.0	30.0	45.0	55.0	73.0
Duration of hospitalization (d)	4.0	9.0	10.0	14.0	20.0
No. of positive COVID-19 test results	1.0	1.0	2.0	2.0	5.0
Total No. of SARS-CoV-2 detection tests given per patient	3.0	4.0	5.0	8.0	14.0
Maximum body temperature (°C)	36.6	36.9	37.0	37.5	39.3
Body temperature at admission (°C)	35.8	36.5	36.7	36.8	37.6
Systolic blood pressure at admission (mmHg)	82.0	110.0	118.0	123.0	131.0
Diastolic blood pressure at admission (mmHg)	50.0	67.3	78.5	85.0	90.0
Heart rate at admission	71.0	80.0	84.0	90.0	120.0
Respiration rate at admission (per min)	15.0	18.0	20.0	20.5	24.0
Blood oxygen saturation (%)	90.0	98.5	99.0	100	100

A total of eight cases (34.8%) showed changes on chest computed tomography (CT) imaging. Three children showed bilateral imaging changes, including two with ground-glass opacity and one with ground-glass opacity mixed with consolidation shadows. Five cases showed unilateral ground-glass opacity, with two on the left side of the chest and three on the right side.

The overall description of the results of the routine blood tests conducted for all 23 included patients on admission are shown in Fig. 2. The median level of each parameter was within normal reference ranges. Of note, three patients had white blood cell counts higher than the normal reference range. Two patients had neutrophil percentages higher than the reference range, whereas three patients had percentages lower than the reference range. Two patients had neutrophil counts lower than the reference range, whereas neutrophil counts were higher than the reference range for two patients. Four patients had lymphocyte percentages lower than the reference range, but three patients showed marginally higher lymphocyte percentages. The hemoglobin levels in two patients were slightly higher than reference ranges, whereas those of two patients were slightly lower. The platelet counts in two patients were

slightly higher than the reference range. The additional results of the laboratory tests for children from the Fuyang City center are presented in Table 2.

Table 2

Results of additional laboratory tests for the pediatric patients at the Fuyang City center included in this study

Variable	No.	Minimum	25th Percentile	Median	75th Percentile	Maximum
Prothrombin time (s)	7	10.30	10.4	11.1	12.8	12.90
Activated partial thromboplastin time (s)	7	12.30	25.5	25.7	31.2	35.30
D-Dimer (μg/L)	7	0.12	0.15	0.21	0.29	0.52
Albumin (g/L)	8	9.30	40.125	41.7	45.05	48.80
Alanine aminotransferase (U/L)	10	1.00	7.75	11.0	18.75	34.00
Aspartate aminotransaminase (U/L)	10	17.00	17.75	21.0	27.0	40.00
creatine kinase (U/L)	10	40.00	64.0	73.5	86.25	115.00
creatine kinase myocardial band (U/L)	10	2.00	7.0	9.0	16.0	28.00
Total bilirubin (μmol/L)	10	4.00	5.15	7.65	9.65	29.30
K ⁺ (mmol/L)	10	3.56	3.9025	4.26	4.515	4.71
Na ⁺ (mmol/L)	10	134.90	137.825	139.0	141.1	141.90
Blood urea nitrogen (mmol)	10	2.50	2.925	3.7	4.125	5.00
Creatinine (μmol/L)	10	31.00	38.0	55.0	78.0	81.00
Lactate dehydrogenase (U/L)	10	143.00	178.0	232.5	264.5	284.00
Glucose (U/L)	10	4.77	4.97	5.115	5.965	8.18
C-reactive protein (mg/L)	9	0.00	0.30	1.2	11.15	46.00
Procalcitonin (ng/mL)	7	0.02	0.03	0.05	0.07	0.07
T lymphocyte (%)	8	49.78	65.52	69.41	72.765	75.72
B lymphocyte (%)	8	11.28	12.07	16.46	21.45	23.76
CD4 (%)	8	25.84	28.93	33.38	38.285	44.60
CD8 (%)	8	23.36	25.76	30.72	36.71	38.74
CD4/CD8	8	0.82	0.8525	1.13	1.32	1.78
Natural killer cells(%)	8	61.00	101.75	230.0	309.75	354.00

For treatment, all patients received antiviral therapy, which included interferon, lopinavir plus ritonavir, or arbidol hydrochloride. One child (4.3%) received gamma globulin treatment, and one received aerosol inhalation of budesonide combined with terbutaline. Other therapies, included ibuprofen suspension as well as traditional Chinese medicine, mainly Lianhua Qingwen Granule, a Chinese herb decoction, and Shufeng Jiedu Capsule. Eight pediatric patients received nasal continuous positive airway pressure therapy. Overall summaries of the antiviral and traditional Chinese medicine therapeutic strategies are shown in Fig. 3.

Discussion

In this study, we reported on 23 pediatric patients with confirmed SAR-CoV-2 infection. Most patients had a definite family source of exposure. None of the patients experienced severe pneumonia, and their laboratory values showed few results beyond normal reference ranges. Studies have found that lower angiotensin-converting enzyme 2 levels and the immature function of the immune system in children may hamper production of a robust immune response, cytokine storm, and severe complications [7–9], which may underlie the differences in clinical manifestations, complications, and prognoses between children and adults [10–12]. Adverse prognostic factors in COVID-19 include older age (> 70 years), diabetes, uncontrolled hypertension, chronic obstructive pulmonary disease, and coronary artery disease, which are more common among adults than children [13].

The most common clinical features observed among children with COVID-19 included mild symptoms, such as dry cough, fever, sore throat, or diarrhea. Severe symptoms, such as dyspnea, acute renal failure, abnormal coagulation, sepsis, sepsis shock, and death, have been reported in children with COVID-19 [5, 14, 15], but the number of such severe cases is less than in adults [16–20]. These symptoms are also common in respiratory infections caused by other viruses, such as influenza, adenovirus, respiratory syncytial virus, parainfluenza, and rhinovirus [21, 22]. The results of laboratory tests conducted in adults with COVID-19 have shown elevated levels of serum ferritin, alanine aminotransferase, C-reactive protein, interleukin 6, and cardiac troponin [23]. Few studies have examined laboratory markers in children. Some studies have found that children with COVID-19 had leucocyte counts and lymphocyte levels and proportions that are within normal reference ranges [13, 24–26] although there have been a few cases of children with lymphocytopenia, neutrophilia, or neutropenia [27, 28]. Zou et al. and others have found that lower platelet counts are associated with higher risk of severe COVID-19 [29, 30]. However, the children assessed in our study had laboratory markers that were generally within normal reference ranges.

Chest CT may aid in the clinical diagnosis of COVID-19 in children [31]. Commonly reported imaging findings among patients with COVID-19 include ground-glass opacity, consolidation, or interlobular septal thickening [21–34]. The lesions observed in our study were consistent with those that found ground-glass opacity and consolidation [25, 28, 32, 34]. CT imaging may differentiate among other virus infections for assisting in clinical diagnoses. Adenovirus tends to cause higher density, fewer subpleural, and more consolidation lesions. Influenza virus has been reported to have grid like changes. Respiratory syncytial

virus may cause thickening of the bronchial wall. However, some patients with mild or moderate symptoms also have normal chest CT imaging results^[34–37]; thus the value of radiologic approaches in the diagnosis of COVID-19 among pediatric patients will require further study and discussion.

At present, there are no specific inhibitors of SARS-CoV-2, and vaccines against the virus are under research and development. The National Health Commission of the People's Republic of China published guidelines for the treatment of novel coronavirus pneumonia that include general treatment, oxygen support, antiviral treatment, circulatory support treatment, convalescent plasma therapy, and Chinese medicine treatment^[38, 39]. For most patients with COVID-19 displaying mild symptoms, the therapeutic effects of symptomatic and supportive treatments, traditional Chinese medicine^[40, 41], and antiviral treatments, are acceptable. However, an inflammatory cytokine storm is commonly observed in patients with severe symptoms who become critically ill with COVID-19. Thus, control of the inflammatory response at an early stage by treatment with cytokine antagonists, immunomodulators, or corticosteroids may avoid poor prognoses; however, the correct therapeutic timing, usage, dosage, and indications for corticosteroid use all need to be considered^[42]. In addition, convalescent blood products and blood purification, such as through plasma exchange, adsorption, perfusion, or blood/plasma filtration^[43], should also be considered. Some studies have also assessed the effects of angiotensin-converting enzyme 2 activators^[44–46]. Further understanding of the pathogenesis of SARS-CoV-2 will contribute to more effective treatment of the disease.

In our study, all patients had mild symptoms and were in the early stage of the infection. Nasal continuous positive airway pressure was performed and antiviral therapies were provided, which mainly included lopinavir/ritonavir and arbidol hydrochloride, and traditional Chinese medicine was administered. Although the prognoses of these patients were good, they were not followed-up after hospital discharge. In addition, the number of cases was limited; thus, the value of these treatment strategies will need to be further studied.

Conclusions

In conclusion, it is necessary to distinguish SARS-CoV-2 infections from other viral infections when pediatric patients present with fever, dry cough, fatigue, nasal congestion, runny nose, nausea, diarrhea or vomiting. In addition to nucleic acid detection tests for SARS-CoV-2, detailed epidemiologic information and Chest CT imaging should be considered for children with suspected COVID-19.

Abbreviations

COVID-19: coronavirus disease 2019

SARS-COV-2: severe acute respiratory syndrome coronavirus 2

ACE2: angiotension-converting enzyme 2

CT: computerized tomography

Declarations

Ethics approval and consent to participate

This study was approved by Ethics Committee of The First Affiliated Hospital of Anhui Medical University (Approval No.Quick-PJ-2020-09-09) and was conducted consistent with the Declaration of Helsinki. All participants or their parents/guardians provided written informed consent before participating in the study.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Lulu Fang, Wang Wang, Shaohu Huo and Hui Gao analyzed and interpreted patients data. Lulu Fang was a major contributor in writing the manuscript. Jun Liu^{2#}, Ming-Feng Han^{3#}, Ming Wei⁴ and Sheng-Gang Ding collected patients data. All authors read and approved the final manuscript.

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Figures

Figure 1

Characteristics of binary variables for all 23 pediatric patients. Values of P are for male vs. female patients.

Figure 2

Box plot showing the results of routine blood tests for all included patients. The horizontal line in each box represents the median value; the box bottom, the first quartile; the box top, the third quartile; and the error bars, the minimum and maximum values. WBC represents white blood cell; N, neutrophils; and L, lymphocytes.

Figure 3

Summary of drug treatments for all included patients.