

# Clinical and Epidemiological Features of 46 Children <1 Year Old With Coronavirus Disease 2019 in Wuhan, China: A Descriptive Study

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The number of coronavirus disease 2019 (COVID-19) cases has exceeded 10 million. However, little is known about the epidemiology and clinical characteristics of COVID-19 infants. We collected medical information of 46 confirmed patients (<1 year old) and retrospectively analyzed epidemiological history, clinical symptoms, and laboratory test results. The median age was 5 (interquartile range, 2–7) months. Sixteen cases had fever and 27 cases had cough. Moderate disease was present in 40 cases and cardiac injury occurred in 38 cases, following by liver dysfunction in 20 cases and lymphocytosis in no cases. Of all infant patients, 2 received invasive mechanical ventilation and 1 died with multiple organ dysfunction syndrome.

**Keywords.** children; clinical features; SARS-CoV-2; outcome.

In December 2019, Wuhan Municipal Health Commission, China, reported an unexplained cluster of pneumonia cases in Wuhan, Hubei Province. Soon after, the etiology of this pneumonia was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease was eventually named as coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) [1, 2]. COVID-19 has rapidly

spread across the globe via person-to-person transmission [3, 4]. As of 9 May 2020, the WHO has confirmed 3 855 788 cases of COVID-19 and 265 862 deaths worldwide, including 84 416 cases and 4 643 deaths in China [5].

Persons of all ages are generally susceptible to SARS-CoV-2 infection, including children and infants [6]. Based on the COVID-19 situation report published by WHO, approximately 2.4% of confirmed cases in China were made up of pediatric cases [7, 8]. A review that enrolled pediatric patients published on 30 January 2020 showed that among 9692 confirmed cases of SARS-CoV-2, 28 cases were aged from 1 month to 17 years [8]. Compared with cases in adults, pediatric COVID-19 cases were apt to experience milder symptoms or no symptoms and tended to have quicker recovery and better prognosis [8, 9]. Up to now, only 1 pediatric death due to COVID-19 was reported in China, an infant who was 10 months old and complicated with intussusception [10].

Although the pandemic is still accelerating, studies in pediatric patients, especially younger child cases, with COVID-19 are limited. Our primary aim was to reveal more data on epidemiological features, clinical characteristics, diagnostic tests, treatment, and prognosis of COVID-19 in children aged <1 year.

## METHODS

A total of 46 infants (aged <1 year) with confirmed COVID-19 were enrolled from 26 January to 15 March 2020 at Wuhan Children's Hospital, China. Confirmed COVID-19 cases were diagnosed by positive reverse-transcription polymerase chain reaction on SARS-CoV-2 nucleic acid via throat swab. Epidemiological history, clinical characteristics, examination and test results, and treatment and outcome data were extracted from hospital electronic medical records. The severities of COVID-19, including asymptomatic, mild, moderate, severe, and critical, were defined on the basis of the clinical features, laboratory testing, and chest radiography [7]. Continuous variables were shown as median and interquartile range (IQR). Categorical variables were expressed as frequency or percentage. This was a retrospective case series study.

## RESULTS

### Clinical Characteristics

A total of 46 pediatric patients <1 year old (IQR, 2–7 months) infected with SARS-CoV-2 were included in this study. Of these cases, 39 (84.78%) occurred in children aged 28 days to 1 year, 5 (10.87%) were infants aged 0–7 days, and 2 (4.37%) were 7–28 days old. Twenty-five (54.35%) patients were male, and 21

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(45.65%) were female. Thirty-three infant patients had a history of household contact with their SARS-CoV-2–infected family members. The majority of the 46 pediatric patients had no comorbidities, whereas 4 (8.70%) cases presented atrial septal defect, 4 (8.70%) had hypogammaglobulinemia, 1 (2.17%) experienced intussusception, and 1 (2.17%) underwent brain trauma. Among these infant patients, 2 (4.35%) were asymptomatic, 2 (4.35%) had mild disease, another 2 (4.35%) suffered severe or critical disease, and the remaining 40 (86.96%) experienced moderate disease. The most frequent symptoms were cough (27 [58.7%]) and fever (16 [34.78%]). Other symptoms were less common, including vomiting (5 [10.87%]), nasal congestion, and rhinorrhea (3 [6.52%]), dyspnea (1 [2.17%]), tachypnea (1 [2.17%]), diarrhea (1 [2.17%]), and sneezing (1 [2.17%]) (Table 1).

### Laboratory Examination

White blood cells were depressed in 3 patients (6.52%) and abnormally elevated in 4 (8.70%) cases. Six patients (13.04%) showed decreased levels of neutrophils and 3 (6.52%) had aberrant high levels. Lymphocytosis occurred in one-third of infants (13 [28.26%]). The serum albumin level was decreased in 8 cases (18.18%) and bilirubin, alanine aminotransferase, and aspartate aminotransferase were increased in 6 (13.64%), 11 (25.00%), and 20 (45.45%) patients, respectively. Elevated levels of lactate dehydrogenase, creatine kinase, and creatine kinase MB were documented in 23 (52.27%), 10 (22.72%), and 38 (86.36%) cases, respectively (Table 1).

The inflammatory biomarkers procalcitonin and high-sensitivity C-reactive protein were significantly elevated in 3 (6.52%) and 8 (19.05%) patients, respectively. CD3<sup>+</sup> T-cell and CD4<sup>+</sup> T-cell values were increased in 10 (28.57%) and 14 (40.0%) cases, respectively, along with CD19<sup>+</sup> B-cell elevation in 16 (47.51%) patients. Elevated levels of cytokines were present in a proportion of patients, including interleukin (IL)–4 in 2 (5.88%), IL-6 in 1 (2.94%), IL-10 in 15 (44.12%), tumor necrosis factor alpha (TNF- $\alpha$ ) in 3 (8.82%), and interferon- $\gamma$  in 4 (11.76%) patients (Table 1).

### Treatment and Clinical Outcomes

Among the 46 pediatric cases, 41 (91.30%) were treated with interferon- $\alpha$ , 21 (45.65%) received budesonide suspension, 13 (28.26%) received antibiotic therapy, and 7 (15.22%) were treated with antiviral therapy. Only 2 (4.35%) severe cases needed invasive mechanical ventilation. Of these infants, complications occurred in 41 cases (89.13%) including 20 (45.45%) with liver dysfunction, 38 (86.36%) with cardiac injury, 3 (6.52%) with acute gastroenteritis, and 1 (2.17%) with multiple organ dysfunction syndrome. The duration of viral shedding, the time from the onset of symptoms till the negative detection of SARS-CoV-2 RNA, was 13 days (IQR, 8–15 days) and the

**Table 1. Clinical Characteristics and Laboratory Findings of 46 Pediatric Patients <1 Year Old Infected With Coronavirus Disease 2019**

Characteristic	No. (%)
Age	
Median (range), mo	5 (2–7)
Subgroup	
0–7 d	5 (10.87)
7 d–28 d	2 (4.37)
28 d–1 y	39 (84.78)
Male sex	25 (54.35)
Comorbidities	
Atrial septal defect	4 (8.70)
Hypogammaglobulinemia	4 (8.70)
Intussusception	1 (2.17)
Brain trauma	1 (2.17)
Infection in a family member	
No	13 (28.26)
Yes	36 (71.74)
Signs and symptoms	
Fever	16 (34.78)
37.3°C–38.5°C	5 (10.87)
38.5°C–39.0°C	6 (13.04)
>39.0°C	5 (10.87)
Cough	27 (58.70)
Vomiting	5 (10.87)
Nasal congestion and rhinorrhea	3 (6.52)
Dyspnea	1 (2.17)
Tachypnea	1 (2.17)
Diarrhea	1 (2.17)
Sneezing	1 (2.17)
Type of severity of illness	
Asymptomatic	2 (4.35)
Mild	2 (4.35)
Moderate	40 (86.96)
Severe and critical	2 (4.35)
Laboratory tests	
Total bilirubin, $\mu\text{mol/L}$ (ref: 2–19) <sup>a</sup>	7.25 (5.33–11.50)
Increased	6 (13.64)
Normal	37 (84.10)
Decreased	1 (2.27)
Albumin, g/L (ref: 39–53) <sup>a</sup>	43.05 (39.70–44.90)
Increased	0
Normal	36 (81.82)
Decreased	8 (18.18)
ALT, U/L (ref: 7–45) <sup>a</sup>	29 (21.00–46.50)
Increased	11 (25.00)
Normal	33 (75.00)
Decreased	0
AST, U/L (ref: 0–50) <sup>a</sup>	48.00 (38.00–61.00)
Increased	20 (45.45)
Normal	24 (54.55)
Decreased	0
Blood urea nitrogen, mmol/L (ref: 2.9–7.1) <sup>a</sup>	2.56 (1.86–4.05)
Increased	2 (4.55)
Normal	18 (40.91)
Decreased	24 (54.55)
Creatinine, $\mu\text{mol/L}$ (ref: 27–62) <sup>a</sup>	21.05 (17.80–25.70)
Increased	2 (4.55)
Normal	5 (11.36)

**Table 1. Continued**

Characteristic	No. (%)
Age	
Decreased	37 (84.09)
LDH, U/L (ref: 120–300) <sup>a</sup>	326.50 (265.00–403.25)
Increased	23 (52.27)
Normal	21 (47.73)
Decreased	0
Creatine kinase, U/L (ref: 20–250) <sup>a</sup>	122.50 (81.75–227.50)
Increased	10 (22.72)
Normal	34 (77.27)
Decreased	0
CKMB, U/L (ref: 0–25) <sup>a</sup>	35.50 (29.50–51.50)
Increased	38 (86.36)
Normal	6 (13.64)
hs-CRP, mg/L (ref: 0–3) <sup>a</sup>	4.60 (1.23–12.00)
Increased	8 (19.05)
Normal	34 (80.95)
Procalcitonin, ng/L (ref: 0–0.5) <sup>a</sup>	0.27 (0.23–0.36)
Increased	3 (6.52)
Normal	43 (93.48)
White blood cell count, ×10 <sup>9</sup> cells/L (ref: 5.5–12.0) <sup>a</sup>	8.16 (6.70–10.18)
Increased	4 (8.70)
Normal	39 (84.78)
Decreased	3 (6.52)
Neutrophil count, ×10 <sup>9</sup> cells/L (ref: 1.08–5.9) <sup>a</sup>	1.86 (1.34–3.00)
Increased	3 (6.52)
Normal	37 (84.09)
Decreased	6 (13.04)
Lymphocyte count, ×10 <sup>9</sup> cells/L (ref: 1.15–6.0) <sup>a</sup>	5.09 (3.91–6.53)
Increased	13 (28.26)
Normal	33 (71.74)
Decreased	0
Neutrophil/lymphocyte <sup>a</sup>	0.40 (0.22–0.71)
CD3 <sup>+</sup> T cells/μL (ref: 805–4459) <sup>a</sup>	3523 (2499–4597)
Increased	10 (28.57)
Normal	24 (68.57)
Decreased	1 (2.86)
CD8 <sup>+</sup> T cells/μL (ref: 314–2080) <sup>a</sup>	967 (654–1536)
Increased	2 (5.71)
Normal	30 (85.71)
Decreased	3 (8.57)
CD4 <sup>+</sup> T cells/μL (ref: 345–2350) <sup>a</sup>	2072 (1700–3019)
Increased	14 (40.00)
Normal	20 (57.14)
Decreased	1 (2.86)
CD19 <sup>+</sup> B cells/μL (ref: 240–1317) <sup>a</sup>	1172 (718–1776)
Increased	16 (47.51)
Normal	18 (51.43)
Decreased	1 (2.86)
Natural killer cells, μL (ref: 210–1514) <sup>a</sup>	382 (236–804)
Increased	1 (2.86)
Normal	27 (77.14)
Decreased	7 (20.00)
IL-2, pg/mL (ref: 0–11.4) <sup>a</sup>	1.58 (1.33–1.83)
Increased	0
Normal	34 (100)
IL-4, pg/mL (ref: 0–12.9) <sup>a</sup>	2.91 (2.02–3.41)
Increased	2 (5.88)

**Table 1. Continued**

Characteristic	No. (%)
Age	
Normal	32 (94.12)
IL-6, pg/mL (ref: 0–120.9) <sup>a</sup>	7.20 (3.63–15.51)
Increased	1 (2.94)
Normal	33 (97.06)
IL-10, pg/mL (ref: 0–5.9) <sup>a</sup>	5.22 (4.36–8.81)
Increased	15 (44.12)
Normal	19 (55.85)
TNF-α, pg/mL (ref: 0–5.5) <sup>a</sup>	1.90 (1.49–2.23)
Increased	3 (8.82)
Normal	31 (91.18)
IFN-γ, pg/mL (ref: 0–17.3) <sup>a</sup>	3.70 (2.83–7.48)
Increased	4 (11.76)
Normal	30 (88.24)
Other pathogen infection	
Cytomegalovirus	3 (6.52)
Epstein-Barr virus	2 (4.35)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CKMB, creatine kinase MB; hs-CRP, high-sensitivity C-reactive protein; IFN-γ, interferon gamma; IL, interleukin; LDH, lactate dehydrogenase; TNF-α, tumor necrosis factor alpha.

<sup>a</sup>Values are presented as median (range).

mean length of stay (the time from hospitalization to discharge) was 13 days (range, 8–16 days). Up to the endpoint of this study, 45 pediatric patients (97.83%) were discharged alive and 1 patient died, who was 10 months old and complicated with intussusception (Table 2).

## DISCUSSION

The number of newly diagnosed COVID-19 cases is still accelerating, and people of all ages are susceptible to infection with SARS-CoV-2 [11]. Studying the clinical characteristics, laboratory tests, and interventions of infant patients (<1 year of age) is essential to improve the cure rate of infants. In this study, we collected a total of 46 confirmed infant cases at the Pediatrics Department of Wuhan Children's Hospital, China from 26 January 2020 to 15 March 2020, and retrospectively analyzed the clinical data of patients.

Different from adult patients, where more cases had comorbidities and suffered severe COVID-19 [12, 13], infant patients had fewer comorbidities and the majority experienced moderate illness. Lymphocytes are depleted in a majority of adult COVID-19 patients, and lymphocytosis is a prominent feature for adult patients [12, 13]. However, infant patients showed different profiles of immune cells, and lymphocyte counts were normal or even increased in most infant cases. Inflammatory cytokines such as IL-6, IL-7, granulocyte colony-stimulating factor, and TNF-α have been shown to be significantly increased in adult patients [12, 13], but in infant patients, the commonest cytokine altered was IL-10, which increased in 15 (44.12%) cases. Infant patients were also demonstrated to have higher frequency of heart and liver injuries by

**Table 2. Complications, Treatment, and Clinical Outcomes in 46 Children <1 Year Old Infected With Coronavirus Disease 2019**

Variable	No. (%) of Patients
<b>Treatment</b>	
Antiviral therapy <sup>a</sup>	7 (15.22)
Antibiotic therapy <sup>b</sup>	13 (28.26)
Interferon- $\alpha$	41 (91.30)
Budesonide suspension	21 (45.65)
<b>Oxygen support</b>	
Nasal cannula	0
IMV	2 (4.35)
<b>Complications</b>	
Liver dysfunction	20 (45.45)
Cardiac injury	38 (86.36)
Acute gastroenteritis	3 (6.52)
MODS	1 (2.17)
Duration of viral shedding <sup>c</sup> , d, median (range)	13 (8–15)
Waiting time <sup>d</sup> , d, median (range)	5 (3–7)
Length of stay <sup>e</sup> , d, median (range)	13 (8–16)
<b>Clinical outcome</b>	
Discharge	45 (97.83)
Death	1 (2.17)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: IMV, invasive mechanical ventilation; MODS, multiple organ dysfunction syndrome.

<sup>a</sup>Any of oseltamivir, ganciclovir, or ribavirin.

<sup>b</sup>Any of teicoplanin, amoxicillin, cefoperazone, cefmetazole, latamoxef, cefmetazole, azithromycin, or meropenem.

<sup>c</sup>Time from the onset of symptoms till the negative detection of severe acute respiratory syndrome coronavirus 2 RNA.

<sup>d</sup>Time from illness onset to hospitalization.

<sup>e</sup>Time from hospitalization to discharge.

SARS-CoV-2, as abnormalities of myocardial and liver enzymes occurred dramatically more often in infant patients compared with adult patients [1]. As for clinical treatment, 76.8% of adult patients were reported to require oxygen inhalation, which was significantly higher than that of infant patients; in addition, >20% of adult patients received intensive care and assisted breathing whereas only 4.35% of infant patients needed intensive care and mechanical ventilation.

Our study demonstrated that COVID-19 in infants (<1 year old) was moderate disease and milder than that in adult patients. The prognosis of COVID-19 was favorable for infant patients, although they were more vulnerable to attack of the heart and liver. One interpretation may be that the depletion of immune cells, especially lymphocytes, seldom occurred in infant COVID-19 patients, and that lymphocytes play an irreplaceable role in clearing virus within our bodies. These differences in clinical characteristics derived from data statistics provide a new strategy for treating infant COVID-19 patients.

## Notes

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