


# Clinical features and characteristics of pediatric patients with COVID-19 infection

## Experiences in a Tertiary Taiwan Hospital

Geng-Hao Bai, MD<sup>a</sup>, Ping-Yi Shih, MD<sup>b</sup>, Shih-Yen Chen, MD, PhD<sup>b,c,d</sup>, Kai-Sheng Hsieh, MD<sup>b,e</sup>, Cheng-Che Chou, MD<sup>b,f</sup>, Po-Hao Feng, MD, PhD<sup>g,h</sup>, Shu-Sing Kong, MD<sup>b,f</sup>, Wen-Chuan Lin, MD<sup>b,i</sup>, Meng-Che Lu, MD<sup>b,j</sup> 

### Abstract

Coronavirus disease 2019 (COVID-19) patients have distinct clinical features in the pediatric groups. However, there is a paucity of research focused on clinical manifestation within pediatric group in Taiwan. This study is to conduct a retrospective study of the clinical features of COVID-19 in Taiwan pediatric patients.

A retrospective study was conducted on pediatric patients (Aged  $\leq 18$  years) in a Northern Taiwan hospital from May 1st, 2021 to June 30th, 2021. Thirty-eight patients were included from emergency room. They were laboratory confirmed COVID-19 through specimens from nasopharyngeal swab by real-time reverse-transcription polymerase chain reaction (RT-PCR). Data including RT-PCR cycle threshold (Ct) values, clinical and epidemiological features were collected and analyzed.

Thirty-eight patients aged from 7-month to 18-year-old were included. The median age of patients was 15-year-old. The patients had sex ratio of 23 males to 15 females. More than half patients were infected from family members. Asymptomatic patients were 47.37%. In the symptomatic patients, fever (34.21%) was the most predominant symptom. Cough, nasal obstruction and sore throat were also common. Asymptomatic children had significantly higher Ct-values than symptomatic children, and diagnosed patients with Ct-values more than 19 were associated with asymptomatic infection ( $P = .0084$ ).

Ct-values higher than 19 were associated with asymptomatic infection, which may be a predictor of pediatric disease severity. Our results highlight the distinct clinical manifestations and outcomes in pediatric COVID-19 patients. Compared to the adults, pediatric patients aged  $\leq 18$  years with COVID-19 in Taiwan mainly had mild disease.

**Abbreviations:** COVID-19 = coronavirus disease 2019, Ct = cycle threshold, RT-PCR = real-time reverse-transcription polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

**Keyword:** covid-19, pediatrics, symptomatic, viral load

## 1. Introduction

Coronavirus disease 2019 (COVID-19) firstly appeared in Wuhan, China during December 2019.<sup>[1]</sup> This ongoing pandemic disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and now has spread around the world.<sup>[2]</sup> Many COVID-19 patients especially in adults develop

pneumonia, acute respiratory distress syndrome or multiple organ failure rapidly.<sup>[3-5]</sup> However, literature in different countries reveal that pediatric COVID-19 patients have distinct clinical features comparing to the adult groups.<sup>[6-15]</sup> Though some studies notice increased risk in infants and adolescent groups, most of the children with COVID-19 infection only get mild symptoms.<sup>[11-15]</sup> The most common symptoms in children are

Geng-Hao Bai and Ping-Yi Shih contributed equally to this paper.

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<sup>a</sup> Department of Education, National Taiwan University Hospital, Taipei city, Taiwan, <sup>b</sup> Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, <sup>c</sup> Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, <sup>d</sup> Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, School of Medicine, College of Medicine, Taipei Medical University, Taipei city, Taiwan, <sup>e</sup> Taipei Heart Institute, Taipei Medical University, Taipei, Taiwan, <sup>f</sup> Division of Pediatric Neurology, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, <sup>g</sup> Division of Pulmonary Medicine, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, <sup>h</sup> Division of Pulmonary Medicine, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei city, Taiwan, <sup>i</sup> Division of

Pediatric Infectious Disease, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, <sup>j</sup> Division of Allergy, Asthma and Immunology, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan.

\*Correspondence: Meng-Che Lu, MD, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, No. 291, Zhongzheng Rd., Zhonghe District, New Taipei City, 23561, Taiwan (ROC) (e-mail: 13490@s.tmu.edu.tw).

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fever and cough.<sup>[7,11]</sup> Including pediatric multisystem inflammatory syndrome, severe illness in the pediatric groups is around 1–6%.<sup>[16]</sup> Because most of the pediatric COVID-19 patients have mild symptoms and less frequency of exposure to some sources of transmission, testing for diagnosis is less frequent. Real-world clinical and epidemiological data in pediatric groups may be understated.<sup>[17–20]</sup> Due to the Taiwan government's early and appropriate measures, incidences of newly confirmed COVID-19 cases are relatively low.<sup>[21]</sup> Even though real-world research focused on initial clinical manifestation within pediatric group in Taiwan has been published,<sup>[22]</sup> the relation of viral load between asymptomatic and symptomatic group should be further explored. Therefore, the aim of this research is to conduct a retrospective study not only to identify the clinical features and characteristics of COVID-19 in Taiwan pediatric patients but also to investigate the viral load in our pediatric patients who were asymptomatic or mild disease.

## 2. Methods

We conducted a retrospective chart review study at Taipei Medical University Shuang Ho Hospital, Ministry of Health and Welfare in New Taipei City, Taiwan. The chart review period was from May 1 to June 30, 2021. We included pediatric patients (aged 0–18 years) with laboratory confirmed COVID-19 infection. The COVID-19 infection was diagnosed and confirmed by real-time reverse-transcription polymerase chain reaction (RT-PCR). All the patients received real-time RT-PCR test at our emergency department, screening station or at the time of admission. The samples were taken from upper nasopharyngeal swabs. The diagnostic definition of COVID-19 was based on guidelines issued by the Taiwan Centers for Disease Control.<sup>[23]</sup>

Since the wide effort to increase testing, SARS-CoV-2 testing has been offered at select primary care sites including Shuang Ho Hospital emergency department to all patients with suspected SARS-CoV-2 exposures regardless of symptoms. A positive result on RT-PCR was defined to a confirmed case. For children tested more than once, only their first-time positive RT-PCR results were included in this study. We screened all the confirmed cases and collected relevant new onset clinical data through electronic medical record, including gender, age, symptoms, cycle threshold (Ct) value while diagnosed, laboratory hemogram and biochemistry data, image study and treatments. Epidemiological investigation was focused on the possible route of transmission and the contact history. BD MAX System (Becton, Dickinson and Company) was used as RT-PCR platform. RT-PCR reagent kit targeted RNA from the nucleocapsid phosphoprotein gene (N1 and N2 regions) of the SARS-CoV-2 coronavirus, and the human RNase P gene.

Disease severity in this article was decided by whether the included patients were asymptomatic or symptomatic. Children were determined to be symptomatic when they had newly onset symptoms within 7 days prior to positive RT-PCR test at our emergency department related to COVID-19, including fever, cough, nasal discharge, sore throat, diarrhea, myalgia, headache, and dysosmia. Asymptomatic children were determined by no symptoms that mentioned above documented at our emergency department. Patients were divided into 2 groups according to age; one was younger than 12 years old and the other was from 12 to 18 years old. Respiratory symptoms in this article were defined as children with cough, nasal obstruction or sore throat. Ct-values were compared in regard to disease severity, age and respiratory symptoms.

We searched PubMed for previous similar studies published from their inception until January 2022. A combination of subject headings and text words was used for the literature search: (1) COVID-19 or SARS-CoV-2 and (2) Pediatric or Children or Adolescent and (3) Ct-value or Viral load and (4) Asymptomatic or Symptomatic. The summary of comparison Ct-value between

asymptomatic and symptomatic patients in previous studies was presented at Table 3 which also included author, year, country, study period, median or mean age, type of swabs, and Ct-value in 2 groups.

This study has been approved by expedited review process of the ethics committee Taipei Medical University Joints Institutional Review Board in the meeting #110-08-3 with approval number N202108049 and followed the Declaration of Helsinki.

### 2.1. Statistical analysis

Two-sample test for equality of proportion was used to examine the demographic features between asymptomatic and symptomatic groups. A Student *t* test and Wilcoxon-Mann-Whitney test were used to compare Ct-value between the groups including disease severity, age, and respiratory symptoms. Fisher exact tests and 2 by 2 tables were used to assess the cutoff point of Ct-value for symptomatic patients. Means with standard deviation (SD) and median with interquartile range (IQR) of clinical data were reported in tables. Statistical tests were 2-sided and a *P* value < 0.05 was determined statistically significant. The statistical calculations were performed through SPSS (Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.)

## 3. Result

Thirty-eight patients aged from 7-month to 18-year-old were positive for SARS-CoV-2 by PCR at our hospital during the study period. The median age of patients was 15 years old with interquartile range (12–16 years old). The patients had sex ratio of 23 males to 15 females. More than half patients (63.2%) were infected from family members with COVID-19. All the included children were either asymptomatic or presented with mild symptoms, and almost half (47.4%) of them were asymptomatic. Only 3 patients (7.9%) need hospital admission for care problem because all family members were isolated (Table 1).

Among 20 symptomatic patients, fever (65%) was the most predominant symptom. Respiratory symptoms such as cough (50%), nasal obstruction or discharges (50%), and sore throat (35%) were also common. Few patients developed diarrhea, myalgia, headache, and dysosmia. There was no dyspnea, desaturation, critically ill or death in the included patients (Table 1).

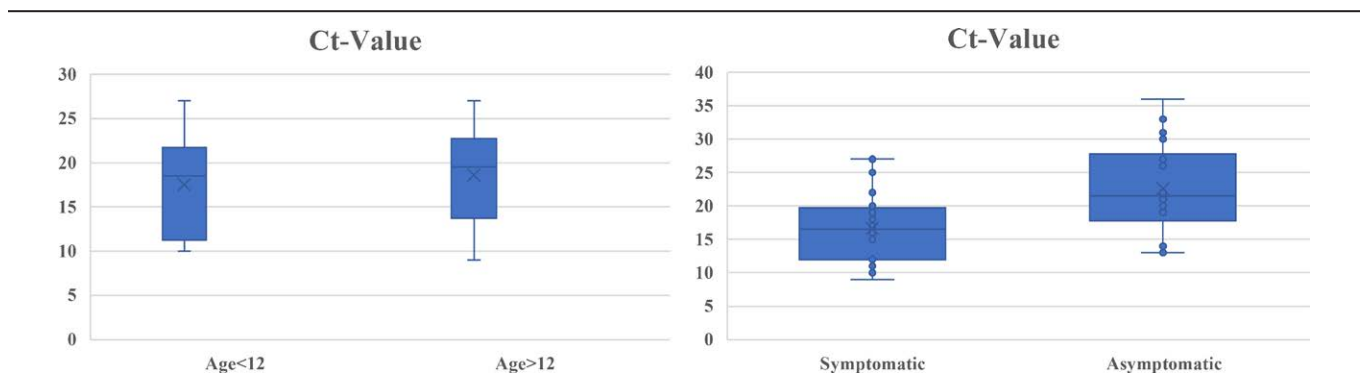
Comparing demographic features between asymptomatic and symptomatic patients, neither sex ratio or median age was significantly different between 2 groups. Interestingly, patients who

**Table 1**  
Demographic and clinical characteristics of children with SARS-CoV-2 infection (N = 38).

Characteristic	No (%)
Age, yr, median (IQR)	15 (12–16)
Sex	
Female, n (%)	15 (39.5)
Male, n (%)	23 (60.5)
Household transmission, n (%)	24 (63.2)
Clinical symptoms	
Asymptomatic, n (%)	18 (47.4)
Mild symptomatic, n (%)	20 (52.6)
Fever	13 (65)
Cough	10 (50)
Nasal discharge	10 (50)
Sore throat	7 (35)
Diarrhea	3 (15)
Myalgia	2 (10)
Headache	2 (10)
Dysosmia	1 (5)
Admission rate, n (%)	3 (7.9)

**Table 2****The difference of demographic features between asymptomatic and symptomatic children.**

	Asymptomatic N = 18, n (%)	Symptomatic N = 20, n (%)	P
Age (median, IQR)	15 (14–16)	13.5 (1–16.25)	.122
0–11 yrs old	1 (5.6)	7 (35)	.045*
12–18 yrs old	17 (94.4)	13 (65)	
Sex			
Female	7 (38.9)	8 (40)	.944
Male	11 (61.1)	12 (60)	
Transmission from family	8 (44.4)	16 (80)	.023*
Ct-value, mean (SD)	22.61 (7.07)	16.65 (5.61)	.006**
CT 6–19	5 (27.8)	15 (75)	
CT 20–36	13 (72.2)	5 (25)	
Admission	2 (11.1)	1 (5)	.595

**Figure 1.** Ct-Value comparison by age and disease severity.

were younger than 12 years old were almost in symptomatic group (87.5%). Moreover, children who were transmitted by their family were significantly more in symptomatic group than asymptomatic group ( $P = .023$ ). Furthermore, using Fisher exact test, we found that newly diagnosed patients with Ct-values  $> 19$  was highly associated with asymptomatic infection ( $P = .0084$ ) (Table 2).

The mean Ct-value of symptomatic children ( $16.65 \pm 5.61$ ) was significantly lower than asymptomatic children ( $22.61 \pm 7.07$ ) ( $P = .006$ ; 95% CI = 1.78–10.14) (Fig. 1). In regard to different age group, the mean Ct-value did not show significant difference between patients younger and older than 12 years old (Fig. 1). Children with respiratory symptoms including cough, nasal obstruction, and sore throat had significantly lower mean Ct-value than the children without those symptoms ( $P = .014$ ; 95% CI = 1.86–14.65).

Table 3 presented the summary of 14 previous studies that compared Ct-value or viral loads between asymptomatic and symptomatic children. Eight studies were from United States, another 3 studies were from Europe and the others were from Asia. The samples were mostly from nasopharyngeal swabs. Over 70% of studies showed symptomatic children had higher viral loads (lower Ct-value) than asymptomatic children, and only 4 studies presented no significant difference between 2 groups. The correlation between age and Ct-value was varied among the included studies. Some of them showed younger children had lower Ct-value; however, the others showed no difference among different age groups. Two of the included studies investigated the relation between presented symptoms and viral loads, one showed no difference,<sup>[24]</sup> the other presented children with cough or sputum production had lower Ct-value.<sup>[25]</sup>

#### 4. Discussion

This study revealed more than half patients were household transmission. This finding is consistent with several observational

studies<sup>[22,37–40]</sup> and literature reviews<sup>[41]</sup> which pointed out children are more likely to contract virus from adult household members. Moreover, the clinical features of the disease were mild in this study and almost one-half patients were asymptomatic. The asymptomatic rate of the patients was slightly higher than most of systematic reviews had reported<sup>[42–46]</sup>; however, the asymptomatic rate was the same as the study of pediatric group in Taiwan.<sup>[22]</sup> This study revealed fever and cough as the most typical manifestations in symptomatic patients. This finding was similar to the pooled results from the systematic reviews.<sup>[42,44–47]</sup> In addition to respiratory symptoms, few patients developed gastrointestinal or neurological symptoms in this study. Symptomatic children were more significantly transmitted by their family. The result was in contrast to Ustundag et al which revealed household contact didn't have significant effect on the presence of symptoms.<sup>[39]</sup>

We also investigated the correlation of viral loads in regard to disease severity, age, and respiratory symptoms. We observed that asymptomatic children had significantly higher Ct-value than symptomatic children. Ct-values higher than 19 were associated with asymptomatic infection which may be a predictor of disease severity. This finding was similar to the data reported by several studies which indicated symptomatic children may have a higher viral load in the nasopharynx than asymptomatic children.<sup>[24,25,27,28,30,32,33,36]</sup> However, the data from Chu et al, Ford et al, Hurst et al, and Peaper et al showed no significant difference in viral load between symptomatic and asymptomatic children.<sup>[26,29,31,35]</sup> The results might be respectively related to the number of infected children and the bias toward inclusion of symptomatic children in the study.

No significant difference of Ct-value was observed between younger and older groups. It was in contrast to the findings of Strutner et al<sup>[24]</sup> and Pinninti et al,<sup>[36]</sup> the studies pointed out compared to other age groups, Ct-Value was significantly lower in age  $< 5$  years old and significantly lower in age  $< 1$  years old, respectively. The reasons might be that children from 1 year old

**Table 3**

**Previous studies that have compared Ct-value or viral load between asymptomatic and symptomatic children, median (IQR); mean (SD).**

Author year	Country	Study period	Age	Swab	Target gene	Asymptomatic		Symptomatic		P	Ct-Value outcome summary	Reference
						Ct-value/viral load	(n)	Ct-value/viral load	(n)			
Chu 2021	Korea	February 18–April 30, 2020	Mean (range) 9.8 (1–18)	NP	RdRp E gene	E: 30.3 [28.3–32.2] RdRp: 33.0 [31.3–35.0]	13	E: 31.8 [29.5–34.3] RdRp: 34.2 [32.0–36.0]	18	0.49 0.33	•Symptomatic and asymptomatic: No difference	[26]
Chua 2021 [Viral load]	Hong Kong	March 12–August 8, 2020	8.6 [4.3–11.0] 9.2 [4.0–15.0]	NP or Saliva	N gene RdRp	N: 34.8 [32.1–37.2] NP: 5.7 [4.3–7.4] Saliva: 4.5 [3.6–5.1] [Mean log RNA]	28	N: 35.1 [33.1–37.0] NP: 6.8 [5.6–8.3] Saliva: 5.8 [4.9–6.7] [Mean log RNA]	63	0.63 NP: <0.001	•Symptomatic < asymptomatic •With (Cough, sputum or headache): Lower	[25]
Chung 2021	USA	March 23–November 9, 2020	7.5 (5.3)	MTB or AN	S gene	N/A	47	Mean difference –3.0, 95% CI(–5.5 to –0.6)	76	0.02	•Symptomatic < asymptomatic •Adults and Children: No difference	[27]
Cotugno 2021 [Viral load]	Italy	March–July, 2020	AS: 4.6 (3.4) SY:7.4 (5.6)	NP	RdRp E gene	N/A	15	N/A	51	0.004	•Symptomatic < asymptomatic	[28]
Ford 2021	USA	November 16–December 15, 2020	5–8 yrs	AN	N gene ORF1ab	N: 22.2 [21.6–31.6]	18	N: 24.3 [21.4–27.3]	24	N/A	•Symptomatic and asymptomatic: No difference	[29]
Ford 2021	USA	November 16–December 15, 2020	9–12 yrs	AN	N gene ORF1ab S gene	N: 25.4 [23.2–27.6]	29	N: 19.6 [17.8–26.9]	33	N/A	•Symptomatic < asymptomatic	[29]
Huillier 2021 [Viral load]	Switzerland	November 10–March 26, 2021	11.8 [9.0–14.3]	NP	N gene E gene	4.1 (1.9) [Mean log RNA]	30	5.9 (1.8) [Mean log RNA]	89	<0.001	•Symptomatic < asymptomatic •Age < 12 yrs old: Higher	[30]
Hurst 2020 [Viral load]	USA	April 7–July 16, 2020	10.4 [4.8–16.4]	NP or MTB	E gene	3.8 [2.8–6.5]	52	4.1 [3.0–5.5]	126	0.56	•Symptomatic and asymptomatic: No difference •0–5, 6–13, 14–20 yrs old: No difference	[31]
Kam 2021	Singapore	March 23–April 5, 2020	7.7 [0.3–15.8]	NP	E gene	36.7	7	28.6	10	0.02	•Symptomatic < asymptomatic	[32]
Kociotek 2021	USA	March–July, 2020	N/A	NP or oropharyngeal	N/A	Adjusted: 8.6 [2.5–12.2]	339	Adjusted: –1.7 [–6.0–4.8]	478	< 0.0001	•Symptomatic < asymptomatic •Ct difference narrowed with increasing age	[33]
Ollier 2022	France	January 15–May 28, 2021	1.7 [0.4–5.2]	NP	N gene RdRp	N: 29.8 (8.5) RdRp: 29.2 (8.0)	11	N: 22.2 (5.8) RdRp: 22.7 (5.5)	35	0.002 0.005	•Symptomatic < asymptomatic	[34]
Peaper 2020	USA	March 1–September 26, 2020	12.0 [5.0–16.0]	NP or MTB	N/A	N/A	38	N/A	44	N/A	•Symptomatic and asymptomatic: No difference	[35]
Pinninti 2021	USA	March 24–August 20, 2020	9.78 (6.56)	NP, nasal, saliva, or rectal	N gene	34 (median)	45	26 (median)	57	0.001	•<=10, >10 yrs old: No difference •Inpatient and Outpatient: No difference •Symptomatic < asymptomatic •Age < 1 yrs old: Lower than Age 1–5, 6–17 yrs old	[36]
Strutner 2021	USA	April 1–August 1, 2020	7.5 [2.0–14.0]	AN or NP	ORF1ab S gene N1&N2	23.5 (6.9)	210	19.9 (6.3)	518	<0.001	•Comorbid condition: No difference •Symptomatic < asymptomatic •Age < 5 yrs old: Lower than other age groups	[34]
Zachariah 2020	USA	March 14–April 24, 2020	Infants and 1–21 yrs old	NP	E gene	N/A	N/A	N/A	N/A	N/A	•Respiratory symptoms (With or without): No difference •Age < 1 yr old: Lower than Age 1–21 yrs old •Symptomatic infants: Higher viral load	[15]

Ct, Cycle threshold; AN, Anterior nares; MTB, Middle turbinate; NP, Nasopharyngeal; SD, Standard deviation; IQR, Interquartile range; N/A, not applicable; E, envelope; RdRp, RNA-dependent RNA polymerase; N, nucleocapsid; S, spike glycoprotein; ORF1ab, open reading frame 1ab.

to 11 years old were not presented at our hospital, and also the small sample size might lead to no significant results. Among mild symptomatic children, children with respiratory symptoms had significant lower mean Ct-Value than children without respiratory symptoms. Due to the small sample sizes, it cannot come to a conclusion. However, the pathophysiology of virus invasion can explain the finding, when increased amount of the virus migrated from the nasal epithelium to the upper respiratory tract, the involvement of the upper airways may present with respiratory symptoms of dry cough.<sup>[48]</sup> Further studies in the future can investigate the possible factors that may influence the viral loads measured from infected children such as RNA extraction kit, rt-PCR assay, targeted gene, the time points of the diseases and the variants of SARS-CoV-2.

To date, the Omicron variant is the most rapidly transmitted SARS-CoV-2 variant. In the United States, till February 02/12/2022, Omicron variant is the dominant variant with 3 common lineages, BA.1.1, B.1.1.529, and BA.2. BA.1.1 accounts for 73.2% of the total cases infected with SARS-CoV-2.<sup>[49]</sup> Although a preprint study revealed the emergence of the Omicron variant in the United States was associated with significantly milder disease in the early phase of infection as compared to the Delta variant period,<sup>[50]</sup> researchers from Denmark found that Omicron is about 2.7–3.7 times more infectious than Delta among vaccinated individuals.<sup>[51]</sup> A retrospective cohort study of electronic health record data pointed out the less severe outcome for the infected children under age 5 during Omicron predominated period than during Delta variant predominated.<sup>[52]</sup> However, nowadays, there was no enough evidence of clinical presentation in children with the Omicron variant. Pediatric acute upper airway infection cases have increased during the Omicron variant surge and nearly a third of affected children develop severe disease.<sup>[53]</sup> Croup, one of the most severe manifestations of upper respiratory infections in children has been reported a sharp rise in cases during this period.<sup>[54]</sup> Therefore, in order to prevent this highly contagious variant and the severe upper airway infection, it is important for preventive measures including increasing the rate of vaccination,<sup>[55]</sup> universal masking in schools, other indoor public spaces and child care centers.<sup>[56]</sup>

There were several limitations in our study. First, it was a retrospective and single-center study. Second, generalizability was limited by the small sample size of this study. Next, the inconsistency of the record from emergency department may lead to incomplete information. Moreover, symptoms are reported by patients themselves, and children may not be able to clearly describe their symptoms. Finally, the Ct-values were collected when children presented at our hospital; thus, the various time points of the infection diseases may affect the result of viral load.

## 5. Conclusion

Ct-values higher than 19 were associated with asymptomatic infection, which may be a predictor of pediatric disease severity. Asymptomatic children had significantly higher mean Ct-value than symptomatic children. Household transmission of asymptomatic children with COVID-19 infection should be more closely guarded. Fever and cough were prevalent symptoms in children with SARS-CoV-2. Further studies should recruit larger sample sizes and assess the pathophysiology of the difference between asymptomatic and symptomatic children.

## Author contributions

All the research team designed and conducted the research. GHB and PYS analyzed the data. GHB, PYS, and MCL wrote the article. GHB, PYS, and MCL had primary responsibility for final content.

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