


# How should our testing behaviour change with time in children in current COVID-19 pandemic?

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## Abstract

**Backgrounds:** More paediatric-confirmed cases have been reported with the global pandemic of COVID-19. This study aims to summarize the key points and supply suggestions on screening paediatric COVID-19 patients more appropriately.

**Materials and Methods:** We retrospectively included paediatric patients who have accepted SARS-CoV-2 RT-PCR testing in Children's Hospital of Chongqing Medical University (30 January 2020 to 13 February 2020) and compared them with paediatric-confirmed COVID-19 cases. Besides, a review was carried out by analysing all current literature about laboratory-confirmed paediatric cases with COVID-19.

**Results:** There were 46 suspected cases included in the descriptive study. The results of SARS-CoV-2 RT-PCR testing were all negative. Compared with paediatric-confirmed cases, the incidence of epidemic history was lower in suspected cases ( $P < .001$ ). The rate of fever ( $P < .001$ ), cough ( $P < .001$ ), headache or dizziness ( $P < .001$ ), vomiting ( $P < .001$ ) and abdominal discomfort or distention ( $P = .01$ ) were more observed in the included suspected children. There were more children having decreased WBC count in the confirmed group. In the literature review, twenty-nine studies were obtained with 488 paediatric COVID-19 cases. 88.6% of them had epidemiological history. Cough and fever were the most common symptoms. Compared with older patients, the incidence of fever, respiratory symptoms, lethargy and headache or dizziness was lower, while gastrointestinal symptoms were reported more.

**Conclusions:** Children with a history of close contact with confirmed cases, manifested as cough and fever should be paid more attention to after excluding infection of other common pathogens. Atypical symptoms should not be over-emphasized in screening paediatric COVID-19. More studies are needed for guiding efficient recognition in paediatric COVID-19.

## KEYWORDS

COVID-19, paediatric, SARS-CoV-2, suspected cases

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## 1 | INTRODUCTION

In December 2019, a series of pneumonia cases with coronavirus disease 2019 (COVID-19) occurred in Wuhan, Hubei Province, China.<sup>1-3</sup> This study aims to share clinical experience in screening paediatric cases suspected with COVID-19 in a Chinese children's hospital. Besides, we will discuss the differences in epidemiological, clinical, laboratory and radiological characteristics between adults and children in the COVID-19 pandemic by reviewing the current literature reporting laboratory-confirmed paediatric cases with COVID-19. We hope to improve the measures of screening paediatric suspected cases to avoid missed diagnosis and save medical sources in the current COVID-19 pandemic.

## 2 | METHODS

### 2.1 | A descriptive analysis

Reporting of the descriptive analysis in this study conforms to broad EQUATOR guidelines.<sup>4</sup>

#### 2.1.1 | Data source

We included paediatric patients who have accepted SARS-CoV-2 RT-PCR testing in Children's Hospital of Chongqing Medical University, China from 30 January 2020 to 13 February 2020 and retrospectively collected the clinical data.

#### 2.1.2 | Study population

The inclusion criteria were as follows: (a) under 18 years old, and (b) having accepted SARS-CoV-2 RT-PCR testing for nasal and pharyngeal swab or anal swab specimens. Children were excluded if they met any of the following criteria: (a) not having accepted SARS-CoV-2 RT-PCR testing, (b) the clinical data were not obtained or seriously absent.

#### 2.1.3 | Criteria for paediatric suspected cases

Included suspected paediatric patients should meet the criteria for paediatric suspected cases according to 'Diagnosis and Treatment Protocol for pediatric COVID-19(the 2nd Revised Version)' carried out by experts on COVID-19 in Children's Hospital of Chongqing Medical University, China<sup>5</sup> or recognized with high risk of infected with SARS-CoV-2 by experts.

### 2.1.4 | Data collection

The demographic characteristics, clinical symptoms, signs, laboratory findings and radiologic assessments were extracted from electronic medical records. Demographic characteristics included gender, age and epidemiological history; clinical symptoms included cough, fever, runny nose, stuffy nose, sore throat, nausea, vomiting, diarrhoea, abdominal discomfort or distension and headache/dizziness; signs included moist rales and wheezing; Laboratory findings included WBC count, the ratio of lymphocyte (L%) and CRP. Radiologic assessments included chest X-ray and/or computed tomography scan (CT).

## 2.2 | Literature review

### 2.2.1 | Literature search strategy

A comprehensive search for case or case series studies on paediatric confirmed cases was conducted using the following databases: PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CKNI), CQ VIP Database, Wanfang Data from 1 January 2019 to 25th March 2020, without any restriction. Search strategies as (COVID 19 OR coronavirus disease 2019 OR 2019 novel coronavirus OR 2019-nCoV OR Wuhan coronavirus OR SARS-CoV-2 OR severe acute respiratory syndrome coronavirus 2) AND (infants OR neonates OR newborns OR toddlers OR child OR children OR adolescents OR paediatric) were used. The corresponding Chinese key terms were used in Chinese databases. We reviewed the reference lists of articles for other studies to supplement our search.

### 2.2.2 | Study selection and data extraction

The inclusion criteria of studies: (a) included children were under 18 years old, and (b) included children were laboratory-confirmed COVID-19 cases and the SARS-CoV-2 RT-PCR testing was positive for nasal and pharyngeal swab or anal swab specimens. The exclusion criteria were as follows: (a) unpublished studies or (b) duplicate studies. Data including epidemiological history, clinical symptoms, laboratory findings and radiologic assessments were extracted.

## 2.3 | Statistical analysis

Categorical variables were summarized as counts (n) and percentages (%). In comparison of clinical features between paediatric suspected and confirmed cases, proportions for

categorical variables were compared using Chi-square tests or Fisher's exact tests as appropriate. Children's age was described using medians and interquartile ranges (IQR) because the data were not normally distributed. A *P* value less than .05 was considered statistically significant, and all tests were two-tailed. All statistical analyses were performed using SPSS 25.0.

### 3 | RESULTS

#### 3.1 | The descriptive analysis

##### 3.1.1 | Characteristics of included suspected cases

According to the inclusion criteria, there were 46 children included in this study. The results of SARS-CoV-2 RT-PCR testing were all negative in the included children. The age of the 46 included children (19 girls and 27 boys) ranged from 1 day to 14 years old. There were 23 children having a history of epidemiology (50%). Thirty-four children had fever (73.9%); 34 children had cough (73.9%); 12 children had runny nose (26.1%); nine children had vomiting (19.6%); four children had diarrhoea (8.7%); four children had headache or dizziness (8.7%); four children had stuffy nose (8.7%); and three children had abdominal discomfort or distention (6.5%). Clinical signs were mild in most cases. The WBC count was lower than normal in 4 children (8.7%) and normal in 34 children (73.9%). The lymphocyte ratio was decreased in 21 children (45.7%) and normal in 20 children (43.5%). CRP was increased in 15 children (32.6%). COVID-like pneumonia signs were obtained in radiologic assessments in 32 children (69.6%). Cloudy opacity was observed in 47.8% of all suspected cases. The descriptive data of the included cases are presented in Table 1.

#### 3.2 | Literature review

A rapid secondary analysis and review were conducted to analyse the characteristics of paediatric COVID-19 cases based on current literature. Consequently, a total of 29 studies were obtained.<sup>6-34</sup> A total of 488 paediatric cases with COVID-19 were included. We re-analysed the data on epidemiological history, clinical symptoms, laboratory findings and radiologic assessments. The analysis showed 88.6% of the paediatric cases had epidemiological history. There were 24.2% of paediatric COVID-19 patients having no symptoms. Cough and fever were the top two symptoms and consisted of 45.3% and 45.1% in included paediatric cases, respectively, which is similar to a descriptive study with a total of 171 paediatric cases.<sup>17</sup> In laboratory findings, paediatric confirmed

**TABLE 1** The clinical features of paediatric suspected and confirmed COVID-19 patients

	Suspected cases n = 46	Confirmed cases n = 488	P
Demographic characteristics			
Gender (boy/girl)	27/19	287/201	.99
Age (months)	37 (11-90)	—	—
Epidemiological history (%)	23 (50%)	410/463 (88.6%)	<.001
Clinical symptoms (%)			
Cough	34 (73.9%)	221/488 (45.3%)	<.001
Fever	34 (73.9%)	220/488 (45.1%)	<.001
Runny nose	12 (26.1%)	74/488 (15.2%)	.054
Stuffy nose	4 (8.7%)	66/488 (13.5%)	.354
Headache or dizziness	4 (8.7%)	4/488 (0.8%)	.003
Vomiting	9 (19.6%)	25/488 (5.1%)	<.001
Diarrhoea	4 (8.7%)	32/488 (6.6%)	.806
Abdominal discomfort or distention	3 (6.5%)	3/488 (0.6%)	.01
Clinical signs (%)			
Moist rales	4 (8.7%)	—	—
Wheezing	3 (6.5%)	—	—
Laboratory findings			
WBC			
Decreased	4 (8.7%)	53/270 (19.6%)	.075
Normal	34 (73.9%)	196/270 (72.6%)	.852
Increased	8 (17.4%)	21/270 (7.8%)	.07
L%			
Decreased	21 (45.7%)	13/34 (38.2%)	.507
Normal	20 (43.5%)	14/34 (41.2%)	.837
Increased	5 (10.9%)	7/34 (20.6%)	.229
Increased CRP	15 (32.6%)	37/101 (36.6%)	.636
Radiological assessments			
Pneumonia signs (%)	32 (69.6%)	355/452 (78.5%)	.164
Cloudy opacity (%)	22 (47.8%)	—	—
Patchy shadow (%)	8 (17.4%)	—	—
Ground-glass opacity (%)	2 (4.3%)	—	—
Nodular shadow (%)	3 (6.5%)	—	—

cases often have decreased or normal level of WBC count (19.6%, 72.6%, respectively) and lymphocyte ratio (38.2%, 41.2%, respectively). Abnormal CRP was observed in 36.6%

of cases; 78.5% radiologic assessments were abnormal with pneumonia signs.

To compare the data with paediatric confirmed cases, a single-arm meta-analysis including COVID-19 patients with no restriction of age was also included.<sup>35</sup> In the comparison, the incidence of fever and cough is much lower than that of older patients. Furthermore, the incidence of exploration, dyspnoea, lethargy and headache/dizziness was lower, while gastrointestinal symptoms (nausea, vomiting and diarrhoea) were reported more in paediatric confirmed cases. Less abnormalities in WBC count, the ratio of lymphocyte and CRP were recorded in paediatric cases with COVID-19. The detailed information is shown in Table 2 and Table S1.

### 3.3 | Comparing paediatric suspected cases with confirmed cases

We compared the clinical features between the included paediatric suspected cases and paediatric confirmed cases. The incidence of epidemic history was lower in suspected cases than that in confirmed cases ( $P < .001$ ). The rate of fever ( $P < .001$ ), cough ( $P < .001$ ), headache or dizziness ( $P = .003$ ), vomiting ( $P < .001$ ) and abdominal discomfort or distention ( $P = .01$ ) was more observed in the included suspected children. The WBC count was normal in the majority of both suspected and confirmed cases, while there were more children having decreased WBC count in the confirmed group. The comparison is shown in Table 1.

## 4 | DISCUSSION

In this study, we conducted a review summarizing the clinical features of paediatric confirmed COVID-19 patients and compared them with adult COVID-19 patients. In rapidly reviewing literature reporting confirmed cases with COVID-19, the results showed that the incidence of fever and cough was lower in paediatric cases than that in older infected ones although these symptoms still occupied vital positions of all. However, gastrointestinal symptoms (nausea, vomiting and diarrhoea) were reported more in paediatric confirmed cases.

To share experience and give suggestions on screening paediatric suspected cases more appropriately, this study also collected clinical information of paediatric suspected cases in a children's hospital and analysed the features of them. After the outbreak of COVID-19 in China, a team with experts dedicating to respiratory, infectious disease, critical care and radiology in Children's Hospital of Chongqing Medical University was established. With paediatric cases with COVID-19 emerging, the criteria of paediatric suspected cases were promulgated by the expert group. The criteria

**TABLE 2** The clinical features of confirmed paediatric and adult cases in literature review

	Paediatric cases n = 488 (%)	Adult cases n = 1995 (%)
Epidemiological history (%)	88.6	—
Clinical symptoms		
Cough (%)	45.3	68.60
Fever (%)	45.1	88.50
Asymptomatic (%)	24.2	—
Exploration (%)	2.3	28.20
Dyspnoea (%)	0.4	21.90
Runny nose (%)	15.2	—
Stuffy nose (%)	13.5	—
Sore throat (%)	18.6	—
Lethargy (%)	4.3	35.80
Headache or dizziness (%)	0.8	12.10
Nausea (%)	1.6	3.90
Vomiting (%)	5.1	—
Diarrhoea (%)	6.6	4.80
Abdominal discomfort or distention (%)	0.6	—
Laboratory findings		
WBC		
Decreased	19.6	29.40
Normal	72.6	—
Increased	7.8	—
L%		
Decreased	38.2	64.50
Normal	41.2	—
Increased	20.6	—
Increased CRP	36.6	44.30
Radiologic assessments		
Pneumonia signs(%)	78.5	—

were based on the recent evidence and emphasized that paediatric cases often present mild manifestations and atypical symptoms should be attached importance to. Consultations would be held in time for those who are likely to be infected with SARS-CoV-2, and then the RT-PCR testing was decided to conduct or not. Although the included paediatric suspected cases all had negative SARS-CoV-2 RT-PCR testing results, we may learn lessons in the screening process by comparing clinical features of the paediatric suspected cases with confirmed cases. In the literature review, most confirmed cases had a definite history of epidemiology and had close contact with family members who were infected with SARS-CoV-2. However, only a half of the included suspected cases had



possible epidemic history, and none of them reported close contact with confirmed COVID-19 cases. Therefore, the history of contact with confirmed cases provided by caregivers is vitally important in the screening process. We suggest parents and clinicians keep following the trends of COVID-19 pandemic with the global outbreak of COVID-19.

In the global COVID-19 pandemic, we have to focus more on clinical symptoms in view that more unclear information about the epidemic history would be obtained. To our knowledge, fever and cough are important hints in COVID-19, no matter in adults or children. The evidence may remind clinicians to pay attention to fever and cough, but in order to avoid the wrong judgement, we still suggest clinicians to exclude the infection of other pathogens which were more common in the peak time of respiratory tract infection. Current evidence indicated that paediatric confirmed cases would present more abnormal gastrointestinal symptoms than adults; however, some patients only present gastrointestinal symptoms but were treated wrongly as suspected cases. Clinicians should notice that rare cases start with only gastrointestinal symptoms in previous reports and no research confirmed that atypical symptoms such as abnormal gastrointestinal symptoms, headache or dizziness were in close relationship with COVID-19. Besides, the difference in WBC count between suspected and confirmed cases indicated that decreased or normal WBC count is more valuable for screening paediatric COVID-19, although increased WBC count should not be the reason to rule out the infection.

The highlight of this study should be noted. First, we summarized the key points and supplied suggestions on screening paediatric COVID-19 more appropriately by comparing suspected cases who had negative SARS-CoV-2 RT-PCR testing results and laboratory-confirmed cases. Second, this study conducted a literature review, analysing the clinical features of paediatric confirmed COVID-19 cases and comparing them with adult patients.

However, there are limitations in this study. Firstly, there was no direct evidence to conclude the characteristics of paediatric COVID-19 because no one was confirmed with COVID-19 in this study. Besides, the sample size was too small, more large-scaled studies are needed urgently to provide more reliable evidence for protecting children in current COVID-19 pandemic.

## 5 | CONCLUSIONS

Nausea, vomiting and diarrhoea are more observed in paediatric COVID-19 patients than older ones. However, cough and fever were the most common symptoms in paediatric confirmed cases with COVID-19. Children with a history of close contact with confirmed cases, manifested as cough and fever should still be paid more attention to after excluding

infection of other common pathogens. Atypical symptoms such as abnormal gastrointestinal symptoms, headache or dizziness should not be over-emphasized in screening paediatric COVID-19. More studies should be carried out to support efficient recognition in children in current COVID-19 pandemic.

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## CONFLICT OF INTEREST

There is no conflict of interest among all authors in this study.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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