

## Persistent symptoms of novel coronavirus infection in children one month after infection

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### Abstract

**Objective:** To explore the persistent symptoms associated with novel coronavirus infection in children and their influencing factors, and to provide a reference basis for the next step of intervention and health education.

**Methods:** A questionnaire was designed by reviewing the literature and expert consultation method, and a questionnaire star was created. One month after the outbreak of COVID-19 in December 2022, a convenience sampling method was used to select 117 family members of children who attended the pediatric department of a tertiary care hospital with a history of new coronavirus infection from January 18 to January 21, 2023, as the respondents to investigate the information related to persistent symptoms after new coronavirus infection in children. The raw data were entered by an Excel sheet, and spss26.0 was applied for statistical analysis using univariate and multi-factor logistic regression analysis.

**Results:** Among the 117 children, 69(59%) were male and 48(41%) were female, and 37(31.6%) children had persistent symptoms associated with one month after infection. Persistent symptoms were mainly cough, loss of appetite, and coughing sputum in 24(44.44%), 7(12.96%), and 6(11.11%) children, respectively. Logistic regression analysis showed that children with general paediatric hospitalization (OR=4.745, 95% CI=1.392-16.180) and coughing during infection (OR=5.273, 95% CI=1.767-15.742) were at high risk for the development of associated persistent symptoms ( $p<0.05$ ).

**Conclusion:** Nearly one-third of children had some persistent symptoms 1 month after novel coronavirus infection, and this population should be given focused attention with symptomatic treatment, timely intervention and follow-up.

**Keywords:** Children; Novel coronavirus; Persistent symptoms; Investigation.

## Introduction

On December 7, 2022, after the State Council heavily released 10 epidemic prevention policies, many places began to adjust their prevention and control measures one after another. The number and severity of infections in children have varied at different times since the outbreak of the COVID-19 pandemic. Since February 2022, the Omicron variant has become the predominant epidemic strain, with a surge in the number of infections in children compared to the Delta variant, with household gatherings and school-based transmission common [1]. It is also of concern that although Omicron variant infections rarely cause severe disease compared to previous variants, a large number of Omicron variant infections may be associated with long-term symptoms [2]. Among them, most children recovering from novel coronavirus pneumonia (coronavirus disease 2019, COVID-19) also develop persistent symptoms [3], and some international guidelines propose to define COVID-19 with signs and symptoms lasting 4-12 weeks as «COVID-19 with persistent symptoms» [4]. A domestic study defined short-term persistent symptoms of COVID-19 in children as a series of recurrent, persistent symptoms or health problems that exist 4-5 weeks after the child's SARS-CoV-2 nucleic acid turned negative [5]. A study from England reported that 4.4% of children were still symptomatic 4 weeks after the onset of COVID-19 [6]. These persistent symptoms may be new after recovery from an acute episode of COVID-19 or may persist from the initial illness [7]. The current reports of persistent symptoms associated with COVID-19 are mainly for adult patients [8], and there are fewer reports for children in China. After the adjustment of the epidemic policy at the end of 2022, the number of children with COVID-19 in Mianyang area increased. In this study, we investigated the persistent symptoms of children attending the pediatric department of a tertiary hospital one month after infection and analyzed the influencing factors for the next step of intervention and health. In this study, we investigated the persistent symptoms and analyzed the factors influencing them after one month of infection in the pediatric department of a tertiary care hospital to provide a reference for further intervention and health education.

## Subjects and Methods

**Subjects:** This study adopted a convenience sampling method to select 117 patients who attended the pediatric department of a tertiary care hospital from January 18 to January 21, 2023, and the families of 117 patients with a history of neocoronavirus infection after the outbreak in December 2022, including general pediatric wards, pediatric surgical wards, and pediatric outpatient clinics, as subjects for investigation. The subjects investigated were also divided into four age groups: <1 year old, 1~3 years old, 4~6 years old, and 7~14 years old.

### Inclusion criteria:

1. Children aged 28 days-14 years;
2. Informed consent and voluntary participation of the child and family in the survey (informed consent of the family for children under 7 years of age, verbal consent and informed consent of the family for children over 7 years of age);

3. Children who met the clinical diagnosis of novel coronavirus infection [9];

4. One month (4-5 weeks) after novel coronavirus infection.

**Exclusion criteria:**

1. Family members who could not use cell phones to complete the questionnaire;

2. Family members who could not provide accurate information about the child's infection.

**Survey instrument:** The researchers designed the questionnaire through literature review, combined with the study content and research objectives, and revised and determined the questionnaire through expert consultation. The contents of the questionnaire included the general information of the patient, the situation during the infection, and the situation of persistent symptoms after the infection.

**Data collection method:** The researcher of this survey conducted relevant training for the group members to ensure the authenticity of the survey results. The survey QR code was made by questionnaire star, and the panel members informed the families of the purpose and content of the study, and after obtaining their consent, the families scanned the survey QR code through WeChat to answer, and the questionnaire was filled out only once per person using a uniform guideline.

**Statistical methods:** The raw data were entered by Excel table, and spss26.0 was applied for statistical analysis, and the count data were expressed using frequency and percentage, and the chi-square test was used for comparison between groups. Multi-factor logistic regression was used to analyze the factors influencing the persistent symptoms associated with the children.  $P < 0.05$  was set as the difference was statistically significant.

## Results

**General information of children with COVID-19:** In this study, 117 valid questionnaires were returned. Of the 117 children, 69(59%) were male and 48(41%) were female; <3 years old 43 cases (36.8%), 4-6 years old 30 cases (25.6%); 7-14 years old 44 cases (37.6%); 100(85.5%) had no underlying disease and 17(14.5%) had underlying disease; 75(64.1%) were vaccinated and 42(35.9%) were unvaccinated; 72(61.5%) were treated at home, 27(23.1%) were treated as outpatients, and 18(15.4%) were treated in general pediatric hospitalization; no medication was taken in 8 cases (6.8%) and medication was taken in 109 cases (93.2%), details and other demographic information are shown in Table 1.

**Table 1:** General information of 117 children with COVID-19 (n,%).

	Number of cases (n=117)	Percentage of the number of children (%)
Gender		
Male	69	59
Female	48	41
Age		
<3 year old	43	36.8
4~6 years old	30	25.6
7~14 years old	44	37.6
Underlying diseases		
No	100	85.5
Yes	17	14.5
Vaccination status		
Not vaccinated	42	35.9
One vaccination	3	2.6
Two vaccinations	72	61.5
Access to medical care		
Outpatient treatment	27	23.1
General pediatric inpatient treatment	18	15.4
Home treatment	72	61.5
Medication status		
No	8	6.8
Yes	109	93.2

**Symptoms during infection in children with COVID-19:** The total number of symptoms during infection was 16, with respiratory (148 cases, 44.05%), neurological (147 cases, 43.75%), digestive (32 cases, 9.52%) and skin-muscle related symptoms (9 cases, 2.68%), with fever being the most common symptom (97 cases, 82.91%), followed by cough (73 cases, 62.39%), nasal congestion (28 cases, 23.93%), sore throat (26 cases, 22.22%) and decreased appetite (24 cases, 20.51%), as detailed in Table 2A & 2B.

**Table 2A:** Percentage of each type of symptoms.

Category	Number of cases	Percentage (%)
Total respiratory symptoms	148	44.05
Total Neurological Symptoms	147	43.75
Total digestive symptoms	32	9.52
Skin and muscle-related symptoms	9	2.68

**Table 2B:** Symptoms during infection in 117 children with COVID-19.

Symptoms	Number of cases	Percentage of the number of children (%)
Fever	97	82.91
Cough	73	62.39
Cough and sputum	21	17.95
Stuffy and runny nose	28	23.93
Sore throat	26	22.22
Smell disorder	1	0.85
Taste disorder	2	1.71
Dizziness and headache	21	17.95

Weakness	11	9.4
Drowsiness and lack of energy	14	11.97
Twitching	1	0.85
Loss of appetite	24	20.51
Diarrhea	4	3.42
Vomiting	4	3.42
Skin rash	2	1.71
Muscle Soreness	7	5.98

**Persistent symptoms associated with 1 month of infection in children with COVID-19:** Thirty-seven (31.6%) of the children in this survey presented with associated persistent symptoms. The frequency of cough (24, 44.44%) was the highest of all persistent symptoms, followed by loss of appetite (7, 12.96%) and coughing up sputum (6, 11.11%). Other rare symptoms include weakness, stuffy and runny nose, shortness of breath, chest pain or discomfort, dizziness, nausea at times, diarrhoea, insomnia, drowsiness, skin rash. Of interest is that one of the participating children was diagnosed with Kawasaki disease about 4 weeks after infection with the novel coronavirus (Table 3).

**Table 3:** Persistent symptoms associated with 1 month of infection in children with COVID-19.

Persistent symptoms	Number of cases	Percentage of the number of children (%)
Cough	24	44.44
Loss of appetite	7	12.96
Cough and sputum	6	11.11
Dizziness	2	3.70
Insomnia	1	1.85
Drowsiness	1	1.85
Weakness	3	5.56
Stuffy and runny nose	2	3.70
Chest tightness and shortness of breath	2	3.70
Chest pain or discomfort in the chest	2	3.70
Nausea at times	1	1.85
Diarrhoea	1	1.85
Skin rash	1	1.85
Other (Kawasaki disease)	1	1.85

**Table 4:** Single factor analysis of persistent symptoms associated with 1 month of infection in children with COVID-19.

Persistent symptoms	Number of cases	Without associated persistent symptoms (%) n=80	$\chi^2$	p
Coughing at the time of infection				
Yes	33 (28.2)	40 (34.2)	16.559	0.000
No	4(3.4)	40(34.2)		
Coughing at the time of infection				
Yes	12 (10.3)	9 (7.7)	7.708	0.005
No	25(21.4)	71(60.7)		
Medical treatment				
Outpatient treatment	11(9.4)	16(13.7)	8.749	0.013
General pediatric inpatient treatment	10(8.5)	8(6.8)		
Home treatment	16(13.7)	56(47.9)		

### Single factor analysis of persistent symptoms 1 month after infection in children with COVID-19:

The results of the survey of 117 children with COVID-19 showed that 37 children (31.6%) had persistent symptoms 1 month after infection. A univariate analysis of persistent symptoms 1 month later showed that coughing and sputum at the time of infection and access to medical care had an effect on the occurrence of persistent symptoms 1 month after infection and the difference was statistically significant ( $p < 0.05$ ). This was independent of gender, age, vaccination and the presence of underlying disease, as shown in Table 4.

### Multifactor analysis of persistent symptoms associated with 1 month of infection in children with COVID-19:

The occurrence of relevant off persistent symptoms was used as the dependent variable, and the variables that were statistically significant for univariate analysis were included in the logistic regression equation with the following independent variable assignments. Of the medical treatment, home treatment = 0, outpatient treatment = 1, general pediatric inpatient treatment = 2; no cough = 0, cough = 1; no coughing sputum = 0, coughing sputum = 1. The results showed that children hospitalized in general pediatrics (OR=4.745, 95% CI=1.392-16.180) and those who coughed during the infection (OR=5.273, 95% CI=1.767-15.742) were at high risk for the development of associated persistent symptoms ( $p < 0.05$ ) (Table 5).

**Table 5:** Multifactorial analysis of persistent symptoms associated with 1 month of infection in children with COVID-19.

Projects	Category	$\beta$	Standard error	wald $\chi^2$	P	OR	95%CI
Constant		-2.346	0.522	20.228	0.000	0.096	
Cough	No cough (reference)						
	Cough	1.663	0.558	8.879	0.003	5.273	1.767~15.742
Cough with sputum	No coughing sputum (reference)						
	Coughing sputum	0.896	0.551	2.640	0.104	2.449	0.831~7.213
Medical treatment	Home treatment(reference)						
	Outpatient treatment	0.517	0.514	1.011	0.315	1.677	0.612~4.591
	General pediatric inpatient treatment	1.557	0.626	6.191	0.013	4.745	1.392~16.180

## Discussion

Basic situation of children with COVID-19 in the current outbreak. The current survey showed a higher proportion of people without underlying disease (100 cases, 85.5%) than those with underlying disease (17 cases, 14.5%), and studies have shown that the characteristics and outcome patterns of patients infected with Omicron have changed relative to the previous Delta variant, with significantly fewer patients with combined underlying disease [10], and that both people with and without underlying disease are susceptible, which is consistent with the results of the current study; the vaccinated population (75 patients, 64.1%) was higher than the unvaccinated population (42 patients, 35.9%) in this study, probably because the Omicron variant evades immunity from previous vaccines or infections more extensively than any other variant, making existing vaccines less effective against the variant [11] and thus making the vaccinated population. The vaccinated population is equally susceptible. Currently, inactivated novel coronavirus vaccination is promoted for people aged 3-17 years [12], and children under the age of 3 years cannot be vaccinated, which is why some children were not vaccinated in this investigation. This study



showed that after novel coronavirus infection, most of the population chose home treatment and less chose outpatient and inpatient treatment, probably because the Omicron variant rarely caused serious illness compared with the Delta variant, and the clinical symptoms of infected patients were relatively mild [13], while the Omicron variant spread faster and was more contagious, leading most parents to be reluctant to take their affected children. The Omicron variant is also faster spreading and more contagious, leading most parents to be reluctant to take their children to crowded places such as hospitals, thus opting for home treatment. The total number of symptoms during infection was 16, with respiratory, neurological, digestive and skin-muscle related symptoms, with fever and cough being the most common symptoms, followed by cough, stuffy and runny nose, sore throat and decreased appetite, which is consistent with the findings of X Cui [14] and Chen Jun [15].

Persistent symptoms associated with COVID-19 children 1 month after infection and their influencing factors of the 117 children, 37 children (31.6%) presented with persistent symptoms, with cough frequency (24, 44.44%) accounting for the highest proportion of all persistent symptoms, followed by loss of appetite (7, 12.96%) and cough (6, 11.11%), showing that respiratory symptoms accounted for the highest proportion of persistent symptoms. Some studies have analysed the prevalence, risk factors, type and duration of new coronary [16] and found that persistent symptoms most commonly manifested in the neurological and cognitive systems and digestive system, with children with prolonged COVID-19 infection experiencing fatigue, post-exercise discomfort, cognitive dysfunction, memory loss, headache, upright intolerance and sleep difficulties [17,18]. In this study, due to the young age of infants and children, who cannot autonomously express symptoms such as subjective feelings of dizziness, nausea, chest tightness, chest discomfort, palpitations, and altered cognitive and memory function, there may have been instances of missing persistent symptoms, or it may be related to the use of convenience sampling and limiting the study population to patients attending a particular hospital. Seven cases of digestive and seven cases of neurological symptoms were seen in this study, namely loss of appetite, dizziness, drowsiness, insomnia and fatigue, which is inconsistent with the initial view of COVID-19 as a respiratory disease. These symptoms suggest the pathophysiological processes that the virus undergoes in the patient's organism after COVID-19 infection, including the possibility that the virus may harbour in multiple tissues and organs throughout the body for a long period of time, thereby causing chronic inflammation [19], and the need for such patients with persistent symptoms to be followed up for a long period of time and to receive the necessary interventions.

The present investigation showed that children who were hospitalized and had cough symptoms during infection were at high risk for the development of associated persistent symptoms ( $p < 0.05$ ). [1] Hospitalization. According to a Danish study in 2021 [20], only 0.08% of children with COVID-19 required hospitalization, and children with milder symptoms were less likely to be hospitalized compared to adults. The results of this study showed that the total number of children treated at home and in outpatient clinics was 84.6%, while the total number of children who attended a doctor was only 15.4%, and children who were hospitalized were more likely to develop persistent symptoms compared to home and outpatient treated Hospitalized children are more likely to have persistent symptoms than children treated at home or in outpatient clinics. This is because hospitalized patients tend to have more severe new coronary symptoms

that fail to resolve with the application of relevant medications or worsen, are at higher risk of long-term disability in severe/critical cases compared to mild and moderate cases [21] and have a slower recovery, as they are more severely infected and may develop functional impairment of multiple organs. Children, on the other hand, are mostly asymptomatic and mildly ill, and with aggressive treatment most have a good prognosis and generally no significant ongoing symptoms develop. Interventions and rehabilitation measures should therefore be actively implemented in hospitalised patients to prevent exacerbation of the condition and reduce the likelihood of developing associated persistent symptoms [2]. Cough during infection. The results of this study showed that cough was an obvious and common symptom of COVID-19 in children, accounting for 62.39% of patients, and the most common persistent symptom, accounting for 44.44% of total symptoms. One study [22] showed that cough was the most common respiratory symptom of COVID-19, persisting for at least 20 months in 40% of patients. This is because some patients with neocoronavirus infection have a prolonged cough that develops into a subacute or even chronic cough after the symptoms have disappeared in the acute phase, and the mechanism may be related to damage to the tracheal and bronchial mucosa caused by the infection, and non-specific airway inflammation [23]. Therefore relevant systematic investigations should be performed in patients with cough to improve the cure rate of cough.

In this study, a child with Kawasaki disease was diagnosed at our hospital about 4 weeks after contracting the novel coronavirus. The child's medical history and relevant examination reports revealed recurrent high fever (with a maximum temperature of 40.3°C), a generalized red rash, conjunctival congestion and hard swollen toes. The occurrence of Kawasaki disease is currently thought to be the result of a multifactorial genetic, environmental, and immune response, with external infectious factors promoting the activation of the body's immune system, which in turn promotes the development of Kawasaki disease [24], which is more prevalent in children in East Asia and far less prevalent in Europe and the United States than in Asia, and is most prevalent in winter and spring, coinciding with the clustered onset of the new coronavirus at the end of 2022, in this case. It is also possible that the presence of Kawasaki disease in this child may be coincidental. There is a lack of reports on the association between neocoronavirus infection and Kawasaki disease in China, and scientific studies and epidemiological investigations are still needed to investigate whether neocoronavirus induces Kawasaki disease.

## Conclusion

In summary, fever and cough are the most common symptoms during neocoronavirus infection, and nearly one third of children develop persistent symptoms one month after infection, with respiratory symptoms accounting for the highest proportion of persistent symptoms, along with neurological, digestive, skin and muscle damage. Children who were hospitalized and had cough symptoms during infection were at high risk for the development of associated persistent symptoms ( $p < 0.05$ ). The limitations of this study are that a convenience sample was used to investigate the same hospital, which is not representative of the entire population of children with persistent symptoms, and because the children were too young to express some subjective feelings on their own, the survey was mainly based on family members' statements, which may have missed persistent symptoms. Further analysis should be carried out by expanding the survey



area and combining it with the corresponding laboratory reports. In addition, the study currently only summarises the situation around one month after infection, and longer follow-up data are needed to obtain more detailed characteristics of persistent symptoms of COVID-19 in children.

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