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PROCEEDINGS OF THE LATVIAN ACADEMY OF SCIENCES. Section B,
Vol. 78 (2024), No. 1 (748), pp. 44–49.

DOI: 10.2478/prolas-2024-0007

Original Paper

# LONG COVID-19 SYMPTOM PROFILE IN CHILDREN AND ADOLESCENTS TESTED FOR SARS-COV-2

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Communicated by Dace Gardovska

*Even though more than two years have passed since the global pandemic started, COVID-19 continues to impact children all over the world. The most common course of SARS-CoV-2 infection in children is short term with no or mild symptoms. However, there are two long-term consequences: long COVID and multisystem inflammatory syndrome (MIS-C). A post-COVID19 programme for children has been created in Latvia; however, we know that the availability of this service is limited. We developed an online survey so that we could screen for those paediatric patients with long COVID who needed to see a specialist as soon as possible. The cross-sectional study from 1 November 2021 to 27 March 2022 included 220 patients. In our study, the most frequent symptoms in the age group < 1.5 years were irritability (50%), mood swings (50%), persistent cough (33.3%) and loss of appetite (33.3%). In the group aged 1.5–5 years, a persistent cough (54.4%), mood swings (43.9%) and irritability (42.1%) were the most common symptoms, while in the group aged 6–10 years, fatigue (56.6%), abdominal pain (55.3%), headache (50%), and mood swings (50%) were seen most often. Meanwhile in the 11–18 age group, impaired physical activity (66.7%), fatigue (62.3%) and drowsiness (62.3%) were the most frequently seen symptoms.*

**Keywords:** *SARS-CoV-2, long COVID, children, adolescents.*

## INTRODUCTION

On 11 March 2020, the World Health Organisation announced that the spread of novel SARS-CoV-2 had reached the scale of a global pandemic (WHO, 2020). In Latvia, a national state of emergency was declared on 12 March 2020 by the country's government (Ministry of Foreign Affairs, Republic of Latvia, 2020; SPKC, 2021). Even though more than two years have passed since then, COVID-19 continues to impact people severely all over the world (Buonsenso *et al*., 2022). During the global pandemic, SARS-CoV-2 caused significant mortality and morbidity among the global adult population, but in children and adolescents acute infection was often asymptomatic or with mild symptoms and life-threatening complications and death were rare (Li *et al*., 2020). However, there are two long-term consequences of SARS-CoV-2 in children: long COVID and multisystem inflammatory syndrome (MIS-C) (Fainardi *et al*., 2022).

The World Health Organisation's definition of post-COVID condition is as follows: post-COVID-19 condition occurs in young people who have a history of confirmed SARS-CoV-2 infection, with at least one physical symptom persisting for a minimum duration of 12 weeks after initial testing, which cannot be explained by any other diagnosis. The

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symptoms have an impact on daily functioning, may continue or develop after COVID infection and may fluctuate or relapse over time (Soriano *et al*., 2021; Munblit *et al*., 2022; Stephenson *et al*., 2022). The prevalence of long COVID-19 in children and adolescents varies between 4% and 66%, depending on the study (Fainardi *et al*., 2022). The underlying pathophysiology mechanism causing long COVID is still poorly understood (Hoffmann *et al*., 2020), and long COVID is a heterogeneous multisystem condition including symptoms which persist or develop after acute SARS-CoV-2 infection (Lopez-Leon *et al*., 2022).

With the growing incidence of COVID-19 in Latvia, the number of children facing long-term consequences after acute COVID-19 infection also increased rapidly. As a result, the previously formed multi-disciplinary team could not consult patients onsite in a short period of time to provide help as quickly as it was required. We needed to devise a screening tool to identify those patients who needed help as quickly as possible. Therefore, an online screening survey was created to identify those who required an in-person visit most urgently.

Online surveys have also been developed and are being used in other countries to reach as many patients infected with COVID-19 as possible, and to collect data on the associated long-term consequences. For example, thanks to the ZOE mobile application created in the United Kingdom, staff there reached 258,790 respondents (Molteni *et al*., 2021).

The aim of the study was to identify long COVID following SARS-CoV-2 infection in children at least one month after acute COVID-19.

## MATERIALS AND METHODS

**Study design and participants.** This was a cross-sectional study focused on a paediatric population with the aim of identifying long COVID following SARS-CoV-2 infection in children at least one month after acute COVID-19. From 1 November 2021 to 27 March 2022, 220 paediatric patients (aged younger than 18 years) and their parents were enrolled in the study at least four weeks after SARS-CoV-2 infection. Only patients whose SARS-CoV-2 infection had been confirmed by PCR test were included in the study. All enrolled patients and their parents participated voluntarily and self-reported data through the online survey. Afterwards, the children or their parents answered questions and noted the symptoms that appeared after the child became ill with COVID-19. Persistent symptoms were classified according to the organ systems involved, and were divided into three categories according to their severity — green, yellow and red. If a patient developed at least one red symptom following acute SARS-CoV-2 infection, we recommended that they applied for in-person consultation in the post-COVID19 programme.

**Statistical analysis.** Statistical analysis was performed using SPSS 26.0 software. For research purposes the overall and age-stratified prevalence rates (expressed as percentages) of the symptoms were calculated. The statistical significance of the differences in prevalence of symptoms across the age groups was detected using Chi Square or Fisher's Exact tests. A $p$ level below 0.05 was considered to be statistically significant.

## RESULTS

A total of 220 children aged under 18 years with a laboratory-confirmed SARS-CoV-2 infection was included in the study from 1 November 2021 to 27 March 2022. The study is ongoing and still taking on new patients.

Of the patients included in the study, 56.8% (n = 125) were girls and 43.2% (n = 95) were boys. Respondent median age was 8 years and mean age — 8.16 years.

We analysed post-SARS-CoV-2 symptoms in four age groups:

< 1.5 years (8.2% (n = 18) from all respondents);

1.5–5 years (25.9% (n = 57) from all respondents);

6–10 years (34.5% (n = 76) from all respondents);

11–18 years (31.4% (n = 69) from all respondents).

All symptoms evaluated using the screening tool and then analysed are shown in Table 1. The symptoms were analysed according to age group (< 1.5 years, 1–5 years, 6–10 years, and 11–18 years). Those age groups where specific symptoms were not analysed are marked with N/A. Additionally, symptoms were analysed according to organ systems.

Most frequent symptoms across each age group are shown in Table 2. From the respiratory organ system, the most frequent symptoms at least four weeks after acute COVID-19 infection were a cough, still present in 39.5% of all respondents (n = 87; $p < 0.05$) and nasal congestion (39.5%; n = 75). For cardiovascular sequelae, the symptom prevalence was higher in older children: rapid heartbeat (19.7%, n = 15; 6–10-year-olds vs. 46.4%, n = 32; 11–18-year-olds; $p = 0.001$) and chest pain (14.5%, n = 11; 6–10-year-olds vs. 43.5%, n = 30; 11–18-year-olds; $p < 0.001$). As for gastrointestinal symptoms, the only symptom that was statistically significant was weight loss, observed in 7.3% of respondents (n = 16; $p = 0.02$). The prevalence of cognitive complaints increased considerably among the older age groups, with the highest rates for statistically significant symptoms seen in teenagers; for example, memory disturbance (7%, n = 4; 1.5–5-year-olds vs. 10.5%, n = 8; 6–10-year-olds vs. 29%, n = 20; 11–18-year-olds; $p = 0.001$), difficulty in concentrating (19.3%, n = 11; 1.5–5-year-olds vs. 31.6%, n = 24; 6–10-year-olds vs. 53.6%, n = 37; 11–18-year-olds; $p < 0.001$) and an inability to maintain focus (19.3%, n = 11;

*Table 1*. Prevalence of symptoms across all age groups

| Signs/Symptoms | < 0.5 years | | 1.5–5 years | | 6–10 years | | 11–18 years | | *p* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | | n | % |
| **Respiratory sequelae** | | | | | | | | | | | |
| Shortness of breath | 3 | 16.7 | 6 | 10.5 | 12 | 15.8 | 20 | 29.0 | 0.050 | 41 | 18.6 |
| Cough | 6 | 33.3 | 31 | 54.4 | 30 | 39.5 | 20 | 29.0 | **0.03** | 87 | 39.5 |
| Nasal congestion | 3 | 16.7 | 23 | 40.0 | 23 | 30.3 | 26 | 37.7 | 0.23 | 75 | 39.5 |
| Runny nose | 3 | 16.7 | 22 | 38.6 | 15 | 19.7 | 20 | 29.0 | 0.07 | 60 | 27.3 |
| Sore throat | N/A | N/A | 14 | 24.6 | 21 | 27.6 | 26 | 37.7 | 0.23 | 61 | 30.2 |
| Sneezing | N/A | N/A | 8 | 14.0 | 13 | 17.1 | 18 | 26.1 | 0.19 | 39 | 19.3 |
| **Cardiovascular sequelae** | | | | | | | | | | | |
| Rapid heartbeat | N/A | N/A | N/A | N/A | 15 | 19.7 | 32 | 46.4 | **0.001** | 47 | 32.4 |
| Chest pain | N/A | N/A | 1 | 1.8 | 11 | 14.5 | 30 | 43.5 | **< 0.001** | 42 | 20.8 |
| **Skin and mucosa sequelae** | | | | | | | | | | | |
| Exanthema | 4 | 22.2 | 12 | 21.1 | 18 | 23.7 | 12 | 17.4 | 0.82 | 46 | 20.9 |
| Conjunctivitis | 4 | 22.2 | 6 | 10.5 | 9 | 11.8 | 16 | 23.2 | 0.14 | 35 | 15.9 |
| Mouth ulcers | N/A | N/A | 4 | 7.0 | 3 | 3.9 | 10 | 14.5 | 0.07 | 17 | 8.4 |
| Altered tongue | N/A | N/A | 5 | 8.8 | 8 | 10.5 | 9 | 13.0 | 0.74 | 22 | 10.9 |
| **Gastrointestinal sequelae** | | | | | | | | | | | |
| Diarrhoea | 3 | 16.7 | 7 | 12.3 | 14 | 18.4 | 10 | 14.5 | 0.80 | 34 | 15.5 |
| Constipation | 4 | 22.2 | 11 | 19.3 | 7 | 9.2 | 4 | 5.8 | 0.050 | 26 | 11.8 |
| Weight loss | 1 | 5.6 | 2 | 3.5 | 2 | 2.6 | 11 | 15.9 | **0.02** | 16 | 7.3 |
| Weight gain | N/A | N/A | 3 | 5.3 | 1 | 1.3 | 6 | 8.7 | 0.12 | 10 | 5.0 |
| Abdominal pain | 5 | 27.8 | 20 | 35.1 | 42 | 55.3 | 31 | 44.9 | 0.054 | 98 | 44.5 |
| Decreased appetite | 6 | 33.3 | 20 | 35.1 | 25 | 32.9 | 21 | 30.4 | 0.96 | 72 | 32.7 |
| Nausea, vomiting | 3 | 16.7 | 4 | 7.0 | 15 | 19.7 | 12 | 17.4 | 0.22 | 34 | 15.5 |
| **Otorhinolaryngological sequelae** | | | | | | | | | | | |
| Pain in the ears | N/A | N/A | 8 | 14.0 | 6 | 7.9 | 7 | 10.1 | 0.52 | 21 | 10.4 |
| Change in sense of smell | N/A | N/A | 5 | 8.8 | 4 | 5.3 | 20 | 29.0 | **< 0.001** | 29 | 14.4 |
| Tinnitus | N/A | N/A | 3 | 5.3 | 3 | 3.9 | 10 | 14.5 | **0.04** | 16 | 7.9 |
| Hoarseness of voice | N/A | N/A | 9 | 15.8 | 12 | 15.8 | 16 | 23.2 | 0.44 | 37 | 18.3 |
| Change in sense of taste | N/A | N/A | 8 | 14.0 | 8 | 10.5 | 19 | 27.5 | **0.02** | 35 | 17.3 |
| **Musculoskeletal sequelae** | | | | | | | | | | | |
| Myalgias | N/A | N/A | 17 | 29.8 | 22 | 28.9 | 30 | 43.5 | 0.13 | 69 | 34.2 |
| **General sequelae** | | | | | | | | | | | |
| Fatigue | N/A | N/A | 19 | 33.3 | 43 | 56.6 | 43 | 62.3 | **0.003** | 105 | 52.0 |
| Fever | 1 | 5.6 | 5 | 8.8 | 6 | 7.9 | 7 | 10.1 | 0.98 | 19 | 8.6 |
| Difficulty climbing to the 3rd floor | N/A | N/A | N/A | N/A | 15 | 19.7 | 28 | 40.6 | **0.006** | 43 | 29.7 |
| Hard to walk for 15 min. | N/A | N/A | 16 | 28.1 | 20 | 26.3 | 24 | 34.8 | 0.51 | 60 | 29.7 |
| Subfebrile temperature | 2 | 11.1 | 14 | 24.6 | 16 | 21.1 | 13 | 18.8 | 0.64 | 45 | 20.5 |
| Exercise intolerance | N/A | N/A | N/A | N/A | 36 | 47.4 | 46 | 66.7 | **0.02** | 82 | 56.6 |
| Sleeps during the day | N/A | N/A | 8 | 14.0 | 32 | 42.1 | 43 | 62.3 | **< 0.001** | 83 | 41.1 |
| Does not play | 4 | 22.2 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | 4 | 22.2 |
| More passive | 3 | 16.7 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | 3 | 16.7 |
| **Neurological sequelae** | | | | | | | | | | | |
| Trembling | 0 | 0 | 2 | 3.5 | 6 | 7.9 | 12 | 17.4 | **0.02** | 20 | 9.1 |
| Seizure(s) | 0 | 0 | 1 | 1.8 | 0 | 0 | 11 | 15.9 | **< 0.00 1** | 12 | 5.5 |
| Altered speech | N/A | N/A | 3 | 5.3 | 4 | 5.3 | 4 | 5.8 | 0.99 | 11 | 5.4 |
| Balance impairment | 2 | 11.1 | 2 | 3.5 | 5 | 6.6 | 15 | 21.7 | **0.005** | 24 | 10.9 |
| Photophobia | 0 | 0 | 6 | 10.5 | 9 | 11.8 | 16 | 23.2 | **0.04** | 31 | 14.1 |
| Headache | N/A | N/A | 9 | 15.8 | 38 | 50.0 | 33 | 47.8 | **< 0.001** | 80 | 39.6 |
| Dizziness | N/A | N/A | N/A | N/A | 19 | 25.0 | 24 | 34.8 | 0.20 | 43 | 29.7 |
| Deterioration of vision | N/A | N/A | 1 | 1.8 | 4 | 5.3 | 7 | 10.1 | 0.14 | 12 | 5.9 |
| Altered gait | 0 | 0 | 1 | 1.8 | 3 | 3.9 | 6 | 8.7 | 0.28 | 10 | 4.5 |
| Sleep disturbance | 5 | 27.8 | 15 | 26.3 | 24 | 31.6 | 27 | 39.1 | 0.46 | 71 | 32.3 |
| Tingling sensation | N/A | N/A | N/A | N/A | 10 | 13.2 | 14 | 20.3 | 0.25 | 24 | 16.6 |

*Continuation of Table 1.* Prevalence of symptoms across all age groups

| Signs/Symptoms | .5 years | | 1.5–5 years | | 6–10 years | | 11–18 years | | *p* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | | n | % |
| Cognitive sequelae | | | | | | | | | | | |
| Drowsiness | 4 | 22.2 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | 4 | 22.2 |
| Irritability | 9 | 50.0 | 24 | 42.1 | 35 | 46.1 | 34 | 49.3 | 0.86 | 102 | 46.4 |
| Memory disturbance | N/A | N/A | 4 | 7.0 | 8 | 10.5 | 20 | 29.0 | **0.001** | 32 | 15.8 |
| Difficulty concentrating | N/A | N/A | 11 | 19.3 | 24 | 31.6 | 37 | 53.6 | < **0.001** | 72 | 35.6 |
| Communication difficulties | N/A | N/A | 5 | 8.8 | 3 | 3.9 | 18 | 26.1 | < **0.001** | 26 | 12.9 |
| Mood swings | 9 | 50.0 | 25 | 43.9 | 38 | 50.0 | 38 | 55.1 | 0.67 | 110 | 50.0 |
| Unable to maintain focus | N/A | N/A | 11 | 19.3 | 22 | 28.9 | 33 | 47.8 | **0.002** | 66 | 32.7 |
| Other symptoms | | | | | | | | | | | |
| Hair loss | 2 | 11.1 | 7 | 12.3 | 4 | 5.3 | 14 | 20.3 | 0.06 | 27 | 12.3 |
| Swollen neck lymph nodes | 4 | 22.2 | 4 | 7.0 | 3 | 3.9 | 10 | 14.5 | **0.04** | 21 | 9.5 |
| Exacerbation of allergies | 1 | 5.6 | 2 | 3.5 | 4 | 5.3 | 6 | 8.7 | 0.65 | 13 | 5.9 |
| Menstrual disturbance | N/A | N/A | N/A | N/A | N/A | N/A | 4 | 5.8 | N/A | 4 | 5.8 |
| Urinary problems | 2 | 11.1 | 5 | 8.8 | 10 | 13.2 | 7 | 10.1 | 0.87 | 24 | 10.9 |
| Other | 5 | 27.8 | 14 | 24.6 | 25 | 32.9 | 15 | 21.7 | 0.48 | 59 | 26.8 |

*p*-value below 0.05 is marked in bold

1.5–5-year-olds vs. 28.9%, n = 22; 6–10-year-olds vs. 47.8%, n = 33; 11–18-year-olds; $p < 0.001$).

## DISCUSSION

In our study, the most frequent symptoms in the 6–10 age group were fatigue (56.6%), abdominal pain (55.3%), headache (50%), and mood swings (50%), while in the 11–18 age group they were impaired physical activity (66.7%), fatigue (62.3%), and drowsiness (62.3%). In comparison, in a wide systemic review that included 21 observational studies with a minimum of 30 paediatric patients in each, the five most frequent clinical symptoms identified were mood changes (16.5%), fatigue (9.66%), sleep disorders (8.42%), headaches (7.84%), and respiratory symptoms (7.62%) (Hoffmann *et al*., 2020). In our study, symptom prevalence was much higher, most probably because we targeted those patients whose symptoms persisted four weeks after the acute infection. The most commonly reported persistent symptoms in our SARS-CoV-2-positive older children were fatigue and impaired physical activity. Additionally, many studies have shown that fatigue is one of the most common symptoms not only in children, but as also in adults (Carfǵ *et al*., 2020; Townsend *et al*., 2020; Molteni *et al*., 2021; Funk *et al*., 2022). We observed that upper respiratory-tract symptoms, such as a persistent cough, were most commonly reported in younger children. A similar pattern was seen in an Italian study, which found that the paediatric population had prolonged respiratory symptoms (Buonsenso *et al*., 2021).

The main strength of our study was that it included patients from all regions of Latvia whose symptoms persisted four weeks after acute COVID-19 infection in a short time period, with the help of our online survey.

*Table 2.* Most frequent symptoms across each age group

| Age group | Symptom | Frequency in age group, % |
|---|---|---|
| < 0.5 years | Irritability | 50.0 |
| | Mood swings | 50.0 |
| | Persistent cough | 33.3 |
| | Loss of appetite | 33.3 |
| 1.5–5 years | Persistent cough | 54.4 |
| | Mood swings | 43.9 |
| | Irritability | 42.1 |
| 6–10 years | Fatigue | 56.6 |
| | Abdominal pain | 55.3 |
| | Headache | 50.0 |
| | Mood swings | 50.0 |
| 11–18 years | Impaired physical activity | 66.7 |
| | Fatigue | 62.3 |
| | Drowsiness | 62.3 |

Our study also faced limitations. First of all, we used an online survey, completed only four weeks after acute SARS-CoV-2 infection. Of course, we reached a large group of respondents in a really short period of time this way, but had no detailed medical data or history for each individual. And because the survey was anonymous, it was impossible to follow up these patients in the long term. This is also mentioned as one of the main limitations in a publication from a paediatric post-COVID unit in Rome (Buonsenso *et al*., 2021). This unit also emphasised the need for reliable control groups, real-time clinical investigations, further research and long-term follow-up of paediatric long COVID patients (Buonsenso *et al*., 2021). The second limitation was that we had no control group for our study. However, recent discussions have stressed that it is almost impossible

to find control groups for a project like this, because a very large part of the population has already had acute SARS-CoV-2 infection at least once. Additionally, in children, for example, home tests can yield false positive/negative results, while they can also quite often be asymptomatic (Lopez-Leon *et al*., 2022).

## CONCLUSIONS

An online survey is a great way to reach today's children and adolescents about healthcare issues. This study has shown that SARS-CoV-2 infection affects children's physical health with a wide range of symptoms for at least four weeks after an acute infection, with fatigue being the most common one in older children.

## ETHICS

Before starting with the screening tool, participants or their parents gave consent for their data to be analysed and used in the research.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available upon request to the corresponding author.

## CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## AUTHOR CONTRIBUTIONS

AM, LS, and JP conceptualised the study. AK-U performed statistical analyses. All authors contributed to the article and approved the submitted version.

## ACKNOWLEDGEMENTS

We thank the patients and their families who are enrolled in this study.

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Received 4 October 2022
Accepted in the final form 23 January 2024

## ILGTERMIŅA COVID-19 SIMPTOMU IZVĒRTĒJUMS BĒRNIEM

Lai arī Covid-19 pandēmija tika izsludināta pirms vairāk nekā diviem gadiem, tomēr joprojām SARS-CoV-2 ilgtermiņa ietekme bērnu populācijā saglabā savu aktualitāti. Visbiežāk SARS-CoV-2 infekcijas gaita bērniem ir viegla vai pat asimptomātiska. Tomēr ir divas ļoti nopietnas ilgtermiņa sekas: garais Covid-19 un daudzsistēmu iekaisuma sindroms, asociēts ar Covid-19 (MIS-C). Dinamiskās novērošanas programma bērniem pēc Covid-19 pārslimošanas tika izveidota arī Latvijā, taču pakalpojuma pieejamība ir ierobežota, līdz ar to bija nepieciešams izveidot tiešsaistes skrīninga rīku, lai varētu atlasīt tos pacientus, kuriem nepieciešama profesionāla palīdzība pēc iespējas ātrāk. Pētījuma un tiešsaistes skrīninga rīka izstrādes mērķis bija atlasīt tos bērnus ar ilgstošu Covid-19, kuriem pēc iespējas ātrāk nepieciešama klātienes vizīte pie specializēta medicīnas personāla. Šķērsgriezuma pētījums tika uzsākts 2021. gada 1. novembrī un norisinās līdz šim brīdim, tomēr šajā rakstā tiek analizēti tie pacienti, kuri aizpildījuši tiešsaistes anketu līdz 2022. gada 27. martam. Datu analīzē kopumā tika iekļauti 220 pacienti. Pētījumā biežākie konstatētie simptomi četras nedēļas pēc akūtās infekcijas vecuma grupā < 1,5 gadiem bija aizkaitināmība (50%), garastāvokļa svārstības (50%), pastāvīgs klepus (33,3%) un samazināta apetīte (33,3%). Vecuma grupā no 1.5 līdz 5 gadiem pastāvīgs klepus (54,4%), garastāvokļa svārstības (43,9%), aizkaitināmība (42,1%) un vecuma grupā no 6–10 gadiem nogurums (56,6%), sāpes vēderā (55,3%), galvassāpes (50%), garastāvokļa svārstības (50%), bet vecuma grupā 11–18 gadi grūtības veikt fiziskās aktivitātes (66,7%), nogurums (62,3%) un miegainība (62,3%).