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ACTA PÆDIATRICA NURTURING THE CHILD WILEY

BRIEF REPORT

Preliminary evidence on long COVID in children

1 | INTRODUCTION

There is increasing evidence that adult patients diagnosed with acute COVID-19 suffer from Long COVID initially described in Italy.[1] A recent large cohort of 1733 patients from Wuhan found persistent symptoms in 76% of patients 6 months after initial diagnosis.[2] To date, data on Long COVID in children are scarce, with the exception of an earlier description of five children with Long COVID in Sweden.[3] We assessed persistent symptoms in paediatric patients previously diagnosed with COVID-19.

2 | METHODS

This cross-sectional study included all children ≤18 year old diagnosed with microbiologically confirmed (PCR analysis on nasopharyngeal swab) COVID-19 (through a nasopharyngeal swab from March 2020 to October 2020) in Fondazione Policlinico Universitario A. Gemelli IRCCS (Rome, Italy). Only children with a SARS-CoV-2 infection diagnosed 30 days before the assessment were included. Patients >18 years old or with severe neurocognitive disability were excluded, since this would have not allowed a proper assessment of signs and symptoms included in the survey. Caregivers were interviewed about their child's health using a questionnaire (Appendix S1) developed by the Long COVID ISARIC study group,[4] for evaluation of persisting symptoms. Participants were interviewed by two paediatricians, either by phone or in the outpatient department, from 1 September 2020 to 1 January 2021. For those assessed in the outpatient settings, the same survey was used and symptoms reported were collected even if not present at the moment of the visit (eg tachycardia). Also, investigations were not performed at the moment of the assessment, in order to rule-out other causes, although the survey has a section to ask whether other possible causes have been detected in the meantime. Participants were categorised into groups according to symptoms status during the acute phase (symptomatic/asymptomatic), need for hospitalisation and time from COVID-19 diagnosis to follow-up evaluation (<60, 60–120, >120 days). Numerical variables were compared using t test or ANOVA and categorical variables with chi-square or Fisher's exact test where appropriate. All analyses were performed using R version 4.0.3 (R Foundation). This study was approved by the Institutional Ethic Committee of the Fondazione Policlinico Universitario A. Gemelli IRCCS—Università Cattolica del Sacro Cuore (ID 3777), and all participants consented to participate.

3 | RESULTS

One hundred and twenty-nine children diagnosed with COVID-19 between March and November 2020 were enrolled (mean age of 11 ± 4.4 years, 62 (48.1%) female). Six children with severe neurocognitive impairment were excluded due to impossibility to report signs/symptoms included in the survey. Hundred and nine children (84.5%) were interviewed by phone call, and the remaining during outpatient assessment. During the acute COVID-19, 33 children (25.6%) were asymptomatic, and 96 (74.4%) had symptoms. Overall, 6 (4.7%) children were hospitalised, and 3 (2.3%) needed paediatric intensive care unit admission. After the initial diagnosis of COVID-19, three developed multisystem inflammatory syndrome (2.3%) and two myocarditis (1.6%). Patients were assessed on average 162.5 ± 113.7 days after COVID-19 microbiological diagnosis. 41.8% completely recovered, 35.7% had one or two symptoms and 22.5% had three or more (Table S1).

Table 1 provides details about persistence of symptoms according to severity and length of follow-up. Insomnia (18.6%), respiratory symptoms (including pain and chest tightness) (14.7%), nasal congestion (12.4%), fatigue (10.8%), muscle (10.1%) and joint pain (6.9%), and concentration difficulties (10.1%) were the most frequently reported symptoms. These symptoms, described both in children with symptomatic and asymptomatic acute COVID-19, were particularly frequent in those assessed >60 days after the initial diagnosis.

Twenty out of 30 children (66.6%) assessed between 60 and 120 days after initial COVID-19 had at least one persisting symptom (13 had one or two symptoms, seven had three or more); 35 of 68 children (27.1%) had at least one symptom 120 days or more after diagnosis (21 had one or two symptoms, 14 had three or more). Twenty-nine out of the 68 (42.6%) children assessed ≥120 days from diagnosis were still distressed by these symptoms.

4 | DISCUSSION

This is a large series study providing evidence of Long COVID in children, and currently to our knowledge in literature, there is

TABLE 1 Persisting symptoms in children with COVID-19, according to symptoms, need of hospitalisation and distance from diagnosis of acute COVID-19

	All	According to symptoms			According to hospitalisation			According to days from COVID−19 diagnosis		
Persisting symptoms	*N* 129	Asymptomatic *N* 33	Symptomatic *N* 96	*p* value	Not Hospitalised *N* 123	Hospitalised *N* 6	*p* Value	<60 *N* 31	60–119 *N* 30	>120 *N* 68
Fatigue (compared to before COVID−19 diagnosis)										
Less	1 (0.8%)	0 (0%)	1 (1%)	0.453	1 (0.8%)	0 (0%)	0.36	0 (0%)	1 (3.3%)	0 (0%)
A bit less	16 (12.4%)	2 (6.1%)	14 (14.6%)		16 (13%)	0 (0%)		6 (19.4%)	4 (13.3%)	6 (8.8%)
Same	98 (75.9%)	29 (87.9%)	69 (71.9%)		94 (76.4%)	4 (66.7%)		24 (77.4%)	21 (70%)	53 (77.9%)
A bit more	13 (10.1%)	2 (6.1%)	11 (11.5%)		11 (8.9%)	2 (33.3%)		1 (3.2%)	4 (13.3%)	8 (11.8%)
More	1 (0.8%)	0 (0%)	1 (1%)		1 (0.8%)	0 (0%)		0 (0%)	0 (0%)	1 (1.5%)
Insomnia	24 (18.6%)	2 (6.1%)	22 (22.9%)	0.059	23 (18.7%)	1 (16.7%)	1	6 (19.4%)	7 (23.3%)	11 (16.2%)
Nasal congestion/ rhinorrhoea	16 (12.4%)	1 (3%)	15 (15.6%)	0.112	15 (12.2%)	1 (16.7%)	1	5 (16.1%)	2 (6.7%)	9 (13.2%)
Persistent muscle pain	13 (10.1%)	1 (3%)	12 (12.5%)	0.221	13 (10.6%)	0 (0%)	0.919	5 (16.1%)	2 (6.7%)	6 (8.8%)
Headache	13 (10.1%)	1 (3%)	12 (12.5%)	0.221	13 (10.6%)	0 (0%)	0.87	1 (3.2%)	7 (23.3%)	5 (7.4%)
Lack of concentration	13 (10.1%)	1 (3%)	12 (12.5%)	0.221	13 (10.6%)	0 (0%)	na	2 (6.5%)	3 (10%)	8 (11.8%)
Weight loss	10 (7.7%)	2 (6.1%)	8 (8.3%)	0.965	9 (7.3%)	1 (16.7%)	0.971	2 (6.5%)	5 (16.7%)	3 (4.4%)
Joint pain or swelling	9 (6.9%)	1 (3%)	8 (8.3%)	0.525	8 (6.5%)	1 (16.7%)	0.838	4 (12.9%)	2 (6.7%)	3 (4.4%)
Skin rashes	9 (6.9%)	3 (9.1%)	6 (6.2%)	0.876	9 (7.3%)	1 (16.7%)	0.838	1 (3.2%)	2 (6.7%)	5 (7.4%)
Chest tightness	8 (6.2%)	0 (0%)	8 (8.3%)	0.196	8 (6.5%)	0 (0%)	na	5 (16.1%)	2 (6.7%)	1 (1.5%)
Constipation	8 (6.2%)	1 (3%)	7 (7.3%)	0.647	7 (5.7%)	0 (0%)	na	1 (3.2%)	0 (0%)	2 (2.9%)
Persistent cough	7 (5.4%)	1 (3%)	6 (6.2%)	0.796	6 (4.9%)	1 (16.7%)	0.761	2 (6.5%)	1 (3.3%)	4 (5.9%)
Altered smell	6 (4.6%)	0 (0%)	6 (6.2%)	0.321	6 (4.9%)	0 (0%)	na	1 (3.2%)	1 (3.3%)	4 (5.9%)
Palpitations	5 (3.8%)	1 (3%)	4 (4.2%)	1	5 (4.1%)	0 (0%)	na	2 (6.5%)	3 (10%)	4 (5.9%)
Chest pain	4 (3.1%)	1 (3%)	3 (3.1%)	1	4 (3.3%)	0 (0%)	na	2 (6.5%)	1 (3.3%)	1 (1.5%)
Altered taste	4 (3.1%)	0 (0%)	4 (4.2%)	0.542	4 (3.3%)	0 (0%)	na	1 (3.2%)	0 (0%)	3 (4.4%)
Hypersomnia	4 (3.1%)	2 (6.1%)	2 (2.1%)	0.579	4 (3.3%)	0 (0%)	1	1 (3.2%)	0 (0%)	3 (4.4%)
Stomach/abdominal pain	3 (2.3%)	0 (0%)	3 (3.1%)	0.72	3 (2.4%)	0 (0%)	na	1 (3.2%)	1 (3.3%)	0 (0%)
Diarrhoea	2 (1.5%)	0 (0%)	2 (2.1%)	0.985	2 (1.6%)	1 (16.7%)	0.971	3 (9.7%)	2 (6.7%)	5 (7.4%)
Menstruation	2 (1.5%)	0 (0%)	2 (2.1%)	0.985	2 (1.6%)	0 (0%)	na	2 (6.5%)	2 (6.7%)	1 (1.5%)
other: yes	3 (2.3%)	1 (3%)	2 (2.1%)	1	3 (2.4%)	0 (0%)	na	1 (3.2%)	1 (3.3%)	0 (0%)
Any persisting symptoms										
None	54 (41.9%)	21 (63.6%)	33 (34.4%)	**0.009**	53 (43.1%)	1 (16.7%)	**0.041**	11 (35.5%)	10 (33.3%)	33(48.5%)
1–2	46 (35.6%)	9 (27.3%)	37 (38.5%)		41 (33.3%)	5 (83.3%)		12 (38.7%)	13 (43.3%)	21 (30.9%)

(Continues)

TABLE 1 (Continued)

Persisting symptoms	All N 129	According to symptoms Asymptomatic N 33	Symptomatic N 96	p value	According to hospitalisation Not Hospitalised N 123	Hospitalised N 6	p Value	According to days from COVID-19 diagnosis <60 N 31	60–119 N 30	>120 N 68
3 or more	29 (22.5%)	3 (9.1%)	26 (27.1%)		29 (23.6%)	0 (0%)		8 (25.8%)	7 (23.3%)	14 (20.6%)
Do symptoms distress the child?										
Not at all	66 (51.1%)	15 (45.5%)	51 (53.1%)	0.595	64 (52%)	2 (33.3%)	0.52	19 (61.3%)	15 (50%)	32 (47.1%)
Only a little	36 (27.9%)	12 (36.4%)	24 (25%)		36 (10.6%)	0 (0%)		8 (25.8%)	5 (16.7%)	23 (33.8%)
Quite a lot	14 (10.8%)	4 (12.1%)	10 (10.4%)		13 (10.6%)	1 (16.7%)		3 (9.7%)	6 (20%)	5 (7.4%)
A great deal	2 (1.5%)	1 (3%)	1 (1%)		2 (1.6%)	0 (0%)		0 (0%)	1 (3.3%)	1 (1.5%)
Prefer not to say	11 (8.5%)	1 (3%)	10 (10.4%)		8 (6.5%)	3 (50%)		1 (3.2%)	3 (10%)	7 (10.3%)

Note: Others include hair loss (*n* 2) and skin peeling (*n* 1).
Abbreviation: NA, not applicable.
Statistically significant values are indicated in bold.

another report supporting the topic.[4] More than a half of the children assessed during the survey reported at least one symptom. In particular, 42.6% presented at least one symptoms >60 days after infection. Symptoms like fatigue, muscle and joint pain, headache, insomnia, respiratory problems and palpitations were particularly frequent, as also described in adults.[1,2] To date, the only other paediatric study available is a Swedish case series of five children, all suffering from fatigue, dyspnoea, heart palpitations or chest pain after >60 days from initial diagnosis.[3] Importantly, all those Swedish children had persistent symptoms after 6 months. These findings are in line with the patterns of symptoms reported in our cohort. Also, the Swedish children with Long COVID had a median age of 12 years, similar to our children (11.4 years), further supporting that this age group may particularly suffer from Long COVID.

An important and unexpected finding is that also children with an asymptomatic or paucisymptomatic COVID-19 developed chronic, persisting symptoms, although followed-up for a relatively short time after the diagnosis.

Limitations of the study include the single-centre design with a relatively small sample size. All patients were interviewed once, and a control group of children without COVID-19 was not included.

Children have been mostly overlooked during this pandemic, since the clinical course of COVID-19 in this group is much milder than in adults.[5] However, there is an increasing evidence that restrictive measures aimed at limiting the pandemic are having a significant impact on child's mental health.[6] Childhood is a delicate and fundamental period of life, critical for acquisition of social, behavioral and educational development. The evidence that COVID-19 can have long-term impact on children as well, including those with asymptomatic/paucisymptomatic COVID-19, highlight the need for paediatricians, mental health experts and policymakers of implementing measures to reduce impact of the pandemic on child's health. Importantly, further prospective studies, not only based on surveys but with objective clinical assessment and including healthy controls that never had COVID-19, are needed to better understand the burden of Long COVID in children.

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CONFLICT OF INTEREST

The authors have no example conflicts of interest to disclose.

Danilo Buonsenso[1,2,3]
Daniel Munblit[4,5,6]
Cristina De Rose[1]
Dario Sinatti[1]
Antonia Ricchiuto[1]
Angelo Carfi[7]
Piero Valentini[1,3]

[1]*Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*
[2]*Dipartimento di Scienze Biotecnologiche di Base, Cliniche Intensivologiche e Perioperatorie, Università Cattolica del Sacro Cuore, Rome, Italy*
[3]*Global Health Research Institute, Istituto di Igiene, Università Cattolica del Sacro Cuore, Roma, Italy*
[4]*Department of Paediatrics and Paediatric Infectious Diseases, Institute of Child's Health, Sechenov First Moscow State Medical University (Sechenov University, Moscow, Russia*
[5]*Inflammation, Repair and Development Section, National Heart and Lung Institute, Faculty of Medicine, Imperial College London, London, UK*
[6]*Research and Clinical Center for Neuropsychiatry, Moscow, Russia*
[7]*Geriatric Department, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*

Correspondence
Danilo Buonsenso, Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo A. Gemelli 8, 00168, Rome, Italy.
Email: danilobuonsenso@gmail.com

ORCID

Danilo Buonsenso https://orcid.org/0000-0001-8567-2639
Cristina De Rose https://orcid.org/0000-0002-5394-8335

REFERENCES

1. Carfì A, Bernabei R, Landi F, Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA. 2020;324(6):603-605.
2. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021;397(10270):220-232.
3. Ludvigsson JF. Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19. Acta Paediatr. 2021;110(3):914-921.
4. Norton A, Olliaro P, Sigfrid L, et al. ISARIC and GloPID-R Long COVID Forum Working Group. Long COVID: tackling a multi-faceted condition requires a multidisciplinary approach. Lancet Infect Dis. 2021 Feb 3:S1473-3099(21)00043-8. https://doi.org/10.1016/S1473-3099(21)00043-8. Epub ahead of print. Erratum in: Lancet Infect Dis. 2021 Feb 16. PMID: 33548193; PMCID: PMC7906694.
5. Parri N, Magistà AM, Marchetti F, et al. Characteristic of COVID-19 infection in pediatric patients: early findings from two Italian Pediatric Research Networks. Eur J Pediatr. 2020;179(8):1315-1323. https://doi.org/10.1007/s00431-020-03683-8
6. Buonsenso D, Roland D, De Rose C, et al. Schools closures during the COVID-19 pandemic: a catastrophic global situation. Pediatr Infect Dis J. 2021;10: e146-e150.

SUPPORTING INFORMATION

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