PLOS ONE

RESEARCH ARTICLE

A systematic review of post COVID-19 condition in children and adolescents: Gap in evidence from low-and -middle-income countries and the impact of SARS-COV-2 variants

Nina Dwi Putri[1,2,3]*, Ida Safitri Laksanawati[4,5], Dominicus Husada[6,7], Nastiti Kaswandani[1,2], Ari Prayitno[1,2], Rina Triasih[4,5], Irma Sri Hidayati[4,5], Retno Asih[6,7], Robby Nurhariansyah[7], Fabiola Cathleen[2], Dwiana Ocviyanti[8,9], Sri Rezeki Hadinegoro[1,2], Dan Pelicci[3], Julie Bines[3], Stephen M. Graham[3]

1 Department of Pediatrics, Cipto Mangunkusumo Hospital, Jakarta, Indonesia, **2** Department of Pediatrics, Faculty of Medicine, Universitas Indonesia, Depok, Indonesia, **3** Department of Paediatrics, University of Melbourne and Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, Victoria, Australia, **4** Department of Pediatrics, Dr. Sardjito Hospital, Yogyakarta, Indonesia, **5** Department of Pediatrics, Faculty of Medicine, Nursing and Public Health, Universitas Gadjah Mada, Yogyakarta, Indonesia, **6** Department of Pediatrics, Dr. Soetomo Hospital, Surabaya, Indonesia, **7** Department of Pediatrics, Faculty of Medicince, Universitas Airlangga, Surabaya, Indonesia, **8** Department of Obstetrics and Gynaecology, Cipto Mangunkusumo Hospital, Jakarta, Indonesia, **9** Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

* ninadwip@gmail.com

OPEN ACCESS

Citation: Putri ND, Laksanawati IS, Husada D, Kaswandani N, Prayitno A, Triasih R, et al. (2025) A systematic review of post COVID-19 condition in children and adolescents: Gap in evidence from low-and -middle-income countries and the impact of SARS-COV-2 variants. PLoS ONE 20(3): e0315815. https://doi.org/10.1371/journal.pone.0315815

Editor: Muhammad Iqhrammullah, Universitas Muhammadiyah Aceh, INDONESIA

Received: February 15, 2024

Accepted: December 1, 2024

Published: March 3, 2025

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0315815

Abstract

The long-term health consequences following COVID-19 have largely been reported in adult populations living in high-income countries. We therefore did a systematic review of post COVID-19 condition symptoms reported in children and adolescents (<18 years), aiming to identify and include publications from low- or middle-income countries (LMICs). From EMBASE, Medline, and Pubmed until the 30th of October 2023, we searched all studies reporting original and complete data of long-term outcomes of at least 20 children or adolescents under 18 years of age with a history of confirmed acute COVID-19 infection. We excluded non-English publications, pre-prints, unreviewed articles, grey literature, studies with inaccessible full text, and those limited to a specific population. Risk of Bias was assessed using STROBE guidelines for observational studies. We used descriptive narrative analysis to summarize the findings. Forty studies reporting 825,849 children and adolescents; the median age of those with persistent symptoms was consistently in the adolescent age range but not all studies included young children (<5 years). Only one study, with 58 participants aged 6-17 years, population was from a LMIC. Studies relied on symptom reporting rather than objective measures of organ dysfunction. The definition of post COVID-19 condition varied; most studies used persistent symptom duration of two or three months or more. However, since the symptom onset was not specified, it was difficult to identify which study is truly consistent with WHO's definition of post COVID-19 condition. Prevalence of post COVID-19 condition ranged from 1.8% to 70% but with marked

Data availability statement: All relevant data are within the manuscript and its Supporting Information files.

Funding: This research received funding from the Indonesia Endowment Fund for Education Agency on the Partnership in Research Indonesia and Melbourne (PRIME funding code PRJ-120/LPDP/2021) through DO. The funders had no role in study design, data collection and analysis, publication decisions, or manuscript preparation.

Competing interests: The authors have declared that no competing interests exist.

heterogeneity between study populations and reporting criteria including the severity of acute COVID presentation. Most studies were undertaken when the Alpha variant was the predominant strain. The prevalence of post COVID-19 condition ranged from 6.7% to 70% in the Alpha variant-, 23% to 61.9% in the Delta-, 17% to 34.6% in the Omicron-, and 3.7% to 34% in the Other-variant predominated studies. The most reported symptoms were fatigue (70%), headache (37.5%) and respiratory symptoms (35%); fatigue was most reported in all variant subgroups. Only half of the studies included a control group. The variations in study population, reporting methods, reliance on symptom reporting alone and lack of control groups make it challenging to determine the impact of COVID-19 on post COVID health in children and adolescents. The lack of data from LMIC populations especially infants and young children is a major gap.

Introduction

Globally, one-fifth of Coronavirus disease 2019 (COVID-19) reported cases have been in children and adolescents (<18 years) [1]. COVID-19 in children is usually less severe and associated with a lower mortality than in adults [2]. However, severe disease and COVID-related mortality have been observed in neonates and infants, children with comorbidities and those living in low- or middle-income countries (LMICs) [3–5]. Furthermore, there is concern regarding long-term health consequences following acute COVID-19 infection in children and adolescents based on observational evidence in adults with COVID-19 as well as previous experience of severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [6,7].

Post COVID-19 condition in adults have been receiving increasing attention, with over 100 symptoms documented [8]. A meta-analysis of 22 studies found that prolonged fatigue, joint pain, anosmia, headache, and myalgia, were recorded in 21.2%, 15.4%, 9.7%, 8.9%, and 5.6%, of adult COVID-19 survivors, respectively [9]. Similarly, a 2024 meta-analysis identified post COVID-19 symptoms in 30% of 7,912 adult participants, with fatigue being the most prevalent symptom, affecting 28.0% of individuals two years following the acute infection. However, the study reported high heterogeneity and limits generalizability [8]. It is important to have similar analysis for children and to contrast with data in adults.

By the end of 2023, there were eight published systematic reviews of post COVID-19 condition in children [10–17]. The most recent systematic review included over 15,000 study participants and reported that over 16.2% of children and adolescents experienced post COVID-19 condition symptoms [15]. Almost all reported study populations live in high-income countries (HICs) and the definitions of post COVID-19 condition used by studies were highly variable. A standardized clinical case definition was published by the World Health Organization (WHO) in 2023 [18] but this has not been applied in previously published reviews.

There are other variables between populations related to COVID epidemiology that may impact on post COVID-19 conditions such as changes over time of the effect of different SARS-COV-2 variants and major differences in the policy and application of COVID-related restrictions, including differences between and within HICs and LMICs. One important example is the wide variation in school closure and re-opening [19–23]. The lack of evidence from LMICs was noted as a concern since the WHO's webinar and expert meetings in August 2022 [24]. While there is a high burden of respiratory infections due to a wide range of pathogens in children living in LMICs, studies of long-term symptoms are rare [25,26]. Furthermore, most studies to date have focused on describing the symptoms and less on the

management of post COVID-19 condition [23]. There is often a lack of access to techniques that measure organ dysfunction at a more sophisticated level beyond reporting of symptoms, especially in LMICs [23].

A prospective cohort study is underway in three sites in Indonesia that is comprehensively assessing abnormalities in a range of bodily systems and quality of life in children and adolescents at follow-up up to 12 months post-COVID [27]. To identify current knowledge gaps and inform future research directions, we conducted a systematic review that aimed to provide an update of the current evidence on post COVID-19 condition in children and adolescents, with consideration of the Gross National Income (GNI) of the country represented by the study population, the dominant variant of SARS-COV-2 at the time of the study and application of the recent WHO definition.

Methods

This systematic review was reported using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) for study design, search procedure, screening, and data reporting guidelines [28].

Eligibility criteria

Types of studies. We included all literature that reported original and complete data of at least 20 children or adolescents, regardless of study design (with or without a control group) or setting. As a result, systematic reviews, reviews, case series, and case reports were excluded.

Types of participants. Children and adolescents less than 18 years of age with confirmed acute COVID-19 infection (hospitalized and non-hospitalized) as determined through either positive SARS-COV-2 Reverse-transcriptase Polymerase Chain Reaction (RT-PCR), antigen test, serology test, or clinical diagnosis by physician. An age cut-off of 18 years was chosen as some search filters still use < 18 years old to categorize children and adolescents.

Types of outcome measures. We focused on the long-term outcomes of children and adolescents previously infected with SARS-CoV-2. Any symptoms and definitions for post COVID-19 condition was accepted; the WHO post COVID-19 condition expert consensus definition in children and adolescents was only published recently, in February 2023 [18].

Exclusion criteria. We excluded publications in a language besides English, pre-prints/pre-published, unreviewed articles, grey literature, unattained full-text, and publications that only provided results to a specific population such as patients with immunodeficiency and Multisystem Inflammatory Syndrome in Children (MIS-C) or reported specific COVID-related symptoms or specific organ involvement only (e.g., radiography or laboratory results, immunology profiles, psychiatric problems only). We also excluded grey literature defined as materials produced outside academic publishing such as government documents, reports, thesis and dissertations, or conference papers.

Search strategy for studies identification

Electronic searches. A single reviewer (NDP) conducted a systematic search with guidance from a medical librarian using the Medline (via Ovid), Embase, and PubMed databases from pandemic onset until the 30 October 2023 (S1 File). The search strategy was structured using Medical Subject Heading (MeSH) terms including "COVID-19", "children under five years old", "overall category of children age", "adolescents", "post COVID-19 condition", "long-term outcome", and "post-COVID-19". All keywords were combined using the Boolean logic operation "OR"/ "AND". Advanced search terms included "tw" (text word), "kf" (keyword heading word), and "hw" (heading word) for Medline (from Ovid), and "tw"

(text word), "kf", "hw", and "dq" (candidate term word) for Embase. Additional records were identified through a bibliography search of available systematic reviews and similar article recommendations up to February 13, 2024.

Selection of studies. Study selection was done by lead author (NDP) and reviewed by a second author (SMG or JEB). We used Endnote X9 desktop to combine publications from all databases and remove duplicates. Studies remaining after duplicate removal were screened for eligibility based on their titles and abstracts using Endnote X9 desktop. Publications deemed irrelevant to the topic or objectives of this review were excluded. The process then proceeded to the assessment of full-text articles based on inclusion and exclusion criteria. Additional reference searching was done manually from included studies' bibliographies and similar article suggestions.

Data collection and analysis

Data extraction. One investigator (NDP) extracted data, which was subsequently verified by other investigators (SMG and JEB) for quality control. The characteristics of the included studies were manually extracted into a Microsoft Excel table, including study details (author, time of data collection, study location, study design), participant details (number of subjects, sex, age of overall participants, age of participants in post COVID-19 condition group and control if any, acute SARS-CoV-2 confirmation method, the severity of acute COVID-19,), and outcome details (post COVID-19 condition definition, duration of follow up, post COVID-19 symptom prevalence, and the three most frequently reported persistent symptoms with prevalence of each. Data and numbers of control populations were extracted if available for comparison with cases including age, sex and proportions with persistent symptoms.

Missing data. When data on essential outcomes were reported as unclear or missing, we requested additional data to the included studies' corresponding authors. If no response was received, the study's inclusion was rediscussed based on its relevance to the overall analysis.

Assessment of risk of bias in included studies. Quality assessments within studies were done after the data extraction of all included studies by one investigator (NDP) in consultation with second reviewer (SMG or JEB). The quality of the study was assessed based on the study adherence using Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [29]. To aid the assessment, we quantified "Yes" as two, "Partial" as one, and "No" as zero. The scoring results were considered in determining the studies' quality, and categorized as follows: low (score $\leq$ 29), moderate (score 30–39), and high quality (score $\geq$40). However, this scoring was not be the sole determinant; subjective assessments were integrated into the final evaluation of each study's overall quality.

Data synthesis. We used a descriptive narrative approach to analyze the persistent symptoms reported in all included studies, based on the WHO clinical case definition of post COVID-19 condition in children and adolescents. The definition specifies a symptom lasting at least two months with onset within three months of acute COVID-19 presentation in individuals with a history of confirmed or probable SARS-CoV-2 infection [18]. Symptoms may include new onset following initial recovery, persistence, fluctuation, or relapse from the initial illness. Reported symptoms were categorized into fourteen entities:

1. Fatigue or tiredness
2. Respiratory symptoms: including dyspnea or shortness of breath
3. Headache
4. Weakness or asthenia and exercise intolerance or reduced physical resilience

5. Musculoskeletal symptoms: including myalgia or joint pain
6. Loss of appetite
7. Neurocognitive problems: including difficulty in concentration or memory
8. Neuropsychiatric problems: including sleeping difficulties, depression, or anxiety
9. Sensory problems: including loss of smell or loss of taste
10. Systemic problems: including fever, chills, syncope, dizziness, or weight loss
11. Other respiratory symptoms: including cough, rhinitis, or nasal congestion
12. Gastrointestinal (GI) or esophageal problems
13. Dermatological problems
14. Cardiovascular problems

We summarized the overall prevalence and types of post COVID-19 conditions. All tabulations were visualized with tables and graphs when feasible. We used the World Bank's GNI stratification to categorize the economies of the countries of the study population resided and data were collected. Countries with GNI per capita from $1,136 to $4,255 were regarded as LMICs, $4,256 to $13,845 as upper-middle-income countries (UMICs), and $4,256 or more as HICs [30]. We utilized the Our World in Data website to match the variants of SARS-CoV-2 with each study location and period [31]. If a study encompassed multiple SARS-CoV-2 variants, we analyzed the study according to the predominating Variant of Concern (VOC) density it covers. If the SARS-COV-2 variants were not available on the website, we reported them as "not identifiable" (referring to the first and second waves of the pandemic).

We did not conduct a meta-analysis due to the wide heterogeneity in study design (such as varying definitions of post COVID-19 condition, timing and method of follow-up assessments) and in study participants (including variations in reporting by age groups and the severity of acute COVID).

Institutional review board

This study did not require ethical clearance.

Results

Overall findings

Fig 1 presents the findings of the search strategy as a PRISMA flow diagram. From 951 publications identified, we removed 185 duplicates and 521 ineligible publications using Endnote X9 automation tools. Of 245 abstracts and titles screened, we retrieved 50 publications for eligibility assessment of which we excluded 28 that were reviews or systematic reviews (n = 17), studies which only explored specific symptoms or organ involvement (n = 8), studies which only reported broad symptoms in the text. We identified an additional eighteen studies that met inclusion criteria from reference searching of reviews. Therefore, there were 40 publications were included in the final analysis [32–71] of which six studies were published in 2023 [30,31,34,58,61,63]. Table 1 lists the main study characteristics and findings by publication including age and sex characteristics in controls when reported.

Of the 40 studies, 31 (77.5%) were cohort studies, including 22 (55%) prospective [35,39,41,43,47–50,54–61,64,65,68–71], eight (20%) retrospective [33,36,37,40,53,63,66,67] and one (2.5%) ambidirectional cohort study [62]. The remaining nine (22.5%) were

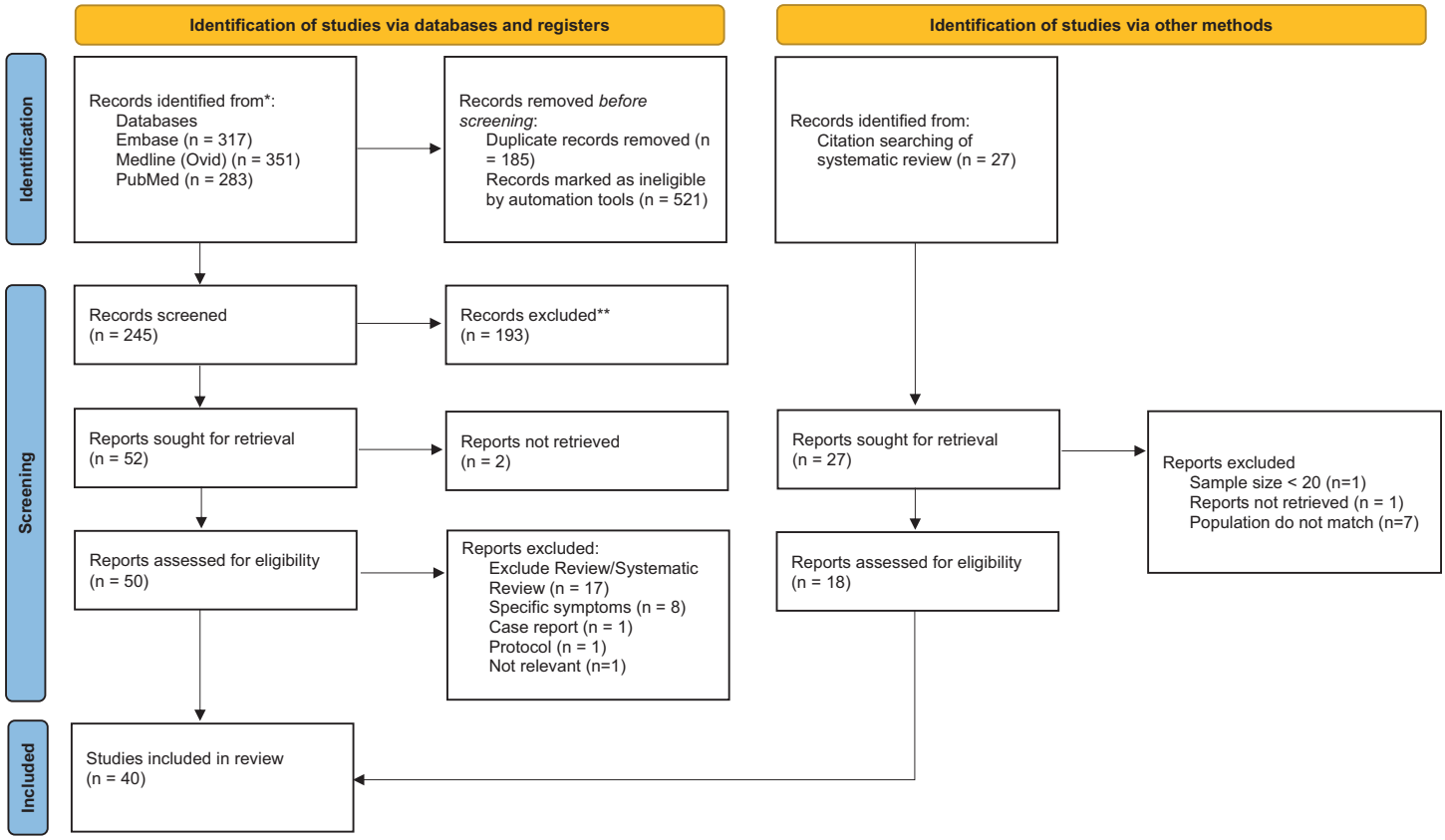

Fig 1. The PRISMA flow diagram of the literature search.

https://doi.org/10.1371/journal.pone.0315815.g001

cross-sectional studies [32,34,38,42,44–46,51,52]. Around half (21, 52.5%) of studies included a control group [32,33,37,39,40,43,46–48,50–53,56,57,60–62,65,68,71]; cases and controls had similar proportions of females and age distribution similar in all but two studies [37,62].

In total, 825,849 children and adolescents with a history of acute COVID-19 infection were included in this study. The median sample size of COVID-19-infected participants was 181, ranging from 16 to 781,419 [53,66]. Eleven studies included less than 100 participants [34,35,39,41,42,49,52,63,66,67,69]. The proportion of females in these studies ranged from 39% to 66% [49,67]. The age distribution ranged from 11 days in one study [41] up to 18 years in most studies, skewed towards older children and adolescents. Ten studies did not include infants or young children (<5 years) and four of these were limited to adolescents (10-18 years); therefore, median or mean age of study participants was commonly within the adolescent age range (18/31 studies, 58.1%). Only six studies documented the age range of those identified with a post COVID-19 condition and the range was similar to the overall study population [34,35,37,38,51,52].

All except two studies include PCR as one of the SARS-CoV-2 confirmatory tests in acute conditions; one study compared seropositive to seronegative patients [61], and the other did not state how they define acute infection [63]. Five studies included only hospitalized patients [34,35,41,47,69], ten on outpatients [32,33,38–40,42,50,60,63,70], and 21 studies included both hospitalized and non-hospitalized patients [36,37,43–46,48,49,51–55,57–59,62,64–67], while the remaining four did not specify [56,61,68,71]. The prevalence of post COVID-19 symptoms ranged from 15% to 45% among studies in only hospitalized patients [32,39] and from 13% to

Table 1. Characteristics of 40 studies included in the analysis.

No	Study	Country income status	SARS-COV-2 confirmation	Study design	N	Female %	Age of participants	Persistent symptoms %	Duration of follow up	Three symptoms most reported %	Inpatient/ Outpatient/ Both
1.	Adler et al [32]	HIC	PCR (+) or antigen test (+)	CS Case Control	3240 1148 2092	62.1% 63.7% 61.3%	Range: 5–18 years Mean 10.8 years Mean: 9.5 years	43.7% 33.3%	Mean: 4.39 ± 1.5 months	Headache (18.4%) Weakness (15.1%) Fatigue (12.3%)	Outpatient
2.	Ahn et al [33]	HIC	PCR (+)	RC Case Control	211 106 105	40.6 41.9	Range: 6 months–18 years Median: 3 years Median: 2 years	17% 4.8%	>12 weeks	Abdominal pain (6.6%) Mild fever (4.7%) Respiratory symptom (4.7%)	Outpatient
3.	Asadi-Pooya, et al [34]	LMIC	Symptomatic and PCR (+)	CS	58	58%	Range: 6–17 years Mean (+SD): 12.3 (3.3)	44·8%	Min 3 months after hospital discharged	Fatigue (20.7%) Shortness of breath (12%) Exercise intolerance (12%)	Inpatient
4.	Ashkenazi-Hoffnung, et al [35]	HIC	PCR (+) or antibody (+)	PC	90	42%	Range: 0– ≤ 18 years Mean (+SD): 12 (5) years	N/A	Median of 112 days (range: 33–410 days)	Fatigue (71.1%) Dyspnea (50.0%) Myalgia (46%)	Inpatient
5.	Baptista de Lima et al [36]	HIC	PCR (+)	RC	144	45.6%	Range: 0–18 years Mean: 79 months	13.3%	>4–24 weeks	Fatigue (7.5%) Behavioral changes (4.5%) Sleep disturbance (3.7%) (12 weeks)	Both
6.	Bergia et al. [37]	HIC	PCR (+) or antigen (+) or antibody (+)	RC Case Control	549 451 98	45% 43%	Range 0–18 years Median: 4.0 years Median 7.8 years	14.6% 19.4%	Median 351 days	Fever (80.3%) Cough (59.1%%) Asthenia (73.3%)	Both
7.	Bloise et al. [38]	HIC	PCR (+)	CS	1413	62%	Range:0–18 years Median (IQR): 10 (6–13) years	20%	Mean 87.49 ± 56.44 days after diagnosis	Asthenia (39.9%) Difficulty in concentration and memory (21.3%) Trouble sleeping-depression and other neuropsychiatric disorders (17.8%)	Outpatient
8.	Blomberg et al [39]	HIC	PCR (+) and Antibody (+)	PC Case Control	33 16 17	56% N/A	Range 0–15 years Median (IQR): 8 (6–12)	13% N/A	6 months	Disturbed taste or smell (13%) Stomach upset (6%)	Outpatient
9.	Borch et al. [40]	HIC	PCR (+)	RC Case Control	30,121 15,041 15,080	N/A	Range: 0–17 years Mean ages similar	25.3% 22.8%	Minimum 4-weeks from PCR test	Fatigue (11%) Loss of smell and taste (10%) Headache (7%)	Outpatient
10	Bossley et al [41]	HIC	PCR (+)	PC	71	41%	Range: 11 days–17 years Mean: 6.7 years	15%	>4 weeks	Dry cough (7%) Shortness of breath (6%) Fatigue (4%)	Inpatient
11.	Brackel et al. [42]	HIC	PCR (+) or antibody (+) or clinical diagnosis or unknown	CS	89	N/A	Range: 2–18 years Median: 13 years	N/A	> 12 weeks	Fatigue (86.5%) Dyspnoea (55.0%) Concentration difficulties (44.9%)	Outpatient
12.	Buonsenso et al (a) [43]	HIC	PCR (+)	PC Case Control	286 249 37	49% 53%	Range:0–18 years Mean: 10.4 years Mean: 10.5 years	32% N/A	Median: 77 days post diagnosis	Insomnia (19%) Asthenia (14%) Cough (12%) (6–9 months post diagnosis)	Both
13.	Buonsenso, et al (b) [44]	HIC	Clinical diagnosis or antibody (+) or PCR (+) or suspected	CS	510	56%	Range: 1–18 years Mean: 10.3 years	25.3%	Mean 8.2 months	Tiredness and weakness (87%) Fatigue (80%) Headache (79%)	Both

(Continued)

Table 1. (Continued)

No	Study	Country income status	SARS-COV-2 confirmation	Study design	N	Female %	Age of participants	Persistent symptoms %	Duration of follow up	Three symptoms most reported %	Inpatient/ Outpatient/ Both
14.	Buonsenso c et al (c) [45]	HIC	PCR (+)	CS	129	48.1%	Range: 0–18 years Mean: 11 ± 4.4 years	66.7%	>60 days after diagnosis, average: 162.5 ± 113.7 days	Insomnia (23.3%) Headache (23.3%) Weight loss (16.7%)	Both
15.	Erol et al [46]	UMIC	PCR (+) or antibody (+)	CS Case Control	216 121 95	46.3% 47.4%	Range: 0–18 years Median: 9.16 years Median: 8.42 years	37.2% N/A	>1 month	Chest and backache (51.1%) Dizziness ± syncope (15.6%) Palpitation (11.1%)	Both
16.	Fink et al [47]	UMIC	PCR (+) or antibody (+)	PC Case Control	105 53 52	58% 60%	Range:8–18 years Median: 14.7 years Median: 14.8 years	23% N/A	Median: 4.4 months (0.8 – 10.7) months post diagnosis	Headache (18.9%) Tiredness (9.4%) Dyspnoea (7.5%)	Inpatient
17.	Funk et al [48]	UMIC and HIC	PCR (+)	PC Case Control	3585 1884 1701	47% NR NR	Range:0–18 years Median: 3 years 73% < 10 years 79% < 10 years	5.8%	90–120 days after SARS-CoV-2 testing	Fatigue (1.1%) Cough (0.7%) Dyspnea (0.7%)	Both
18.	Gonzales et al [49]	HIC	PCR (+) or antibody (+)	PC	50	66%	Range: 5.5–17.9 years Median: 14.1 years	N/A	>12 weeks after infection	Fatigue (100%) Neurocognitive disorder (74%) Muscular weakness (74%)	Both
19.	Haddad et al [50]	HIC	PCR (+) and/or Symptomatic with sero-conversion	PC Case Control	544 210 infected 334 exposed	47% 52%	Range: 1–18 years 72% < 14 years 76% < 14 years	21.4% 8.4%	11-12 months after infections	Fatigue (3.3% Reduced physical resilience (2.9%) Breathlessness (1.9%)	Outpatient
20.	Kikkenborg Berg, et al [51]	HIC	PCR (+)	CS Case Control	28,270 6,630 21,640	58% 57%	Range: 15–18 years Median: 17.6 years Median: 17.5 years	61.9% 57%	At least 2 months after infection	Fatigue (13%) Loss of appetite (6.9%) Headache (6.5%)	Both
21.	Knoke et al [52]	HIC	PCR (+) and/or antibody (+)	CS Control for baseline characteristics only	70	N/A	Range: 5–18 years Mean (+SD): 10.8 (3.3)	27.1%	2.6 months average	Breathing problems (5.7%) Fatigue (7.1%) Loss of smell/taste (5.7%)	Both
22.	Kompaniyets, et al [53]	HIC	PCR (+) or an ICD-10-CM code of B97.29 or U07.1	RC Case Control	3,125,676 781,419 2,344,257	50% 50%	Range: 0–17 years Median: 12 years Median: 12 years	N/A	60 days – 365 days	Respiratory signs and symptoms (10.9%) Musculoskeletal symptoms (8.7%) Gastrointestinal and esophageal disorders (3.9%)	Both
23.	Kuczborska et al [54]	HIC	PCR (+) or antigen (+)	PC	147	47%	Range: 4 months–17 years Median 9 years	34.6% among immuno-competent	Min 3 months	Fever (61%) Cough/Rhinitis (45.5%) Fatigue (42.9%)	Both
24.	Matteudi et al [55]	HIC	PCR (+)	PC	137	N/A	Range: 17 days–15 years Median: 9.3 years	16.8%	10–13 months after diagnosis	Asthenia (9.5%) Learning difficulties (8%) Headache (6%)	Both

(Continued)

Table 1. (Continued)

No	Study	Country income status	SARS-COV-2 confirmation	Study design	N	Female %	Age of participants	Persistent symptoms %	Duration of follow up	Three symptoms most reported %	Inpatient/ Outpatient/ Both
25.	Miller et al [56]	HIC	PCR (+) or antibody (+)	PC Case Control	5032 1062 3970	41% NR NR	Range: 0–17 years NR NR	4.1% 2.2%	≥28 days after symptom onset	General symptom (30.2%) Respiratory symptoms (14%) ENT symptoms (14%)	N/A
26.	Molteni et al [57]	HIC	PCR (+)	PC Case Control	3,468 1,734 1,734	50% 50%	Range: 5–17 years Mean: 13 years Mean: 13 years	1.8% N/A	56 days	Anosmia (84%) Headache (80%) Sore throat (80%)	Both
27.	Osmanov et al [58]	UMIC	PCR (+)	PC	518	52%	Range:0–18 years Median: 10.4 years	24.3%	Median: 256 days	Fatigue (10.7%) Sleep disturbance (6.9%) Sensory problems (5.6%)	Both
28.	Pazukhina, et al [59]	UMIC	PCR (+)	PC	360	52%	Range:0–18 years Median: 9.5 years	20%	>6 months Median: 255 days	Fatigue (9%) Dermatological (5%) Neurocognitive (4%) (6-month follow-up group)	Both
29.	Pinto Pereira et al [60]	HIC	PCR (+)	PC Case Control	12949 6407 6542	62.9% 62.3%	Range: 11–17 years	60.9% 43.2%	>6 months	Tiredness (38.4%) Shortness of breath (22.8%) Headache (18.3%)	Outpatient
30.	Radtke et al [61]	HIC	Antibody (+)	PC Case Control	1355 109 1246	53% 54%	Range: 6–16 years Median: 11 years 61% cases 6-11 years 56% controls 6-11 years	3.7% 2.2%	6 months	Tiredness (2.8%) Difficulty concentrating (1.8%) Increased need for sleep (1.8%)	N/A
31.	Roge et al [62]	HIC	PCR (+) or seroconversion	Ambidirectional cohort Case Control	378 236 142	45% 47%	Range: 1 month–18 years Median: 10 years Median: 2 years	70% 24.8%	Median: 73.5 days Median: 69 days	Irritability (27.6%) Impaired attention (19.2%) Fatigue (19.2%)	Both
32.	Sakurada et al [63]	HIC	N/A	RC	54	57.4%	Range: 11–18 years Mean: 15.3	N/A	Min 4 weeks	Fatigue (55.6%) Headache (35.2%) Dysosmia (30%)	Outpatient
33.	Say et al [64]	HIC	PCR (+)	PC	151	42%	Range:0–18 years Median: 2 years Mean: 3.7 years	8%	3–6 months	Post-viral cough (4%) Fatigue (2%)	Both
34.	Seery et al [65]	UMIC	PCR (+)	PC Case Control	1216 639 577	47% 48%	Range: 1–17 years Median: 7 years Median: 8 years	34% 13%	>3 months	Headache (15.2%) Cough (11.1%) Fatigue (8.7%)	Both
35.	Smane et al (a) [66]	HIC	PCR (+)	RC	30	43%	Range: 3 months–17 years Mean: 9.2 years	30%	Mean: 101 days	Prolonged low-grade fever (6.7%) Joint pain (3.3%) Headache (3.3%)	Both
36.	Smane et al (b) [67]	HIC	PCR (+)	RC	92	39%	Range: 1–18 years Median: 12 years	51%	1-3 months	Tiredness (38%) Loss of taste/smell (16%) Headaches (15%)	Both
37.	Stephenson et al [68]	HIC	PCR (+)	PC Case Control	6,804 3,065 3,739	63.2% 63.5%% 62.9%	Range: 11–17 years 41% 11-14 years 43% 11-14 years	66.50% 53.3%	3 months	Tiredness (39.0%) Headache (23.1%) Shortness of breath (23.4%)	N/A

(Continued)

Table 1. (Continued)

No	Study	Country income status	SARS-COV-2 confirmation	Study design	N	Female %	Age of participants	Persistent symptoms %	Duration of follow up	Three symptoms most reported %	Inpatient/ Outpatient/ Both
38.	Sterky et al [69]	HIC	PCR (+)	PC	55	42%	Range: 0–18 years	22%	Min 4 months (median 219 days, range 123– 324 days)	Fatigue (66.7%) Myalgia (33.3%) Headache (33.3%)	Inpatient
39.	Trapani et al [70]	HIC	PCR (+)	PC	629	48.1%	Range: 0–16 years	24.3%	>8–36 weeks	Fatigue (7%) Neurological (6.8%) Respiratory disorders (6%)	Outpatient
40.	Zavala et al [71]	HIC	PCR (+)	PC Case Control	859 472 387	52% 46%	Range: 2–16 years Median: 10 years Age-matched	6.7% 4.2%	At least >1 month	Anxiety (7%) Difficulty sleeping (7%) Tiredness (7%)	N/A

HIC: high-income-country; LMIC: low-middle-income country; PCR: polymerase chain reaction; N/A: not available; IQR: interquartile range; Ab: antibody; PC: prospective cohort; RC: retrospective cohort; CS; cross sectional; NR; not reported.

https://doi.org/10.1371/journal.pone.0315815.t001

61% among studies in only non-hospitalized patients [37,58] Most studies did not report the severity of symptoms.

All studies assessed outcomes (post COVID-19 conditions) for at least more than four weeks or a month. The longest follow-up duration was 13 months [53]. The most frequently used definition of post COVID-19 condition in children and adolescents was the persistence of symptoms for more than four weeks or a month following diagnosis of acute COVID-19 (used by 14 studies) [32,35,36,40,41,43,44,46,52,56,62,63,67,71]. Other cut-offs after diagnosis included two months (5 studies) [45,51,53,57,70], three months (11 studies) [33,34,37,42,47–49,54,64,65,68], four months [69] or five months (1 study each) [58] and six months or longer (6 studies) [39,50,55,59–61]. six months or longer (used by 6 studies) [39,50,55,59–61]. Two studies did not specify [38,66]. Among the studies, twenty-four studies follow WHO's criteria for symptom duration of "at least 2 months" but failed to specify the onset of symptoms. Therefore, it is difficult to identify which studies reported as consistent with WHO's definition of post COVID-19 condition.

Persistent and common symptoms

Overall, the prevalence of persistent symptoms among all publications varied widely from 1.8% in 3,468 school children who had tested positive in the community in the UK and USA [57] to 70% in 378 Latvian children and adolescents followed after discharge from hospital [62] (Table 1). Similarly, the prevalence ranged from 1.8% to 66.5% in studies that reported symptom persistence of two months or more – i.e., as per WHO definition [57,58].

Among studies that included solely hospitalized patients, the prevalence of post COVID-19 condition ranged from 15% to 45% [34,41], whereas studies of only non-hospitalized patients reported a prevalence range of 13% to 61% [39,60]. Most studies did not provide detailed information on the severity of persistent symptoms.

The number of reporting publications for each persistent symptom type is shown in Fig 2. The most reported symptoms were fatigue (28/40, 70%), headache (15/40, 37.5%), and respiratory symptoms (14/40, 35%). Similar results were found from the 24 studies that reported consistent with WHO definition: fatigue [17/24, 70.8%], respiratory symptoms [10/24, 41.7%], and headache [9/24, 37.5%]. Within those studies, the prevalence of each symptom ranged widely from 1.1%–100% for fatigue [46,47]. 0.7%–55% for respiratory symptoms, [40,46] and

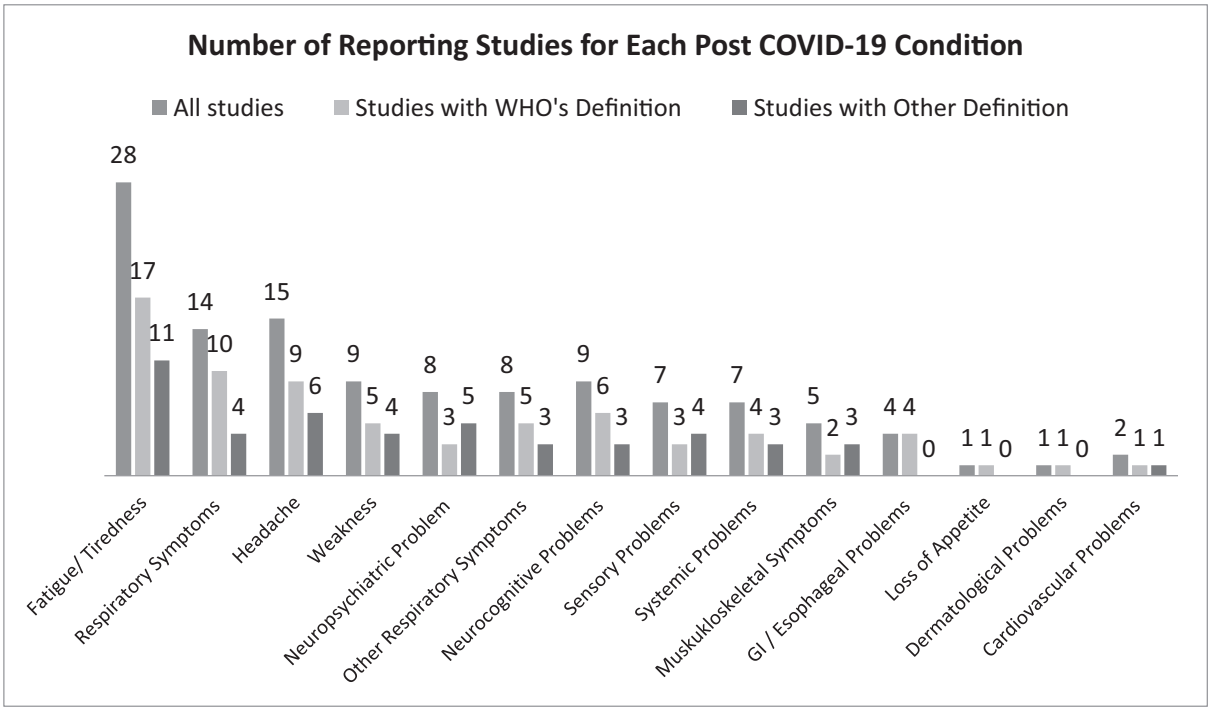

Fig 2. The numbers of publications in which a specific symptom was among the three most commonly reported persistent symptoms.

https://doi.org/10.1371/journal.pone.0315815.g002

6–80% for headache [55,57]. The remaining 16 studies which do not meet WHO's definition of post COVID-19 condition found fatigue (11/16, 68.8%), headache (6/16, 37.5%), and neuropsychiatric problems (5/16, 31.3%) to be the most prevalent persistent symptoms. On the other side, the least reported symptoms in all studies include loss of appetite (1/40, 2.5%) and dermatological problems (1/40, 2.5%) [51,59].

Gross national income

Publication on post COVID-19 condition included children or adolescents (<18 years) from 27 different countries but only one study was from a LMIC [34]. Five studies were from UMICs, [46,47,58,59,65], one study included populations from both UMICs and HICs [48], and the remaining 33 only included populations from HICs (Fig 3, S3 Table). In HIC studies, the prevalence of post COVID-19 symptoms ranged from 1.8% to 70% with fatigue (23/33 studies, 69.7%) and headache (reported in 13/33, 39.4%) being the most commonly reported symptoms. Within the five studies undertaken in an UMICs, the prevalence of post COVID-19 symptoms ranged from 20% to 37%, [46,59] with fatigue (reported in 4/5, 80%) and headache (reported in 2/5, 40%) as the most common symptoms. The single LMIC study conducted in Iran [34] and only included 58 participants who were all aged over five years; a post COVID symptoms were common - prevalence of 45% - and fatigue, shortness of breath and exercise intolerance were the commonest reported symptoms.

SARS-COV-2 variants of concern

The distribution of variants across all included studies is detailed in Table 2. The predominating variant was not identifiable in 14 (35%) studies through electronic search because data of acute

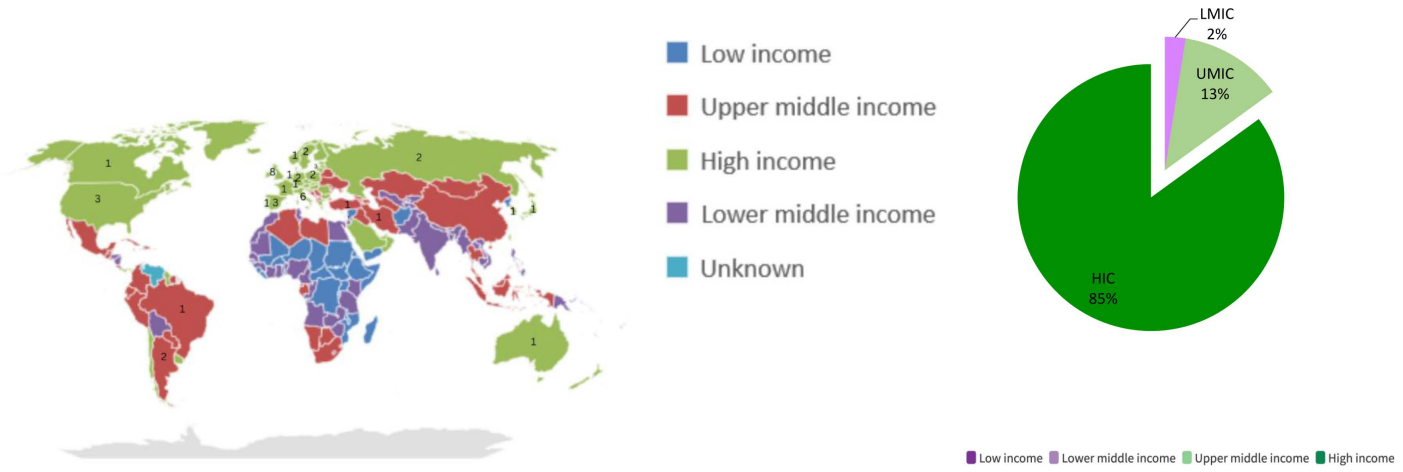

Fig 3. Map and distribution of countries involved in post COVID-19 condition publications in children based on GNI by World Bank.

https://doi.org/10.1371/journal.pone.0315815.g003

COVID were derived within the first and second wave of the pandemic. In the remaining 26 studies, the Alpha variant was predominant in eleven studies [35,36,38,40,43,52,60,62,64,68,71], the Omicron variant in four studies [33,53,54,63], the Delta variant in four studies [32,47,51,70], the Gamma variant in one study [57], and other variants in six studies [42,48,58,59,61,65]. There is no beta variant-predominated study included in this review (Fig 4).

The range of prevalence of reported post COVID-19 condition was 4.1%–66.7% in the studies in which the variant of concern was not identifiable, [45,56] 6.7%–70% in the Alpha variant predominated studies, [62,71] 23%–61.9% in the Delta predominated studies, [45,49] 17–34.6% in the Omicron predominated studies, [33,54] and 3.7%–34% in the Other-variant predominated studies [61,65] Fatigue was the commonest symptom reported in all variant subgroups (9/11 [81.8%] in Alpha, 4/4 [100%] in Delta, 2/4 [50%] in Omicron, 6/6 [100%] in Other-variant predominated studies, and 7/14 [50%] in unidentifiable-variant-predominated studies).

Other findings

Post COVID-19 conditions were more prevalent in older age groups [34,40,48,58] Most pediatric COVID-19 survivors reported one persistent symptom, followed by two with smaller numbers reporting three or more. Most symptoms at follow-up were reported as mild and tolerable by participants, though definition of mild and tolerable varied. Severe and disabling problems were reported in a few studies which were done in specialist medical centers that had referral bias for more. severe illness [34,35,42]. The severity of acute COVID-19 was associated with long-COVID-19 in a number of studies [34,37,48,58]. The prevalence of post COVID-19 symptoms tended to decline over time [43,58,59] and most post COVID-19 symptoms had resolved within a year [34,40,43].

Quality of the study

Quality assessment based on adherence of STROBE recommendation for observational studies was presented in S2 Table. The mean score of all study was 35.0 (moderate quality). We categorized 10 (25%) studies as low quality (score ≤ 29) [33,35,41,42,54,61,64,66,67,69], 17 (42.5%) as moderate (score 30-39) [34,36–40,43–47,52,53,55,58,63,71] and 13 (32.5%) as high (score ≥ 40).

Table 2. SARS-COV-2 variants of concern.

No	Study author	Study period	Density of circulating SARS-COV-2 Variants of Concern at Study Period						Predominant variant
			Alpha	Beta	Delta	Gamma	Omicron	Other	
1.	Adler et al	December 2021 to January 2022	N/A	N/A		N/A		N/A	Delta
2.	Ahn et al	May 2022 to July 2022	N/A	N/A	N/A	N/A		N/A	Omicron
3.	Asadi-Pooya et al	February 2020 to November 2020	N/A (First & second wave of pandemic)						N/A
4.	Ashkenazi-Hoffnung, et al	November 2020 to April 2021				N/A	N/A		Alpha
5.	Baptista de lima et al	March 2020 to September 2021		N/A			N/A	N/A	Alpha
6.	Bergia et al.	March 2020 to December 2020	N/A (First & second wave of pandemic)						N/A
7.	Bloise, et al	March 2020 to March 2021					N/A		Alpha
8.	Blomberg et al	28 February to 4 April 2020	N/A (First wave of pandemic)						N/A
9.	Borch, et al	January 2020 to March 2021			N/A		N/A		Alpha
10.	Bossley et al	March 2020 to January 2021	N/A (First wave of pandemic)						N/A
11.	Brackel, et al	December 2020 to February 2021					N/A		Other
12.	Buonsenso, et al (a)	April 2020 to April 2021					N/A		Alpha
13.	Buonsenso, et al (b)	UK: January 2020 to January 2021	N/A (First wave of pandemic)						N/A
		US: January 2020 to January 2021	N/A (First wave of pandemic)						
14.	Buonsenso, et al (c)	March to October 2020	N/A (First wave of pandemic)						N/A
15.	Erol et al	March 2020 to February 2021	N/A (First wave of pandemic)						N/A
16.	Fink, et al	April 2020 to August 2021		N/A			N/A		Delta
17.	Funk, et al	US: March 2020 to January 2021					N/A		Other
		Costa Rica: March 2020 to January 2021	N/A (First & second wave of pandemic)						
		Canada: March 2020 to January 2021			N/A	N/A	N/A		
		Spain: March 2020 to January 2021		N/A		N/A	N/A		
18.	Gonzales et al	December 2020 – May 2021	N/A (First wave of pandemic)						N/A
19.	Haddad, et al	January 2020 to May 2020	N/A (First wave of pandemic)						N/A
20.	Kikkenborg Berg, et al	Jan 2020 to July 2021					N/A		Delta
21.	Knoke, et al	August 2020 to March 2021					N/A		Alpha
22.	Kompaniyets, et al	March 2020 to January 2022	N/A	N/A		N/A			Omicron
23.	Kuczborska et al	November 2020 and January 2022	N/A	N/A		N/A			Omicron
24.	Matteudi et al	27 February to 15 May 2020	N/A (First wave of pandemic)						N/A
25.	Miller et al	June 2020 to May 2021	N/A (First wave of pandemic)						N/A
26.	Molteni, et al	March 2020 to February 2021					N/A		Gamma
27.	Osmanov, et al	April 2020 to August 2020	N/A	N/A	N/A	N/A	N/A		Other
28.	Pazukhina, et al	April 2020 to August 2020	N/A	N/A	N/A	N/A	N/A		Other
29.	Pereira et al	September 2020 to March 2021			N/A		N/A		Alpha
30.	Radtke, et al	October to November 2020		N/A	N/A	N/A	N/A		Other
31.	Roge, et al	July 2020 to April 2021		N/A	N/A	N/A	N/A		Alpha
32.	Sakurada et al	Februari 2021 to October 2022		N/A		N/A		N/A	Omicron
33.	Say, et al	March 2020 to March 2021					N/A		Alpha
34.	Seery et al	June 2020 to June 2021	N/A	N/A	N/A		N/A		Other
35.	Smane et al (1)	July 2020 to July 2020	N/A (First wave of pandemic)						N/A
36.	Smane, et al (2)	March 2020 to December 2020.	N/A (First wave of pandemic)						N/A
37.	Stephenson, et al	January 2021 to March 2021					N/A		Alpha
38.	Sterky, et al	March 2020 to August 2020	N/A (First wave of pandemic)						N/A
39.	Trapani et al.	June 2021 to August 2021		N/A			N/A	N/A	Delta
40.	Zavala et al.	January 2021					N/A		Alpha
	Predominant of SARS-COV-2 Variants							N/A	
			> 50%	>30-50%	>20-30%	10-20%	< 10%		

https://doi.org/10.1371/journal.pone.0315815.t002

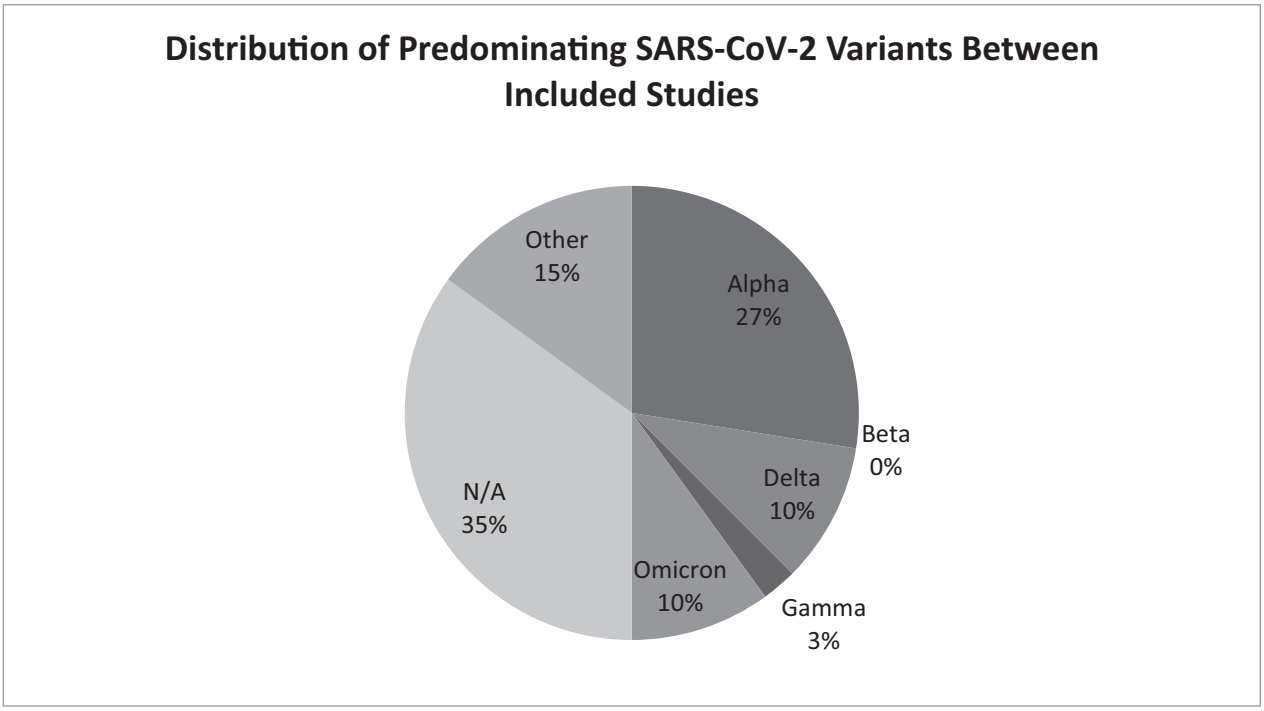

Fig 4. Distribution of predominating SARS-CoV2 variants between included studies.

https://doi.org/10.1371/journal.pone.0315815.g004

Discussion

This systematic review provides a timely update on reported persistent symptoms in children and adolescents following infection with SARS-CoV-2. As SARS-CoV-2 testing for diagnosis and surveillance has diminished since 2022, new data are likely to become infrequent. Since the onset of the global pandemic in 2020, many studies have reported post-COVID symptoms in large numbers of children and adolescents from multiple countries. Our review includes five additional studies published since the most recent previous systematic review, but none from LMICs [15]. Though many studies were undertaken prior to the publication of the WHO consensus definition [18], most used similar criteria, especially as the consensus definition was informed by review of the same published studies. While there are major challenges for interpretation of data limited to symptom reporting, a standardized diagnosis definition is potentially helpful to enable meta-analyses, make comparisons with control populations and to measure impact of interventions.

Fatigue, headache and respiratory symptoms are consistently the most common persistent symptoms reported but there are major limitations relating to the interpretation of the findings. A reliance on symptom reporting alone, often with the lack of an appropriately matched control group, makes it challenging to define the true impact of COVID-19 infection on long-term health or recovery in children and adolescents. The symptoms may not be specific to post COVID-19 condition but could be influenced by numerous psychological effects of the pandemic or other pre-existing conditions of the subjects. The wide range of reported prevalence (1.8%–66.5%) of post COVID-19 condition likely reflects the heterogeneity between studies including study design (e.g., timing and method of follow-up assessment) and study participants such as variations in the severity of acute COVID. Fatigue is also the most prevalent post COVID-19 condition reported in adults along with joint pain, anosmia and headache [8,9]. In those studies that did include adults as well as children from the same

population, a significantly higher prevalence of persistent symptoms was reported in adults [39,43]. A more in-depth analysis comparing children to adults may be useful.

To date, the pathophysiology of post COVID-19 condition in children and adolescents is unknown [72]. A recent systematic review of six studies involving 678 adult COVID-19 survivors suggested a potential link between viral persistence and post COVID-19 conditions. In two months following acute infection, SARS-CoV-2 RNA was detected in 5% to 59% of patients with post COVID-19 condition, depending on the sample. However, the generalizability of the findings is constrained by the lack of a control group of individuals without post COVID-19 symptoms [73].

The systemic inflammatory response observed in acute COVID-19, characterized by elevated levels of cytokines, such as IL-2, IL-10, IL-6, IL-8, C-Reactive Protein (CRP), and Tumor Necrosis Factor (TNF)-alpha, triggers acute phase reactions and, if sustained, may lead to end-organ damage [74,75]. For instance, in lung tissue, the persistent elevation of proinflammatory cytokines is linked to a subset of pathological fibroblasts, which may contribute to the development of pulmonary fibrosis [76,77].

The severity of acute disease is indicated by the number of presenting symptoms, the need for hospitalization, the length of hospital stays, and the need for ICU admission [34,37,48,67]. It is hypothesized that severe COVID-19 triggers a more robust immune response with the resultant cytokine storm leading to more organ damage or that more aggressive and invasive treatment needed is more frequently associated with iatrogenic harm [78]. Increased prevalence of post COVID-19 condition in those with severe acute cases compared to a milder case has been also noted in adults [58]. Mitigating acute disease severity with antiviral treatments such as Remdesivir or Nirmaltrevir was not associated with reduced risk of developing post COVID-19 conditions [79].

Another mechanism of the dysregulated immune response is the development of an autoimmune response. Autoimmune diseases such as Guillain-Barré syndrome, Miller-Fisher syndrome, idiopathic thrombocytopenic purpura, Kawasaki-like disease, and MIS-C have been associated with COVID-19. However, a recent systematic review of five studies concluded that the clinical significance of persistent autoantibodies related to post COVID-19 conditions in adults appears limited and requires future research [80].

Different and more specific mechanisms have been proposed under each organ system in the adult population, and similarities between both groups have already been suggested [81]. Persistent fatigue, one of the most common complaints, arises from multifactorial causes, including brain hypometabolism, brain glymphatic drainage dysfunction, and brain toxin accumulation [82,83]. SARS-CoV-2 typically enters the central nervous system via hematogenous spread, promoting neuroinflammation and resulting in neuronal damage and neurologic symptoms [84]. Sustained neuroinflammation, whether through autoimmune reactions or activation of microglia, could account for neurocognitive and mental health disorders. Regarding the persistent taste and smell disorders, histologic assessments show persistent inflammation and-/or SARS-CoV-2 identification in the cells of taste buds and olfactory neuroepithelium [85,86].

Our review did not identify any additional studies from LMICs, highlighting the scarcity of published data and the uncertainty regarding the long-term health impacts of COVID-19 in these populations. Even before the COVID-19 pandemic, children and adolescents in LMICs had already faced a significant burden of severe disease and death due to infectious diseases [87]. Epidemiological and clinical risk factors, such as high exposure to indoor and outdoor pollution, as well as comorbidities associated with respiratory infections—including malnutrition, HIV infection, and tuberculosis [25,26]—may influence the clinical presentation and outcomes of respiratory infection, including those caused by SARS-CoV-2, in these vulnerable populations [88,89].

It is not known whether the prevalence or nature of post COVID-19 condition in children and adolescents varies according to the SARS-CoV-2 variant. Indeed, we observed a decline in the prevalence of post COVID-19 condition from studies dominated by the Alpha-variant to those dominated by the Omicron variant, a trend also reported in adults. This decline may be attributed to the availability of vaccination during the Omicron surge, which could have resulted in a milder disease course and fewer persistent symptoms [90]. A systematic review of six studies suggested that COVID-19 vaccination before acute infection was associated with reduced risks of long-COVID in adults, with two doses offering greater than one [91]. However, the COVID-19 vaccination status of children and adolescents was not provided in the included studies.

Analysis of post COVID-19 condition by sex and age in this review was limited. Univariate analysis by Asadi-Pooya et al. indicated a female-to-male prevalence ratio of 1.36 for post COVID-19 condition ($p < 0.441$) [34]. Kikkenborg et al. reported a higher proportion of female participants with symptoms persisting beyond two months after initial diagnosis: 71.7% vs 48.4% (OR 2.70; 95% CI 2.40–3.03; $p < 0.0001$) [51]. Previous meta-analysis has also supported female sex as a risk factor for developing post COVID-19 conditions in adults (OR 1.48, 95% CI 1.17 to 1.86). Further investigation is needed to elucidate the mechanism by which females are at increased risk of post COVID-19 condition, beyond the biological and sociocultural differences between sexes [91]. Moreover, the higher representation of the adolescent age group in the included studies may reflect either a greater susceptibility of adolescents to acute and post COVID-19 condition or the possibility that young children with acute COVID-19 were less likely to seek care or be identified, given the high prevalence of acute respiratory illnesses from other pathogens. Alternatively, this representation might also reflect the studies' reliance on symptom reporting [37]. Several studies primarily used self-reported questionnaire data, which increases the risk of recall bias.

Supporting information

S1 File. Search strategy.
(DOCX)

S2 Table. Quality of included studies.
(DOCX)

S3 Table. Additional study details.
(DOCX)

S4 Table. Abstract PRISMA checklist.
(DOCX)

S5 Table. Full Text PRISMA checklist.
(DOCX)

S6 Table. Details of excluded studies.
(DOCX)

S7 Table. Data extraction details.
(DOCX)

Acknowledgments

We would like to thank Poh Chua, medical librarian who helped us in literature search. This systematic review's formal protocol is part of the doctoral degree research proposal and has not been formally published. This review has also not been registered.

Author contributions

Conceptualization: Nina Dwi Putri, Julie Bines, Stephen M. Graham.

Data curation: Nina Dwi Putri.

Formal analysis: Nina Dwi Putri.

Funding acquisition: Nina Dwi Putri, Dwiana Ocviyanti.

Investigation: Nina Dwi Putri, Julie Bines, Stephen M. Graham.

Methodology: Nina Dwi Putri, Julie Bines, Stephen M. Graham.

Project administration: Nina Dwi Putri.

Software: Nina Dwi Putri.

Supervision: Sri Rezeki Hadinegoro, Julie Bines, Stephen M. Graham.

Validation: Nina Dwi Putri, Julie Bines, Stephen M. Graham.

Visualization: Nina Dwi Putri.

Writing – original draft: Nina Dwi Putri, Stephen M. Graham.

Writing – review & editing: Nina Dwi Putri, Ida Safitri Laksanawati, Dominicus Husada, Nastiti Kaswandani, Ari Prayitno, Rina Triasih, Irma Sri Hidayati, Retno Asih, Robby Nurhariansyah, Fabiola Cathleen, Dwiana Ocviyanti, Sri Rezeki Hadinegoro, Dan Pelicci, Julie Bines, Stephen M. Graham.

References

1. American Academy of Pediatrics. Children and COVID-19: State-level data report [Internet]. [cited 2023 Oct 27]. Available from: https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/
2. Izquierdo-Pujol J, Moron-Lopez S, Dalmau J, Gonzalez-Aumatell A, Carreras-Abad C, Mendez M, et al. Post COVID-19 Condition in Children and Adolescents: An Emerging Problem. Front Pediatr. 2022;10:894204. https://doi.org/10.3389/fped.2022.894204 PMID: 35633949
3. Kitano T, Kitano M, Krueger C, Jamal H, Al Rawahi H, Lee-Krueger R, et al. The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: A systematic review of fatality and ICU admission in children worldwide. PLoS One. 2021;16(1):e0246326. https://doi.org/10.1371/journal.pone.0246326 PMID: 33513204
4. Shi Q, Wang Z, Liu J, Wang X, Zhou Q, Li Q, et al. Risk factors for poor prognosis in children and adolescents with COVID-19: A systematic review and meta-analysis. EClinicalMedicine. 2021;41:101155. https://doi.org/10.1016/j.eclinm.2021.101155
5. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review. JAMA Pediatr. 2020;174(9):882–9. https://doi.org/10.1001/jamapediatrics.2020.1467 PMID: 32320004
6. Ahmed H, Patel K, Greenwood D, Halpin S, Lewthwaite P, Salawu A, et al. Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis. J Rehabilitation Medicine. 2020;52(5):jrm00063. https://doi.org/10.2340/16501977-00063
7. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo P, Cuapio A, et al. More than 50 long-term effects of COVID-19: A systematic review and meta-analysis. Sci Rep. 2021;11(1):16144.
8. Fernandez-de-Las-Peñas C, Notarte KI, Macasaet R, Velasco JV, Catahay JA, Ver AT, et al. Persistence of post-COVID symptoms in the general population two years after SARS-CoV-2 infection: A systematic review and meta-analysis. J Infect. 2024;88(2):77–88. https://doi.org/10.1016/j.jinf.2023.12.004 PMID: 38101521
9. Fajar J, Ilmawan M, Mamada S, Mutiawati E, Husnah M, Yusuf H, et al. Global prevalence of persistent neuromuscular symptoms and the possible pathomechanisms in COVID-19 recovered individuals: A systematic review and meta-analysis. Narra J. 2021;1(3):.
10. Lopez-Leon S, Wegman-Ostrosky T, Ayuzo Del Valle NC, Perelman C, Sepulveda R, Rebolledo PA, et al. Long-COVID in children and adolescents: a systematic review and meta-analyses. Sci Rep. 2022;12(1):9950. https://doi.org/10.1038/s41598-022-13495-5 PMID: 35739136

11. Behnood SA, Shafran R, Bennett SD, Zhang AXD, O'Mahoney LL, Stephenson TJ, et al. Persistent symptoms following SARS-CoV-2 infection amongst children and young people: A meta-analysis of controlled and uncontrolled studies. J Infect. 2022;84(2):158–70. https://doi.org/10.1016/j.jinf.2021.11.011 PMID: 34813820
12. Pellegrino R, Chiappini E, Licari A, Galli L, Marseglia GL. Prevalence and clinical presentation of long COVID in children: a systematic review. Eur J Pediatr. 2022;181(12):3995–4009. https://doi.org/10.1007/s00431-022-04600-x PMID: 36107254
13. Zimmermann P, Pittet L, Curtis N. How common is long COVID in children and adolescents? Pediatric Infect Dis J. 2021;40(12):e482-7.
14. Fainardi V, Meoli A, Chiopris G, Motta M, Skenderaj K, Grandinetti R, et al. Long COVID in Children and Adolescents. Life (Basel). 2022;12(2):285. https://doi.org/10.3390/life12020285 PMID: 35207572
15. Jiang L, Li X, Nie J, Tang K, Bhutta ZA. A Systematic Review of Persistent Clinical Features After SARS-CoV-2 in the Pediatric Population. Pediatrics. 2023;152(2):e2022060351. https://doi.org/10.1542/peds.2022-060351 PMID: 37476923
16. Zheng Y-B, Zeng N, Yuan K, Tian S-S, Yang Y-B, Gao N, et al. Prevalence and risk factor for long COVID in children and adolescents: A meta-analysis and systematic review. J Infect Public Health. 2023;16(5):660–72. https://doi.org/10.1016/j.jiph.2023.03.005 PMID: 36931142
17. Franco J, Garegnani L, Oltra G, Metzendorf M, Trivisonno L, Sgarbossa N, et al. Short and long-term wellbeing of children following SARS-CoV-2 infection: A systematic review. Int J Environ Res Public Health. 2022;19(21):14392. https://doi.org/10.3390/ijerph192114392
18. World Health Organization. A clinical case definition for post COVID-19 condition in children and adolescents by expert consensus [Internet]. World Health Organization; 2023 [cited 2023 Oct 29]. Available from: https://iris.who.int/bitstream/handle/10665/366126/WHO-2019-nCoV-Post-COVID-19-condition-CA-Clinical-case-definition-2023.1-eng.pdf?sequence=1
19. UNICEF. With 23 countries yet to fully reopen schools, education risks becoming 'greatest divider' as COVID-19 pandemic enters third year [Internet]. 2022 [cited 2023 Oct 29]. Available from: https://www.unicef.org/press-releases/23-countries-yet-fully-reopen-schools-education-risks-becoming-greatest-divider
20. The Jakarta Post. Jakarta schools to return to full capacity classes [Internet]. The Jakarta Post. 2022 [cited 2024 Aug 30]. Available from: https://www.thejakartapost.com/indonesia/2022/03/31/jakarta-schools-to-return-to-full-capacity-classes.html
21. Aljazeera. Iran fully reopens schools a day after two years of COVID closure [Internet]. 2022 [cited 2023 Oct 21]. Available from: https://www.aljazeera.com/news/2022/4/3/iran-fully-reopens-schools-after-two-years-as-ramadan-begins
22. Yusuf M. Kenyan schools reopen despite coronavirus concerns [Internet]. Voice of America. 2021 [cited 2023 Oct 30]. Available from: https://www.voanews.com/a/africa_kenyan-schools-reopen-despite-coronavirus-concerns/6200298.html
23. Michelen M, Manoharan L, Elkheir N, Cheng V, Dagens A, Hastie C, et al. Characterising long COVID: a living systematic review. BMJ Glob Health. 2021;6(9):e005427. https://doi.org/10.1136/bmjgh-2021-005427 PMID: 34580069
24. World Health Organization. Post COVID-19 condition: children and young persons [Internet]. 2022 [cited 2023 Oct 20]. Available from: https://www.who.int/news-room/events/detail/2022/08/17/default-calendar/post-covid-19-condition--children-and-young-persons
25. Martinez L, Gray D, Botha M, Nel M, Chaya S, Jacobs C, et al. The long-term impact of early-life tuberculosis disease on child health: A prospective birth cohort study. Am J Respir Crit Care Med. 2023;207(8):1080–8.
26. von Mollendorf C, Berger D, Gwee A, Duke T, Graham SM, Russell FM, et al. Aetiology of childhood pneumonia in low- and middle-income countries in the era of vaccination: a systematic review. J Glob Health. 2022;12:10009. https://doi.org/10.7189/jogh.12.10009 PMID: 35866332
27. Long Term Outcome of Children with Covid-19 and Treatment Evaluation in Indonesia. Long COVID [Internet]. 2022 [cited 2023 Nov 11]. Available from: https://www.locatelongcovid.id/
28. Page M, Moher D, Bossuyt P, Boutron I, Hoffmann T, Mulrow C, et al. PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.
29. von Elm E, Altman D, Egger M, Pocock S, Gøtzsche P, Vandenbroucke J. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. BMJ. 2007;335(7624):806–8. https://doi.org/10.1136/bmj.39302.463149.80
30. The World Bank. The World by Income and Region [Internet]. 2023 [cited 2023 Oct 10]. Available from: https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html

31. Our World in Data. SARS-CoV-2 sequences by variant [Internet]. 2023 [cited 2023 Oct 10]. Available from: https://ourworldindata.org/grapher/covid-variants-bar?country=CAN~BWA~ESP~ZAF~AUS~USA~GBR~DEU~ITA~BEL~FRA
32. Adler L, Israel M, Yehoshua I, Azuri J, Hoffman R, Shahar A, et al. Long COVID symptoms in Israeli children with and without a history of SARS-CoV-2 infection: a cross-sectional study. BMJ Open. 2023;13(2):e064155. https://doi.org/10.1136/bmjopen-2022-064155 PMID: 36810170
33. Ahn B, Choi S, Yun K. Non-neuropsychiatric long COVID symptoms in children visiting a pediatric infectious disease clinic after an Omicron surge. Pediatric Infect Disease J. 2023;42(5):e143-5.
34. Asadi-Pooya AA, Nemati M, Nemati H. "Long COVID": Symptom persistence in children hospitalised for COVID-19. J Paediatr Child Health. 2022;58(10):1836–40. https://doi.org/10.1111/jpc.16120 PMID: 35851732
35. Ashkenazi-Hoffnung L, Shmueli E, Ehrlich S, Ziv A, Bar-On O, Birk E, et al. Long COVID in children: observations from a designated pediatric clinic. Pediatric Infectious Disease Journal. 2021;40(12):e509-11.
36. Baptista de Lima J, Salazar L, Fernandes A, Teixeira C, Marques L, Afonso C. Long COVID in children and adolescents: A retrospective study in a pediatric cohort. Pediatr Infect Dis J. 2023;42(4):e109–11.
37. Bergia M, Sanchez-Marcos E, Gonzalez-Haba B, Hernaiz AI, de Ceano-Vivas M, García López-Hortelano M, et al. Comparative study shows that 1 in 7 Spanish children with COVID-19 symptoms were still experiencing issues after 12 weeks. Acta Paediatr. 2022 Aug;111(8):1573–82.
38. Bloise S, Isoldi S, Marcellino A, De Luca E, Dilillo A, Mallardo S. Clinical picture and long-term symptoms of SARS-CoV-2 infection in an Italian pediatric population. Ital J Pediatr. 2022;48:79.
39. Blomberg B, Mohn KG-I, Brokstad KA, Zhou F, Linchausen DW, Hansen B-A, et al. Long COVID in a prospective cohort of home-isolated patients. Nat Med. 2021;27(9):1607–13. https://doi.org/10.1038/s41591-021-01433-3 PMID: 34163090
40. Borch L, Holm M, Knudsen M, Ellermann-Eriksen S, Hagstroem S. Long COVID symptoms and duration in SARS-CoV-2 positive children - a nationwide cohort study. Eur J Pediatr. 2022;181(4):1597–607. https://doi.org/10.1007/s00431-021-04345-z PMID: 35000003
41. Bossley CJ, Kavaliunaite E, Harman K, Cook J, Ruiz G, Gupta A. Post-acute COVID-19 outcomes in children requiring hospitalisation. Sci Rep. 2022;12(1):8208. https://doi.org/10.1038/s41598-022-12415-x PMID: 35581348
42. Brackel CLH, Lap CR, Buddingh EP, van Houten MA, van der Sande LJTM, Langereis EJ, et al. Pediatric long-COVID: An overlooked phenomenon?. Pediatr Pulmonol. 2021;56(8):2495–502. https://doi.org/10.1002/ppul.25521 PMID: 34102037
43. Buonsenso D, Munblit D, Pazukhina E, Ricchiuto A, Sinatti D, Zona M, et al. Post-COVID Condition in Adults and Children Living in the Same Household in Italy: A Prospective Cohort Study Using the ISARIC Global Follow-Up Protocol. Front Pediatr. 2022;10:834875. https://doi.org/10.3389/fped.2022.834875 PMID: 35529336
44. Buonsenso D, Espuny Pujol F, Munblit D, Pata D, McFarland S, Simpson FK. Clinical characteristics, activity levels and mental health problems in children with long coronavirus disease: a survey of 510 children. Future Microbiol. 2022;17(8):577–88. https://doi.org/10.2217/fmb-2021-0285 PMID: 35360923
45. Buonsenso D, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, et al. Preliminary evidence on long COVID in children. Acta Paediatr. 2021;110(7):2208–11. https://doi.org/10.1111/apa.15870 PMID: 33835507
46. Erol N, Alpinar A, Erol C, Sari E, Alkan K. Intriguing new faces of Covid-19: persisting clinical symptoms and cardiac effects in children. Cardiol Young. 2022;32(7):1085–91. https://doi.org/10.1017/S1047951121003693 PMID: 34407902
47. Fink TT, Marques HHS, Gualano B, Lindoso L, Bain V, Astley C, et al. Persistent symptoms and decreased health-related quality of life after symptomatic pediatric COVID-19: A prospective study in a Latin American tertiary hospital. Clinics (Sao Paulo). 2021;76:e3511. https://doi.org/10.6061/clinics/2021/e3511 PMID: 34852145
48. Funk AL, Kuppermann N, Florin TA, Tancredi DJ, Xie J, Kim K, et al. Post-COVID-19 conditions among children 90 days after SARS-CoV-2 infection. JAMA Network Open. 2022;5(7):e2223253.
49. Gonzalez-Aumatell A, Bovo MV, Carreras-Abad C, Cuso-Perez S, Domènech Marsal È, Coll-Fernández R, et al. Social, Academic, and Health Status Impact of Long COVID on Children and Young People: An Observational, Descriptive, and Longitudinal Cohort Study. Children (Basel). 2022;9(11):1677. https://doi.org/10.3390/children9111677 PMID: 36360405

50. Haddad A, Janda A, Renk H, Stich M, Frieh P, Kaier K, et al. Long COVID symptoms in exposed and infected children, adolescents and their parents one year after SARS-CoV-2 infection: A prospective observational cohort study. eBioMedicine. 2022;84:104245. https://doi.org/10.1016/j.ebiom.2022.104245

51. Kikkenborg Berg S, Dam Nielsen S, Nygaard U, Bundgaard H, Palm P, Rotvig C, et al. Long COVID symptoms in SARS-CoV-2-positive adolescents and matched controls (LongCOVIDKidsDK): a national, cross-sectional study. Lancet Child Adolesc Health. 2022;6(4):240–8. https://doi.org/10.1016/S2352-4642(22)00004-9 PMID: 35143771

52. Knoke L, Schlegtendal A, Maier C, Eitner L, Lücke T, Brinkmann F, et al. Pulmonary function and long-term respiratory symptoms in children and adolescents after COVID-19. Frontiers in Pediatrics. 2022;10:851008.

53. Kompaniyets L, Bull-Otterson L, Boehmer T, Baca S, Alvarez P, Hong K. Post-COVID-19 symptoms and conditions among children and adolescents - United States, March 1, 2020-January 31, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(31):993–9. https://doi.org/10.15585/mmwr.mm7131a1

54. Kuczborska K, Buda P, Książyk J. Long-COVID in immunocompromised children. Eur J Pediatr. 2022;181(9):3501–9. https://doi.org/10.1007/s00431-022-04561-1 PMID: 35834042

55. Matteudi T, Luciani L, Fabre A, Minodier P, Boucekine M, Bosdure E, et al. Clinical characteristics of paediatric COVID-19 patients followed for up to 13 months. Acta Paediatr. 2021 Dec;110(12):3331–3.

56. Miller F, Nguyen DV, Navaratnam AM, Shrotri M, Kovar J, Hayward AC, et al. Prevalence and Characteristics of Persistent Symptoms in Children During the COVID-19 Pandemic: Evidence From a Household Cohort Study in England and Wales. Pediatr Infect Dis J. 2022;41(12):979–84. https://doi.org/10.1097/INF.0000000000003715 PMID: 36375098

57. Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Antonelli M, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. Lancet Child Adolesc Health. 2021;5(10):708–18. https://doi.org/10.1016/S2352-4642(21)00198-X PMID: 34358472

58. Osmanov IM, Spiridonova E, Bobkova P, Gamirova A, Shikhaleva A, Andreeva M, et al. Risk factors for post-COVID-19 condition in previously hospitalised children using the ISARIC Global follow-up protocol: a prospective cohort study. Eur Respir J. 2022;59(2):2101341. https://doi.org/10.1183/13993003.01341-2021 PMID: 34210789

59. Pazukhina E, Andreeva M, Spiridonova E, Bobkova P, Shikhaleva A, El-Taravi Y, et al. Prevalence and risk factors of post-COVID-19 condition in adults and children at 6 and 12 months after hospital discharge: a prospective, cohort study in Moscow (StopCOVID). BMC Med. 2022;20(1):244. https://doi.org/10.1186/s12916-022-02448-4 PMID: 35794549

60. Pinto Pereira SM, Nugawela MD, Rojas NK, Shafran R, McOwat K, Simmons R, et al. Post-COVID-19 condition at 6 months and COVID-19 vaccination in non-hospitalised children and young people. Archives of Disease in Childhood. 2023;108(4):289–95.

61. Radtke T, Ulyte A, Puhan MA, Kriemler S. Long-term symptoms after SARS-CoV-2 infection in children and adolescents. JAMA. 2021 Sep 7;326(9):869–71.

62. Roge I, Smane L, Kivite-Urtane A, Pucuka Z, Racko I, Klavina L, et al. Comparison of persistent symptoms after COVID-19 and other Non-SARS-CoV-2 infections in children. Frontiers in Pediatrics. 2021;9:752385. https://doi.org/10.3389/fped.2021.752385

63. Sakurada Y, Otsuka Y, Tokumasu K, Sunada N, Honda H, Nakano Y, et al. Trends in Long COVID Symptoms in Japanese Teenage Patients. Medicina (Kaunas). 2023;59(2):261. https://doi.org/10.3390/medicina59020261 PMID: 36837463

64. Say D, Crawford N, McNab S, Wurzel D, Steer A, Tosif S. Post-acute COVID-19 outcomes in children with mild and asymptomatic disease. Lancet Child Adolesc Health. 2021;5(6):e22–3. https://doi.org/10.1016/S2352-4642(21)00124-3 PMID: 33891880

65. Seery V, Raiden S, Penedo J, Borda M, Herrera L, Uranga M, et al. Persistent symptoms after COVID-19 in children and adolescents from Argentina. International Journal of Infectious Diseases. 2023;129(4):49–56.

66. Smane L, Stars I, Pucuka Z, Roge I, Pavare J. Persistent clinical features in paediatric patients after SARS-CoV-2 virological recovery: a retrospective population-based cohort study from a single centre in Latvia. BMJ Paediatr Open. 2020;4(1):e000905. https://doi.org/10.1136/bmjpo-2020-000905 PMID: 34192185

67. Smane L, Roge I, Pucuka Z, Pavare J. Clinical features of pediatric post-acute COVID-19: a descriptive retrospective follow-up study. Ital J Pediatr. 2021;47(1):177. https://doi.org/10.1186/s13052-021-01127-z PMID: 34446085

68. Stephenson T, Shafran R, De Stavola B, Rojas N, Aiano F, Amin-Chowdhury Z, et al. Long COVID and the mental and physical health of children and young people: national matched cohort study protocol (the CLoCk study). BMJ Open. 2021;11(8):e052838. https://doi.org/10.1136/bmjopen-2021-052838 PMID: 34446502

69. Sterky E, Olsson-Åkefeldt S, Hertting O, Herlenius E, Alfven T, Ryd Rinder M, et al. Persistent symptoms in Swedish children after hospitalisation due to COVID-19. Acta Paediatr. 2021;110(9):2578–80. https://doi.org/10.1111/apa.15999 PMID: 34157167

70. Trapani G, Verlato G, Bertino E, Maiocco G, Vesentini R, Spadavecchia A, et al. Long COVID-19 in children: an Italian cohort study. Ital J Pediatr. 2022;48(1):83. https://doi.org/10.1186/s13052-022-01282-x PMID: 35659358

71. Zavala M, Ireland G, Amin-Chowdhury Z, Ramsay M, Ladhani S. Acute and persistent symptoms in children with polymerase chain reaction (PCR)-confirmed severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) infection compared with test-negative children in England: Active, prospective, national surveillance. Clinical Infectious Diseases. 2022;75(1):e191-200.

72. Thallapureddy K, Thallapureddy K, Zerda E, Suresh N, Kamat D, Rajasekaran K, et al. Long-Term Complications of COVID-19 Infection in Adolescents and Children. Curr Pediatr Rep. 2022;10(1):11–7. https://doi.org/10.1007/s40124-021-00260-x PMID: 35127274

73. Fernández-de-Las-Peñas C, Torres-Macho J, Macasaet R, Velasco JV, Ver AT, Culasino Carandang THD, et al. Presence of SARS-CoV-2 RNA in COVID-19 survivors with post-COVID symptoms: a systematic review of the literature. Clin Chem Lab Med. 2024;62(6):1044–52. https://doi.org/10.1515/cclm-2024-0036 PMID: 38366966

74. Basu-Ray I, Almaddah N k, Adeboye A, Vaqar S, Soos MP. Cardiac manifestations of coronavirus (COVID-19). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Aug 30]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK556152/

75. Sansone F, Pellegrino G, Caronni A, Bonazza F, Vegni E, Lué A, et al. Long COVID in children: A multidisciplinary review. Diagnostics (Basel). 2023;13(12):1990.

76. Mehandru S, Merad M. Pathological sequelae of long-haul COVID. Nat Immunol. 2022;23(2):194–202. https://doi.org/10.1038/s41590-021-01104-y PMID: 35105985

77. Melms JC, Biermann J, Huang H, Wang Y, Nair A, Tagore S, et al. A molecular single-cell lung atlas of lethal COVID-19. Nature. 2021;595(7865):114–9. https://doi.org/10.1038/s41586-021-03569-1 PMID: 33915568

78. García-Salido A, de Carlos Vicente JC, Belda Hofheinz S, Balcells Ramírez J, Slöcker Barrio M, Leóz Gordillo I, et al. Severe manifestations of SARS-CoV-2 in children and adolescents: from COVID-19 pneumonia to multisystem inflammatory syndrome: a multicentre study in pediatric intensive care units in Spain. Crit Care. 2020;24(1):666. https://doi.org/10.1186/s13054-020-03332-4 PMID: 33243303

79. Fernández-de-Las-Peñas C, Torres-Macho J, Catahay JA, Macasaet R, Velasco JV, Macapagal S, et al. Correction: Is antiviral treatment at the acute phase of COVID-19 effective for decreasing the risk of long-COVID? A systematic review. Infection. 2024;52(5):1687. https://doi.org/10.1007/s15010-024-02208-x PMID: 38451416

80. Notarte KI, Carandang THDC, Velasco JV, Pastrana A, Ver AT, Manalo GN, et al. Autoantibodies in COVID-19 survivors with post-COVID symptoms: A systematic review. Frontiers in Immunology. 2024;15(7):1428645. https://doi.org/10.3389/fimmu.2024.1428645

81. 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):914–21. https://doi.org/10.1111/apa.15673 PMID: 33205450

82. Castanares-Zapatero D, Chalon P, Kohn L, Dauvrin M, Detollenaere J, Maertens de Noordhout C, et al. Pathophysiology and mechanism of long COVID: a comprehensive review. Ann Med. 2022;54(1):1473–87.

83. Bouças AP, Rheinheimer J, Lagopoulos J. Why Severe COVID-19 Patients Are at Greater Risk of Developing Depression: A Molecular Perspective. Neuroscientist. 2022;28(1):11–9. https://doi.org/10.1177/1073858420967892 PMID: 33135582

84. Boldrini M, Canoll P, Klein R. How COVID-19 affects the brain. JAMA Psychiatry. 2021;78(6):682–3.

85. de Melo G, Lazarini F, Levallois S, Hautefort C, Michel V, Larrous F. COVID-19-related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters. Science Translational Medicine. 2021;13(596):eabf8396.

86. Doyle M, Appleton A, Liu Q, Yao Q, Mazucanti C, Egan J. Human type II taste cells express angiotensin-converting enzyme 2 and are infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). American Journal of Pathology. 2021;191(9):1511–9.

87. Azzopardi PS, Kerr JA, Sawyer SM, Kennedy EC, Steer AC, Graham SM. The unfinished agenda of communicable diseases among children and adolescents before the COVID-19 pandemic, 1990–2019: A systematic analysis of the Global Burden of Disease Study from 1990 to 2019. Lancet Global Health. 2022;10(12):e1774-81.

88. Ranasinghe L, Achar J, Gröschel MI, Whittaker E, Dodd PJ, Seddon JA. Global impact of COVID-19 on childhood tuberculosis: an analysis of notification data. Lancet Glob Health. 2022;10(12):e1774–81. https://doi.org/10.1016/S2214-109X(22)00414-4 PMID: 36400083

89. Redfern A, van der Zalm MM, Lishman J, Goussard P, Smit L, Dagan R, et al. Clinical Presentation and Outcome of Acute Respiratory Illnesses in South African Children During the COVID-19 Pandemic. Pediatr Infect Dis J. 2023;42(8):672–8. https://doi.org/10.1097/INF.0000000000003951 PMID: 37171967

90. Antonelli M, Pujol JC, Spector TD, Ourselin S, Steves CJ. Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2. Lancet. 2022 Jun 18;399(10343):2263–4.

91. Notarte KI, Catahay JA, Velasco JV, Pastrana A, Ver AT, Pangilinan FC, et al. Impact of COVID-19 vaccination on the risk of developing long-COVID and on existing long-COVID symptoms: A systematic review. EClinicalMedicine. 2022;53:101624. https://doi.org/10.1016/j.eclinm.2022.101624 PMID: 36051247