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REVIEW PAPER

Long COVID-19 in children: a review of key information

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ABSTRACT

Long COVID in children is defined as a syndrome of persistent symptoms following SARS-CoV-2 infection, which appear within three months after the acute phase, last for at least two months, and have a significant impact on the child's daily functioning. The symptoms are heterogeneous and may involve multiple organ systems. The causes and risk factors for developing long COVID in the paediatric population remain incompletely understood, and diagnosis may be challenging due to the nonspecific nature of symptoms and the need for thorough differential diagnosis. Further long-term studies are required to establish the true association between acute SARS-CoV-2 infection and the development of long COVID in children. This paper presents fundamental information on long COVID in the paediatric population, with a focus on key risk factors, pathophysiology, clinical manifestations, diagnostic approaches, the importance of vaccination, and the potential role of viral variants in the pathogenesis of long COVID.

KEY WORDS:

long COVID, post-COVID-19 condition, children, SARS-CoV-2.

INTRODUCTION

At the end of 2019, the World Health Organisation (WHO) received reports of several cases of pneumonia of unknown aetiology in Wuhan, China. The causative pathogen was identified in January 2020 as a novel coronavirus, officially named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in February 2020. The rapid global spread of the virus led the WHO to declare a worldwide pandemic on 11 March 2020 [1].

The clinical manifestations in children of acute COVID-19 (coronavirus disease 2019), caused by SARS-CoV-2, varied widely, ranging from asymptomatic or mildly symptomatic cases to severe pulmonary forms requiring intensive care. Additionally, extrapulmonary symptoms and fatal outcomes were reported [2].

In the majority of paediatric cases, the course of infection was asymptomatic or mild compared to that seen in adults [3]. According to WHO data compiled up to August 2025, more than 778 million cases of COVID-19 were reported worldwide, including over 7 million deaths [4]. Within the paediatric population, infections accounted for approximately 8.5% of all cases, with higher incidence observed in certain countries, such as the United States (18%) [5].

LONG COVID

During the first year of the COVID-19 pandemic, reports began to emerge describing persistent symptoms following acute SARS-CoV-2 infection, commonly referred to as "long COVID", "post-COVID syndrome", or "post-acute sequelae of SARS-CoV-2 (PASC)". Initially, these persistent symptoms were documented in adults [6] and then later also observed in children.

The first scientific report describing long COVID in the paediatric population was a case series from Sweden, involving five children who, following recovery from acute infection, continued to experience nonspecific symptoms for 6–8 months. These symptoms included fatigue, dyspnoea, chest pain, palpitations, headaches, and concentra-

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tion difficulties [7]. Subsequent studies confirmed the existence of long COVID among paediatric patients [8].

In 2022, the first formal definition of long COVID-19 in children was proposed, consistent with the WHO definition for adults [9]. According to this definition: *Post-COVID-19 condition refers to young individuals with a history of confirmed SARS-CoV-2 infection presenting with at least one persistent physical symptom lasting for a minimum of 12 weeks following the initial test, which cannot be explained by an alternative diagnosis. These symptoms affect daily functioning and may represent a continuation of or develop after the acute phase of COVID-19; they may fluctuate or recur over time* [10].

A positive SARS-CoV-2 test was defined as a lateral flow antigen test, polymerase chain reaction, or serological antibody test (IgM and IgG antibody).

In February 2023, the WHO further refined the definition of post-COVID-19 condition in children and adolescents as follows: *A condition occurring in individuals with a history of confirmed or probable SARS-CoV-2 infection, who experience symptoms lasting for at least two months, appearing within three months of the acute COVID-19 infection. These symptoms impact daily functioning, including changes in eating habits, physical activity, behaviour, school attendance, and social functioning (interactions with friends, peers, and family), as well as developmental milestones. Reported symptoms may follow initial recovery from acute infection or persist from the onset of illness. They may fluctuate or recur over time* [11].

PREVALENCE AND SPECTRUM OF LONG-COVID SYMPTOMS IN CHILDREN AND ADOLESCENTS

The reported prevalence of symptoms associated with long COVID in children and adolescents varies widely across available studies, ranging 4–66% [12]. This variability may be attributed to the absence of a standardised paediatric definition of long COVID at the time of study design (before February 2023), heterogeneous inclusion criteria (in some studies, no confirmed history of SARS-CoV-2 infection was required), differences in follow-up duration, low response rates in questionnaire-based studies, reliance on self-reported or parent-reported symptoms without objective clinical evaluation, and the lack of appropriate control groups for comparison [8, 12, 13].

Interestingly, studies that included control groups of COVID-19-negative children revealed that many symptoms were present in both COVID-19-positive and COVID-19-negative cohorts, although they occurred more frequently among infected individuals [14–17]. However, other investigations demonstrated that post-COVID-19 symptoms were uncommon and generally resolved within 12 weeks [18, 19].

A meta-analysis conducted by Lopez-Leon *et al.* [20], encompassing more than 80,000 paediatric patients, reported a pooled prevalence of long COVID of 25%, increasing to 29% among children who had been previously hospitalised for acute COVID-19.

More than 200 different symptoms have been attributed to long COVID to date [21]. Many of these manifestations are nonspecific and frequently occur in the general paediatric population. The most commonly reported symptoms include mood disturbances, fatigue, sleep disorders, headaches, respiratory symptoms, cognitive impairment (such as concentration difficulties, learning problems, or memory loss), loss of appetite, decreased exercise tolerance, and olfactory dysfunction. Less frequent symptoms include palpitations, sore throat, fever, rashes, musculoskeletal pain, and gastrointestinal complaints [20].

Symptom frequency appears to vary by age. Among young children (≤ 3 years), the most commonly reported symptoms by caregivers were skin rashes, behavioural changes, cough, abdominal pain, and reduced appetite. In older children and adolescents, the predominant symptoms included mood disorders, fatigue, and difficulties with concentration and memory [15, 16].

It has been suggested that some long COVID-related symptoms may be more closely linked to the indirect psychosocial consequences of the pandemic – such as social isolation, quarantine, school closures, and bereavement – rather than to the direct effects of SARS-CoV-2 infection itself [17, 22] Table 1.

Several risk factors have been identified as predisposing to the development of long COVID in the paediatric population. These include older age (adolescence), female sex, the presence of chronic comorbidities, particularly allergic diseases, obesity, a greater number of symptoms, and a more severe course of acute COVID-19 infection. Furthermore, poor physical and mental well-being and feelings of loneliness prior to SARS-CoV-2 infection have been associated with an increased likelihood of developing long COVID [1, 20].

In the general population, lower socioeconomic status and insufficient rest or recovery following acute infection have also been recognised as risk factors for the persistence of post-COVID symptoms. However, it is noteworthy that approximately one-third of individuals with long COVID had no identifiable predisposing factors [21].

Conversely, several protective factors have been proposed, including the absence of comorbidities, efficient immune function, and favourable environmental and biological conditions, such as prior vaccinations, optimal nutritional status, and a healthy gut microbiota composition [20].

A Polish study involving 147 children with symptoms of long COVID, including 70 immunocompromised patients (with malignancies under active treatment, post-liver or kidney transplantation, ulcerative colitis on immunosuppressive therapy, or primary immunodeficiencies), demonstrated that long-COVID symptoms were significantly more common among immunocompe-

TABLE 1. The most frequently reported long-COVID symptoms in children

Nervous system [23] 1. Neurological symptoms	• Cognitive dysfunction (2–81%): "brain fog", impaired concentration, memory and attention deficits • Headache (3–80%) • Olfactory or gustatory disturbances (12–70%) • Fatigue (3–87%) • Dizziness (3–20%)
Nervous system [23] 2. Neuropsychiatric symptoms [24, 25]	• Sleep disturbances (2–63%) • Mood disorders (5–24%) • Obsessive–compulsive symptoms (23%) • Tics (9%) • Eating disorders (10.6% – changes in eating habits, 6.6% – restrictive eating) • Psychosis, mania (no exact date – limited number of studies)
Respiratory system [5, 12, 26, 27]	• Cough (1–30%) • Dyspnoea (2–57%)
Cardiovascular system [5, 12]	• Orthostatic intolerance (7%) • Exercise intolerance (5.7%) • Chest tightness or pain (1–31%) • Variations in heart rate (2.3%) • Palpitations (1.2%)
Gastrointestinal system [5, 12, 28, 29]	• Abdominal pain (2.9%; 1–76%) • Constipation (2%) • Chronic diarrhoea (1.7%) • Nausea/vomiting (1.5%) • Dysphagia (0.5%) • Liver injury (case series of 5 children)
Sensory organs [5, 12]	• Nasal obstruction, rhinitis (1–12%) • Ear pain, tinnitus (3%) • Sore throat (≈2%)
Musculoskeletal system [5]	• Myalgia, muscle weakness, arthralgia (1–61%)
Skin [12]	• Rash (2–52%)

tent children compared with those with immune deficiencies (60% vs. 35%, 12 weeks after acute infection) [30].

Among the reported symptoms, fatigue, reduced exercise tolerance, and concentration difficulties predominated in immunocompetent children, whereas gastrointestinal symptoms were somewhat more frequent among immunocompromised patients. Moreover, long-COVID symptoms more frequently interfered with daily functioning in the immunocompetent group.

The authors suggested that immunodeficiency might exert a protective effect against the development of the inflammatory response implicated in the pathogenesis of long COVID, potentially mitigating post-infectious sequelae in these patients [30].

The pathogenesis of long COVID remains incompletely understood; however, several potential mechanisms have been proposed and are summarised in Table 2.

ASSESSMENT OF THE RESPIRATORY SYSTEM IN CHILDREN WITH LONG COVID

The most common respiratory manifestations of long COVID in children include cough, dyspnoea, and exercise intolerance [5, 27]. In a meta-analysis involving 386 paediatric patients, clinical symptoms and pulmonary function were evaluated at least six weeks after acute SARS-CoV-2 infection. The analysis revealed no statistically significant abnormalities in pulmonary function tests [27].

In contrast, an Israeli study including 184 children presenting with persistent respiratory complaints consistent with long COVID demonstrated abnormal pulmonary function in nearly half of the participants (85 children). Among these, approximately 20% exhibited evidence of airway obstruction. Following treatment with inhaled corticosteroids and long-acting β-agonists, normalisation of pulmonary function was observed within 1–6 months of follow-up [32].

Lung ultrasonography (trans-thoracic ultrasound) did not reveal any structural pulmonary abnormalities in children with long-COVID symptoms [33].

A Polish study involving 41 children hospitalised due to moderate to severe SARS-CoV-2-related pneumonia showed that persistent clinical symptoms, such as reduced exercise tolerance, dyspnoea, and cough, were present in nearly 20% of children at three months post-discharge. In 26 patients, residual lung ultrasound abnormalities persisted three months after pneumonia but demonstrated a tendency toward resolution by six months.

TABLE 2. Proposed mechanisms underlying the pathogenesis of long COVID [21, 22, 31]

Persistence of SARS-CoV-2 viral reservoirs [22, 31]	Viral particles may persist in the human body for months following acute infection, particularly in the brain, heart, and intestines, leading to chronic subclinical inflammation. This persistent immune activation may contribute to prolonged symptom such as pain, fatigue, malaise, and neurological manifestations including "brain fog" and disturbances of smell and taste
Reactivation of latent herpesviruses [21, 31]	Reactivation of previously latent viruses–such as Epstein-Barr virus–during acute SARS-CoV-2 infection may indirectly contribute to persistent symptoms, including fatigue and cognitive impairment
Immune dysregulation and autoimmunity [21, 22, 31]	SARS-CoV-2 infection may trigger the production of autoantibodies, including antinuclear antibodies, antineutrophil cytoplasmic antibodies, and antibodies targeting angiotensin II receptors, thereby initiating autoimmune processes. Furthermore, viral protein fragments can induce chronic inflammation, particularly within the central nervous system, sustaining post-infectious symptomatology
Autonomic nervous system dysfunction [21]	SARS-CoV-2 may invade autonomic nerve fibres, leading to dysautonomia, manifested as cardiac rhythm abnormalities, postural orthostatic tachycardia syndrome, and gastrointestinal dysmotility
Intestinal dysbiosis [31]	Through interaction with ACE2 receptors expressed on intestinal epithelial cells, SARS-CoV-2 disrupts gastrointestinal homeostasis, causing microbiome imbalance and increased intestinal permeability. These alterations affect the gut-brain axis, potentially leading to gastrointestinal and neuropsychiatric symptoms
Vascular and endothelial dysfunction [22, 31]	SARS-CoV-2 can induce coagulation abnormalities and endothelial inflammation, predisposing to thromboembolic events. Circulating microthrombi may impair peripheral circulation and tissue oxygenation, resulting in fatigue, post-exertional malaise, and dyspnoea
Direct organ damage [22, 31]	Direct viral injury to organs such as the heart, lungs, kidneys, and brain, particularly in adults following severe COVID-19, may lead to chronic organ dysfunction and subsequent long-term clinical manifestations

Pulmonary function tests were normal in most of the participants; however, restrictive ventilatory defects were observed exclusively in children recovering from severe pneumonia [34].

NEUROLOGICAL ASSESSMENT IN CHILDREN WITH LONG COVID

The most frequently reported neurological manifestations of long COVID in children include brain fog, memory impairment, concentration difficulties, headaches, dizziness, anosmia, ageusia, and fatigue. Less commonly observed symptoms include seizures, encephalitis, and encephalopathy [23].

The pathophysiology of neurological symptoms in long COVID remains incompletely understood; however, several mechanisms have been proposed. Chronic headaches may result from prolonged release of proinflammatory cytokines during the acute phase of COVID-19. Olfactory and gustatory dysfunctions are believed to arise from damage to the olfactory epithelium and oral mucosa caused by SARS-CoV-2 infection [24].

The aetiology of fatigue observed in long COVID is considered multifactorial, involving a systemic inflammatory response, frequent co-occurrence of sleep disturbances, and psychological factors directly related to the pandemic [23].

Neuropsychiatric manifestations–including sleep and mood disorders, eating disturbances, psychosis, and mania – have been reported both in adults and in the paediatric population. These symptoms may stem from direct viral effects on the central nervous system as well as from indirect psychosocial consequences of the pandemic [22, 24, 35].

Interestingly, in both children and adults exhibiting symptoms such as cognitive dysfunction (memory impairment, concentration difficulties), sleep disturbances, fatigue, and olfactory disorders, positron emission tomography imaging revealed hypometabolism in specific brain regions, including the temporal lobes, brainstem, cerebellum, and olfactory gyrus [36].

GASTROINTESTINAL ASSESSMENT IN CHILDREN WITH LONG COVID

Gastrointestinal manifestations of long COVID in children are relatively uncommon, with a prevalence of less than 5%. Reported symptoms include abdominal pain, vomiting, diarrhoea, constipation, and dysphagia [20]. There have been reports of hepatic injury following SARS-CoV-2 infection in children, manifesting as acute liver failure or cholestatic hepatitis [29].

Gastrointestinal symptoms may result from the direct cytopathic effects of the virus. The high expression of angiotensin-converting enzyme II receptors–the primary entry point for SARS-CoV-2–on hepatocytes and intestinal brush border cells may promote gastrointestinal involvement through cytokine dysregulation, inflammatory responses, and increased intestinal barrier permeability.

Additionally, COVID-19-associated gut dysbiosis has been implicated in the development of symptoms not only of the gastrointestinal system, but also of the respiratory and nervous systems [5].

In terms of management, lactoferrin supplementation has demonstrated a beneficial effect in alleviating gastrointestinal symptoms associated with long COVID [28].

CARDIOVASCULAR ASSESSMENT IN CHILDREN WITH LONG COVID

In adult patients with long COVID, cardiovascular symptoms are relatively common and heterogeneous, including chest pain, palpitations, reduced exercise tolerance, and dyspnoea. These symptoms may result, among other mechanisms, from the direct viral impact on the cardiac and vascular endothelium and can be associated with organic pathologies such as myocarditis, pericarditis, or myocardial dysfunction. Similar manifestations have been described in children; however, they generally present with a milder clinical course [37].

In a study by Delogu *et al.* [38], involving 56 children diagnosed with long COVID, no significant differences were observed in left ventricular systolic or diastolic function compared with healthy controls. However, a slightly prolonged QTc interval in electrocardiogram (within normal limits) was noted in long-COVID patients. Additionally, abnormalities in heart rate variability were identified in the long-COVID group, indicating autonomic nervous system dysfunction with **i**ncreased parasympathetic activity, which may explain the reported symptoms such as palpitations and dyspnoea.

Another study including over 100 children post-COVID-19 infection demonstrated significant differences in systolic blood pressure and several echocardiographic parameters compared with a control group, suggesting that the SARS-CoV-2 pathogen may affect the cardiovascular system [39].

Similarly, in a study by Heching *et al.* [40], involving 82 paediatric patients, 65% reported at least one cardiac symptom following acute COVID-19 infection. Electrocardiographic findings were normal in nearly 80% of cases, while transient electrocardiogram changes were observed in 21%, without accompanying echocardiographic abnormalities.

DIAGNOSTIC EVALUATION OF LONG COVID IN CHILDREN

At present, there are no universally accepted guidelines for the diagnostic evaluation of long COVID in paediatric patients. Fainardi *et al.* [41] proposed a three-stage diagnostic framework.

In the first stage, clinicians should actively screen for long-COVID symptoms through a detailed medical history and comprehensive physical examination.

The second stage involves additional investigations guided by the reported symptoms. These may include the following:
- basic laboratory tests,
- pulmonary function assessments (spirometry, impulse oscillometry, exhaled nitric oxide measurement, body plethysmography),
- imaging studies (chest X-ray, lung ultrasound, abdominal ultrasound),
- cardiac evaluation (electrocardiogram, echocardiography),
- sleep assessment (polysomnography),
- psychological evaluation (screening for depression and anxiety disorders).

The third stage focuses on regular follow-up–every three months–and, if indicated, repetition of diagnostic tests to monitor symptom persistence or progression. During the diagnostic process, alternative diagnoses should always be considered, as emphasised in a German study [42]. Among children initially suspected of having long COVID, alternative diagnoses included the following: residual manifestations of pediatric inflammatory multisystem syndrome, myocarditis, autoimmune diseases (such as juvenile idiopathic arthritis, dermatomyositis, inflammatory bowel disease), acute infections (pneumonia, mononucleosis), parasitic diseases, neurological conditions (migraine, neuroborreliosis, myasthenia gravis), asthma, oncologic diseases, as well as psychiatric and somatic symptom disorders, including depression and anxiety.

In a survey among paediatricians in the United States, respondents most frequently identified new-onset cardiovascular or respiratory symptoms, as well as cognitive and neurological disturbances, as indicative of possible long COVID. The detection of postural orthostatic tachycardia during physical examination was also considered a potential clinical marker of the condition [43].

To date, no specific biomarkers have been established to aid in the diagnosis of long COVID. Ongoing research is exploring potential cytokine-based biomarkers; however, as of now, no routine laboratory tests have proven useful in confirming the diagnosis [43].

MANAGEMENT AND PREVENTION OF LONG COVID IN CHILDREN

In most cases, long-COVID symptoms in children are mild and resolve spontaneously within several months [44]. However, in approximately one-third of paediatric patients, symptoms may persist for 12 months or longer, and no standardised therapeutic consensus has yet been established [45].

VACCINATION

The impact of COVID-19 vaccination on the development of long-COVID symptoms in children remains unclear and requires further investigation. Several studies have demonstrated a protective effect of vaccination, particularly when administered prior to the acute SARS-CoV-2 infection, showing a reduction in the risk of developing long-COVID symptoms [46–48].

Nonetheless, reinfections appear to increase the risk of long COVID, even among individuals vaccinated with two or three doses [21].

A more recent study assessed the influence of the SARS-CoV-2 Omicron variant on the occurrence of long-COVID symptoms 12 months after acute infection. The study included two groups of children: one consisting of children infected for the first time with the Omicron variant, and the other comprising those who experienced reinfection during the Omicron-dominant period.

After 12 months of follow-up, the most commonly reported symptoms in both groups were fatigue, sleep disturbances, dyspnoea, headache, and rhinitis. There were no significant differences between the groups in the number or severity of symptoms, nor in their impact on daily functioning. Moreover, COVID-19 vaccination did not appear to significantly influence the risk of developing long COVID. These findings suggest that the number of SARS-CoV-2 infections may not play a decisive role in the development of post-COVID sequelae in paediatric populations [49].

Furthermore, among those who had previously experienced multisystem inflammatory syndrome in children (MIS-C), it was observed that, regardless of the length of follow-up (ranging from 4 to over 24 weeks after MIS-C), most long-COVID symptoms were not associated with the specific SARS-CoV-2 variant. The only exception was a slightly higher prevalence of fatigue among patients whose MIS-C was caused by the Original/Alpha variant [50].

CONCLUSIONS

A possible consequence of SARS-CoV-2 infection is the condition referred to as long COVID. The diagnosis of long COVID in children may be challenging due to nonspecific symptoms affecting multiple organ systems. Further long-term studies are necessary to establish the actual relationship between SARS-CoV-2 infection, including the influence of emerging viral variants, and the development of long-COVID symptoms.

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