"Long-Term Effects of SARS-CoV-2 Infection in Hospitalized Children: Findings from an Italian Single-Center Study"

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Conflicts of Interest: The authors declare no conflict of interest.

Funding: The project received contributions from (1) HORIZON-HLTH-2021-CORONA-01 CoVICIS project number 101046041; (2) Bando Cariplo Networking research &training post-COVID protocol number 2021-4490.

Key words: SARS-CoV-2, infection, COVID, Long COVID, long-term effects, hospitalized, children

Cover title: Long-term Effects of SARS-CoV-2 in Hospitalized Children

Running title: Long-term Effects of SARS-CoV-2 in Children

Abstract

Background: Limited evidence exists regarding the association between COVID-19 and Long COVID manifestations in children, particularly concerning variants of concern (VOCs). We aimed to characterize a cohort of pediatric patients hospitalized with confirmed acute SARS-CoV-2 and monitor them for Long COVID symptoms. Additionally, it seeks to explore any potential correlations between VOCs and clinical symptoms.

Patients and methods: we conducted a prospective study involving children hospitalized from November 2021 to March 2023, with confirmed acute SARS-CoV-2 infection. A telephone survey was conducted at 3-6-12 months after discharge to monitor the symptoms progression over time.

Results: we included 167 patients (76F/91M). Upon hospital admission, 95.9% of patients presented as symptomatic. Regarding patients for whom it was feasible to determine the SARS-CoV-2 variant (n=51), the Delta variant was identified in 11 children (21.6%) and Omicron variant in the remaining 40 patients (78.4%: 27.5% BA.1 variant; 15% BA.2 variant; 57.5% BA.5 variant). 15 patients (13%; 7F/8M) reported experiencing at least one symptom indicative of Long COVID (weight loss 33.3%, inappetence 26.6%, chronic cough 33.3%, fatigue 20%, sleep disturbances 20%). In only 4 patients with Long COVID we could identified a specific SARS-CoV-2 variant (3 Omicron: 2 BA.1 and 1 BA.2; 1 Delta).

Conclusion: long COVID is a significant concern in the pediatric population across all age groups and without gender-specific prevalence difference. Our data reinforce the importance of monitoring the long-COVID impact in children. Further studies are warranted to detail the correlation between VOCs and symptoms related to long COVID.

Introduction

Following the emergence of the COVID-19 pandemic, a notable increase in persistent symptoms has been observed in individuals previously infected with SARS-CoV-2, in contrast to those who have not encountered the virus. The term "Long COVID" is used to describe the continuation or development of these symptoms for at least two months, occurring three months after the initial SARS-CoV-2 infection, with no other plausible explanation.[1] Long COVID affects survivors of COVID-19 across the spectrum of disease severity, including mild-to-moderate cases that did not require respiratory support or hospitalization.[2] Furthermore, Long COVID symptoms have been reported in children and adolescents, including those who experienced asymptomatic or mildly symptomatic COVID-19. It is worth noting that similar post-viral symptoms have been observed in the context of prior human coronavirus diseases, such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS).[3]

Radiological and respiratory function studies have indicated that pulmonary scarring might be a common consequence of COVID-19, potentially explaining the persistent dyspnea and cough seen in Long COVID.[4] Long-term pulmonary dysfunction has been identified in children who have recovered from COVID-19, underscoring the importance of understanding these complications.[5] Additionally, structural and metabolic abnormalities in the brain have been reported among individuals with prior SARS-CoV-2 infection, even in cases with mild symptomatology, possibly attributed to persistent neuroinflammatory processes,[6] supported by the finding of SARS-CoV-2 genes and proteins and pathological immune and vascular activations in the brainstem of deceased COVID-19 victims.[7] Radiological evidence of cardiac injury in Long COVID exists, with uncertain long-term implications, yet it may elucidate the persistence of chest pain, heart palpitations, and tachycardia for up to six months post-recovery.[2] In addition to pulmonary, neurological, and cardiac involvement, radiological damage and functional impairment of other organs, such as the liver, spleen, and kidneys, have been reported, persisting for at least 2-3 months after hospital discharge.[9]

While the precise mechanisms behind Long COVID remain elusive, several hypotheses regarding its pathophysiology have been proposed.[10] Dysfunction of T-cells might contribute to Long COVID development through autoimmune processes,[11] wherein SARS-CoV-2 induces antigen-presenting cells to present antigens to autoreactive T-cells.[12] B-cells may also play a role by producing antiphospholipid autoantibodies detected in 52% of patients in association with neutrophil hyperactivity, and is often associated with more severe clinical outcomes.[13] Furthermore, autoantibodies against interferons, neutrophils, connective tissues, cyclic citrullinated peptides, and cell nuclei have been identified in 10-50% of COVID-19 patients.[14] These autoantibodies, reminiscent of those found in chronic autoimmune diseases like lupus erythematosus and rheumatoid arthritis,[15] may contribute to Long COVID symptoms, including fatigue, joint pain, concentration difficulties, and headaches.[16-17] Other potential contributors to Long COVID pathophysiology in both children and adults, include residual inflammation following SARS-CoV-2 multisystem inflammatory syndrome (MIS), characterized by

lymphopenia and elevated pro-inflammatory markers,[18] as well as deep alterations in the gut microbiome, which have been observed up to 30 days after disease resolution and correlated with prolonged SARS-CoV-2 shedding.[19]

Despite these insights, limited evidence exists regarding the association between COVID-19 and Long COVID manifestations in children, particularly concerning variants of concern (VOCs). Studies have shown that certain VOCs, such as the Delta variant, exhibit significantly higher viral loads in the upper respiratory tract of adults, raising questions about their impact on children.[20] Another study suggests that seizures may be a frequent and early sign of the Omicron variant in children with acute infections.[21]

This study aims to clinically characterize a cohort of pediatric patients who were hospitalized due to SARS-CoV-2 infection and monitor them for Long COVID symptoms following discharge. Additionally, it seeks to explore any potential correlations between variants of concern (VOCs) and clinical symptoms, where relevant.

Patients and Methods

Patients

We conducted a prospective study involving children hospitalized at Milan's Buzzi Children's Hospital in Italy from November 1st, 2021, to March 30th, 2023, with confirmed acute SARS-CoV-2 infection as documented by nasal swab upon admission. During hospitalization, written consent was obtained from both the child and their accompanying parent, allowing for the collection of saliva swabs to determine SARS-CoV-2 variants. Furthermore, the patients were asked to participate in long-term monitoring after discharge, and those with at least six months of follow-up were included in the analysis. A comprehensive clinical assessment was conducted during hospitalization, collecting data on demographics, symptoms, and comorbidities in the acute phase. To assess the development of Long COVID symptoms a structured questionnaire was designed. A telephone survey was conducted at 3, 6, and 12 months after discharge to monitor the progression of symptoms over time (Figure 1).

To safeguard the privacy of patients, all data and biological samples gathered were pseudonymized, and they were identified solely through the assigned barcode. Data collection took place within a database established on the REDCap platform (www.project-redcap.org), based at Harvard Catalyst, Boston, USA, in strict compliance with prevailing GDPR legislation. A data protection impact assessment was implemented.

All procedures adhered to ethical standards set forth by the responsible committee on human experimentation and were in accordance with the Helsinki Declaration of 1975, as amended in 2000. The study received approval from the Ethics Committee (protocol number 0037072).

Methods

Collection of Saliva Swabs

Upon admission, saliva swabs were collected from all patients using Lollisponge (LolliSponge™, Copan, Brescia, Italy),[22] within 24 hours of admission. The LolliSponge™ was placed in the mouth for one minute to allow the sponge to absorb saliva. Samples, which are self-preservative due to the nature of saliva, were stored at room temperature (RT) without transport medium and were subjected to testing for SARS-CoV-2 using quantitative reverse transcription polymerase chain reaction (qRT-PCR) assays.

Viral RNA was manually extracted utilizing the QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany). RT-PCR genotyping assays were conducted using the COVID-19 Ultra Variant Catcher (Clonit Srl., Milan, Italy), the Allplex SARS-CoV-2 Variants (Arrow Diagnostics Srl., Genoa, Italy), or the multiplexed RT-qPCR developed by the English consortium (https://www.protocols.io/view/multiplexed-rt-qpcr-to-screenfor-sars-cov-2-b-1-1-br9vm966?version_warning=no). For samples with a cycle threshold (Ct) <30, full genome sequences were acquired through a modified version of the Artic Protocol (https://artic.network/ncov-2019) using the Illumina DNA Prep and the IDT ILMN DNA/RNA Index kit (Illumina, San Diego, CA, USA). Sequencing was conducted on the Illumina Miseq platform utilizing a 2×200 cycle paired-end sequencing protocol. Results were aligned and mapped to the reference genome obtained from GISAID (https://www.gisaid.org/, accession ID: EPI_ISL_406800) using Geneious Prime software v. 11.1 (http://www.geneious.com, Biomatters, Auckland, New Zealand). The SARS-CoV-2 lineages and clades were determined using the Pangolin COVID-19 Lineage Assigner v. 4.1.1 (https://pangolin.cog-uk.io/) and Nextclade v. 2.4.1 (https://clades.nextstrain.org).

Statistical Analysis

To summarize the data, categorical variables are presented as counts and percentages, and comparisons between groups were performed using the chi-square test or Fisher's exact test as appropriate. Quantitative variables are reported as mean and standard deviation (SD) if the empirical distribution shows a symmetric and unimodal pattern and as median and interquartile range (IQR) otherwise. Comparisons between groups were made using the t-test for independent samples or the Mann-Whitney test, as appropriate.

Results

Our study included 167 patients, comprising 76/167 (45.5%) females and 91/167 (54.5%) males, with a median age 0.74 (IQR 5.6; range 0.02-17.7). Within our cohort, 93 (55.7%) were children under 2 years of age, 46 (27.5%) were aged between 2 and 10 years, and 28 (16.8%) were older than 10 years.

None of the patients required intensive care, and chronic comorbidities were present in 64/167 (38.3%) cases. Table 1 provides a detailed overview of the demographic characteristics of the enrolled patients.

Data Upon Admission

Among the hospitalized children, 70 (41.9%) had a documented history of contact with a SARS-CoV-2 positive individual. Notably, mothers (44.3%) and fathers (28.6%) were the most common sources of contact for our patients.

Upon hospital admission, 7 patients (4.2%) presented as asymptomatic, with SARS-CoV-2 infection incidentally discovered during routine surveillance nasal swabs conducted for non-COVID-related hospitalizations.

Among symptomatic children, the majority (82.6%) were admitted due to a history of fever, often accompanied by cough in 37.7% of cases, runny nose in 26.3% of cases, wheezing in 3.6% of cases, and fatigue or dyspnea in 22.8% of cases. Additionally, hypoalimentation was reported in 41.9% of patients, while gastrointestinal symptoms, including abdominal pain, vomiting, and diarrhea, were observed in 48.5% of patients. Neurological symptoms, such as seizures and altered consciousness, were noted in 13.2% of cases. Symptoms like muscle aches, joint pain, conjunctivitis, skin rashes, and lymphadenopathy were infrequently reported (see Table 2).

It is worth noting that vomiting, diarrhea, and hypoalimentation appeared to be more prevalent among children under 2 years of age, while neurological symptoms were more common in children aged 2-10 years and adolescents. However, none of these symptoms reached statistical significance (all $p>0.05$).

Table 2 summarizes the signs and symptoms observed upon admission in the enrolled patients, categorized according to different age groups.

Regarding patients for whom it was feasible to determine the SARS-CoV-2 variant via saliva swab (n=51), the Delta variant was identified in 11 children (21.6%). These cases were all hospitalized between November 2021 and December 2021, with the exception of one patient admitted in January 2022. Specifically, all of these subjects carried Delta descendant variants within the 21J clade. In contrast, the Omicron variant was detected in the remaining 40 patients (78.4%), all of whom were hospitalized from January 2022 to June 2023. Among these, 27.5% (n=11) had the BA.1 variant and its sublineages (clade 21K), 15% (n=6) carried BA.2 (clade 21L), and 57.5% (n=23) had the BA.5 variant (clade 22B). Additionally, three cases of XBB recombinants were observed (7.5%) between March and May 2023. No statistically significant difference in median age was noted across the various variants ($p=0.7$).

As shown in Table 3, while neurological symptoms appeared to be more prevalent in cases with the Omicron variant, and gastrointestinal symptoms were seemingly more common in Delta variant cases, it's important to note that none of these symptoms reached statistical significance (all $p>0.05$).

Out of the 167 patients enrolled, 153 (91.6%) had not received the SARS-CoV-2 vaccination prior to their infection. Among them, a significant majority (80.4%) were ineligible for vaccination due to their age. The remaining patients (19.6%) did not get vaccinated for various reasons, including a lack of time (3.6%), the child's refusal (7.3%), concerns about vaccine side effects (3.6%), and a lack of awareness about the vaccine's usefulness despite a prior infection (3.6%).

Monitoring for Long COVID

In Figure 2, we present a flowchart depicting the patients' medical history.

Out of the 115 patients who were followed up for at least 6 months after their discharge (comprising 80/115 patients or 69.6% aged < 2 years, 21/115 or 18.3% aged between 2 and 10 years, and 14/115 or 12.2% aged older than 10 years), 15 patients (13%, including 7 females and 8 males) reported experiencing at least one symptom indicative of Long COVID, with most of them presenting a combination of symptoms. All symptoms were reported at 3 months from discharge and lasted at least two months (symptom duration: median 12 months, IQR 4; range 4-12).

The most commonly reported symptoms included weight loss (3/15, 20%), inappetence (4/15, 26.7%), chronic cough (5/15, 33.3%), fatigue (3/15, 20%), and sleep disturbances (3/15, 20%). Additionally, patients reported symptoms such as abdominal pain, headache, cognitive changes, mood disorders, wheezing, muscle aches, joint pain or swelling, and tachycardia (see Table 4). Table 4 summarizes the Long COVID symptoms according to different age groups.

As depicted in Figure 3, fatigue, chronic cough, as well as cognitive and psychological issues like concentration difficulties, mood disorders, and eating disorders were predominantly observed in adolescents. On the other hand, infants and toddlers exhibited recurrent wheezing, failure to thrive, and sleep disturbances more frequently. It's noteworthy that no statistically significant differences were noted between the various age groups.

Of the 15 patients who reported symptoms indicative of Long COVID, only 4 could be identified with a specific SARS-CoV-2 variant through saliva swabs. Among these cases, 3 were associated with the Omicron variant (2 BA.1 and 1 BA.2), and 1 was linked to the Delta variant.

For 13 out of the 15 patients (86.7%), the Long COVID symptoms necessitated consultation with a medical professional, while 6 out of 15 (40%) required medication, and 3 out of 15 (20%) needed hospitalization. The hospitalizations were prompted by a range of issues, including eating disorders, wheezing, and a combination of weight loss and joint pain.

Among preschool-aged children, the majority (7 out of 9, 77.7%) experienced frequent limitations in their daily activities at home, which placed a substantial burden on their families. For all school-aged children in the study (n=6), they faced limitations in their daily lives, both at home and during school activities. Furthermore, in 4 out of these 6 cases (66.6%), Long COVID symptoms interfered with friendships, leisure activities, and physical activities, resulting in high levels of stress within their families.

Patients aged 6 years and older (n=5) were asked to rate their quality of life during the period in which they experienced Long COVID symptoms on a scale from 0 (the worst) to 10 (the best). The responses ranged from 4/10 to 6/10, with an average rating of 5.4.

Discussion

While the definition of long COVID has been established in the literature, there remains a dearth of data on its epidemiology and clinical presentation, particularly in the pediatric population.[23] This study sheds light on the demographic and clinical characteristics of a cohort of hospitalized pediatric patients with SARS-CoV-2 infection, focusing on the development of symptoms associated with long COVID after discharge. Notably, we observed a long-COVID prevalence of 13% in our population.

Our findings align with previous reports indicating that most children hospitalized for COVID-19 are infants or toddlers. This observation is consistent with multicenter studies highlighting the two most susceptible age groups for hospitalization in 2021 as 0-4 years and 12-17 years.[24] The high rate of hospitalization among younger children may be attributed, at least in part, to the widespread circulation of the highly transmissible Delta variant.[25] It's worth noting that the majority of patients in our cohort had not received the SARS-CoV-2 vaccination before infection, primarily due to age restrictions on vaccination eligibility. The availability of COVID-19 vaccines for children aged 5 years and older in Lombardy, Italy, was only extended until December 27, 2022, and was further expanded to include the age group of 6 months to 4 years. Additionally, the lower hospitalization rate among adolescents may be attributed to the availability of COVID-19 vaccines for individuals over 12 years of age since June 2021 in Lombardy, Italy, underscoring the substantial effectiveness of vaccines in preventing severe COVID-19 in this age group.[25]

At hospital admission, the most frequently reported symptoms in our pediatric cohort were fever, respiratory symptoms, hypoalimentation, gastrointestinal symptoms (including abdominal pain, vomiting, and diarrhea), and neurological symptoms (including seizures and altered consciousness). Importantly, these symptoms did not show significant differences based on age. The majority of patients had documented contact with a SARS-CoV-2 positive individual, most commonly one of their parents, which is consistent with data from other Italian pediatric cohorts.[26] This underscores the high incidence of infections within close contacts and familial clusters.

According to the clinical definition proposed by the WHO, Long COVID, also known as Post-Acute Sequelae of SARS-CoV-2 Infection, is defined as the persistence or onset of symptoms within 3 months of SARS-CoV-2 infection, lasting for at least 2 months without any alternative explanation.[1] The reported prevalence of long COVID symptoms varies widely worldwide.[27] According to a recent systematic review, the prevalence of long-COVID in children and adolescents was 25.24%.[23] Bloise et al reported that the pediatric Italian cohort including both hospitalized children and children whose disease was managed at home, the prevalence of long-lasting symptoms was around 20%.[26]

In our cohort, the prevalence of long COVID was lower (13%) compared to literature data.[23] This discrepancy may be partially due to the age distribution of our population, with a higher prevalence in infants, who may not manifest certain symptoms commonly associated with long COVID, such as mood symptoms and fatigue.[23]

Similar to previous studies on pediatric cohorts, we found no statistically significant difference in the prevalence of long COVID symptoms between males and females. Unlike studies in adults where female gender is cited as a risk factor for long COVID,[28,29] gender-related differences in the prevalence of persistent symptoms in children remain inconclusive.[23,30]

The most prevalent long COVID symptoms in our cohort were chronic cough (33.3%), wheezing (13.3%), fatigue (20%), mood disorders (13.3%), sleep disturbances (20%), abdominal pain (13.3%), weight loss (20%) and inappetence (26.7%).[23]

Mental health issues are also noteworthy in children with prior SARS-CoV-2 infection, with symptoms such as anxiety, depression, sleep disturbances, appetite changes, and impaired social interactions being frequently reported.[31] These conditions may be partly attributed to the broader impact of the pandemic on the lives and relationships of children and adolescents. However, there may be underlying functional pathophysiology contributing to these symptoms, as children with long COVID have been found to exhibit brain hypometabolism patterns similar to those seen in adults with long COVID.[32] In line with existing literature findings,[23] our cohort also exhibited frequent occurrences of fatigue, chronic cough, concentration difficulties, mood disorders, eating disorders, sleep disturbances, and respiratory symptoms, without any significant differences among different age groups.

In adults, it is well-established that long COVID symptoms can have a detrimental impact on individuals' functioning and overall quality of life.[33] To the best of our knowledge, previous studies have not delved into how these symptoms affect the daily activities of children and adolescents. In our study, we included a dedicated segment in our telephone survey to assess patients' limitations in their daily lives and their own evaluations of their quality of life. In accordance with findings from adult cohorts, we observed a notable decline in all aspects of daily life, particularly at home and in school. This had a considerable burden on the families of the patients, and school-aged children reported a diminished self-assessment of their quality of life.

These findings underscore the necessity for rehabilitation interventions in these patients, particularly targeting symptoms such as dyspnea, chronic cough, and fatigue, with the aim of achieving functional improvement, as is recommended for adults.[34]

This study has some limitations. Firstly, in nearly 69.5% of cases, it was not possible to identify VOCs through saliva swabs due to negative results or high cycle threshold (Ct) values, limiting our ability to detect statistically significant differences in long-term and short-term symptoms between patients with SARS-CoV-2 Delta or Omicron variants. The issue of viral load determination is in line with recent data suggesting that viral load in nasopharyngeal swabs is higher than in salivary specimens, especially after symptoms onset and irrespective of food or beverage consumption.[35] Furthermore, there were cases where salivary samples were collected with delays due to logistical reasons, such as stays in the emergency room or at other facilities before admission to the Buzzi hospital. Additionally, since intensive care was not required for any patient in our population, we could not compare the prevalence of long COVID based on the severity of the acute phase of infection. Finally, a control group of hospitalized children not experiencing COVID-19 was not included.

In conclusion, our study underscores that long COVID is a significant concern in the pediatric population across all age groups and does not exhibit a gender-specific prevalence difference. Our data reinforce the importance of continuously monitoring the impact of long-COVID in infants, children, and adolescents. A follow-up following SARS-CoV-2 infection is therefore advisable, with symptom investigation tailored to the patient's age. Further studies are warranted to detail the correlation between VOCs and symptoms related to long COVID.

Acknowledgments: the authors thank Dr Spandan Sai Adivishnu for data analysis support

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Tables

Table 1. Demographic characteristics of enrolled patients.

Features	**Number of patients (%)** n=167
Age	
<2 y	93 (55.7%)
2-10 y	46 (27.5%)
>10 y	28 (16.8%)
Gender	
Female	76 (45.5%)
Male	91 (54.5%)
Ethnic group	
Arab	18 (10.8%)
Asian	10 (6.0%)
Latin American	17 (10.2%)
Caucasian	122 (73.1%)
Other	0 (0.0%)
Comorbidities	
-Diabetes	2 (1.2%)
-Obesity	1 (0.6%)
-Chronic malnutrition	1 (0.6%)
-Cardiac congenital malformations	4 (2.4%)
-Asthma	1 (0.6%)
-Chronic_Kidney_Disease	2 (1.2%)
-Gastrointestinal and/or liver disorders	5 (3%)
-Neurological_and/or neuropsychiatric disorders	16 (9.5%)
-Immunological_disorder	1 (0.6%)
-Malignant_neoplasm	2 (1.2%)
-Genetic_syndrome	4 (2.4%)
-Others	25 (14.9%)

Table 2. Admission signs and symptoms of enrolled patients according to age groups.

Symptom	**<2 years (n= 93)**	**2-10 years (n = 46)**	**>10 years (n=28)**	**Total (n=167)**
General symptoms				
Hystory of fever	80 (86%)	35 (76.1%)	23 (82.1%)	138 (82.6%)
Respiratory symptoms				
Cough	37 (39.8%)	15 (32.6%)	11 (39.3%)	63 (37.7%)
Runny nose (rhinorrhoea)	30 (32.9%)	9 (19.6%)	5 (17.9%)	44 (26.3%)
Ear pain	1 (1.0%)	0 (0%)	0 (0%)	1 (0.6%)
Wheezing	4 (4.3%)	2 (4.3%)	3 (10.7%)	9 (3.6%)
Shortness of breath (dyspnea)	9 (9.7%)	6 (13.0%)	9 (32.1%)	24 (14.4%)
Muscoloskeletal symtpoms				
Muscle aches (myalgia)	0 (0%)	3 (6.5%)	5 (17.8%)	8 (4.9%)
Joint pain (arthralgia)	0 (0%)	3 (6.5%)	2 (7.1%)	5 (3.0%)

Fatigue / malaise	2 (2.1%)	6 (13.0%)	6 (21.4%)	14 (8.4%)
Neurological symptoms				
Headache	0 (0%)	5 (10.9%)	7 (25.0%)	12 (7.1%)
Alteredconsciousness/confusion	2 (2.1%)	6 (13.0%)	2 (7.1%)	10 (5.9%)
Seizures	2 (2.1%)	8 (17.4%)	2 (7.1%)	12 (7.2%)
Gastrointestinal symptoms				
Abdominal pain	2 (2.1%)	8 (17.4%)	7 (25.0%)	17 (10.2%)
Vomiting / nausea	20 (21.5%)	11 (23.9%)	11 (39.3%)	42 (25.1%)
Diarrhoea	15 (16.1%)	2 (4.3%)	5 (17.9%)	22 (13.2%)
Hypoalimentation	44 (47.3%)	16 (34.8%)	10 (35.7%)	70 (41.9%)
Skin mucosal symptoms				
Conjunctivitis	4 (4.3%)	2 (4.3%)	0 (0%)	6 (3.6%)
Skin rash	3 (3.2%)	6 (13.0%)	1 (3.6%)	10 (6.0%)
Lymphadenopathy	0 (0%)	4 (8.7%)	3 (10.7%)	7 (4.2%)

Table 3. Distribution of symptoms between Delta variant, Omicron variant and non-detectable variant (ND)

Symptoms	**Delta (n=11)**	**Omicron (n=40)**	**ND (n=65)**	**Total (n=116)**
General symptoms				
Hystory of fever	10 (90.9%)	36 (90%)	49 (75.4%)	95 (81.9%)
Respiratory symptoms				
Cough	6 (54.5%)	18 (45%)	22 (33.8%)	46 (39.6%)
Runnynose (Rhinorrhoea)	5 (45.4%)	8 (2%)	18 (27.7%)	31 (26.7%)
Earpain	1 (9.0%)	0 (0%)	0 (0%)	1 (0.9%)
Wheezing	2 (18.1%)	1 (0.2%)	4 (6.2%)	7 (6.0%)
Shortness of breath (Dyspnea)	2 (18.1%)	3 (0.7%)	9 (13.8%)	14 (12.1%)
Muscoloskeletal symptoms				
Muscle aches (Myalgia)	0 (0%)	0 (0%)	6 (9.2%)	6 (5.2%)
Joint pain (Arthralgia)	1 (9.0%)	0 (0%)	3 (4.6%)	4 (3.4%)
Fatigue / Malaise	1 (9.0%)	1 (0.2%)	10 (25.4%)	12 (10.3%)
Neurological symptoms				
Headache	1 (9.0%)	3 (0.7%)	5 (7.7%)	9 (7.8%)
Altered consciousness/confusion	0 (0%)	1 (2.5%)	7 (10.8%)	8 (6.9%)
Seizures	0 (0%)	4 (10%)	5 (7.7%)	9 (7.8%)
Gastrointestinal symptoms				
Abdominal pain	1 (9.0%)	1 (2.5%)	8 (12.3%)	10 (8.6%)
Vomiting / Nausea	5 (45.4%)	10 (25%)	18 (27.7%)	33 (28.4%)
Diarrhoea	2 (18.1%)	6 (15%)	10 (15.4%)	18 (15.5%)
Hypoalimentation	6 (54.5%)	15 (37.5%)	33 (50.7%)	54 (46.6%)
Skinmucosal symptoms				
Conjunctivitis	0 (0%)	1 (2.5%)	2 (3.1%)	3 (2.6%)
Skin rash	1 (9.0%)	2 (5%)	5 (7.7%)	8 (6.9%)
Lymphadenopathy	0 (0%)	2 (5.4%)	3 (5.0%)	5 (4.3%)

Table 4. Symptoms of long COVID according to age groups.

Symptom	< 2 years (n=7)	2-10 years (n=3)	>10 years (n=5)	Total (n=15)
Weight loss	0 (0%)	0 (0%)	3 (100%)	3 (20%)
Inappetence	1 (25%)	1 (25%)	2 (50%)	4 (26.7%)
Fatigue	0 (0%)	0 (0%)	3 (100%)	3 (20%)
Sleep disorders	3 (100%)	0 (0%)	0 (0%)	3 (20%)
Chronic cough	2 (40%)	1 (20%)	2 (40%)	5 (33.3%)
Wheezing	2 (100%)	0 (0%)	0 (0%)	2 (13.3%)
Abdominal pain	1 (50%)	1 (50%)	0 (0%)	2 (13.3%)
Mood disorders	0 (0%)	0 (0%)	2 (100%)	2 (13.3%)
Headache	0 (0%)	0 (0%)	1 (100%)	1 (6.7%)
Cognitive alterations	0 (0%)	0 (0%)	1 (100%)	1 (6.7%)
Muscle aches	0 (0%)	0 (0%)	1 (100%)	1 (6.7%)
Joint pain or swelling	0 (0%)	1 (100%)	0 (0%)	1 (6.7%)
Tachycardia	0 (0%)	0 (0%)	1 (100%)	1 (6.7%)

Figures

Figure 1. Flowchart illustrating the monitoring process.

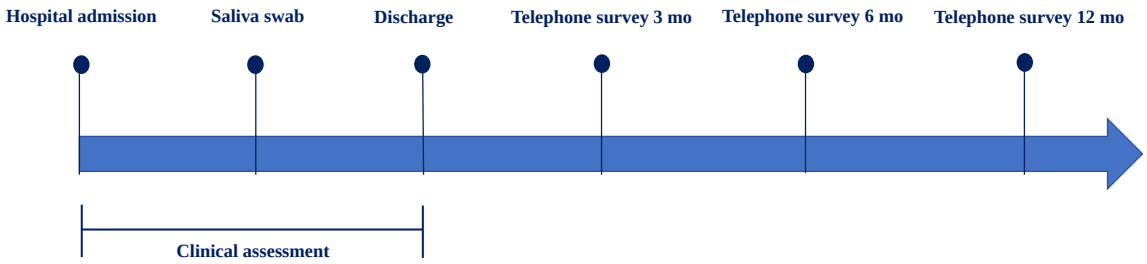

Figure 2. Flowchart illustrating the patients' medical history.

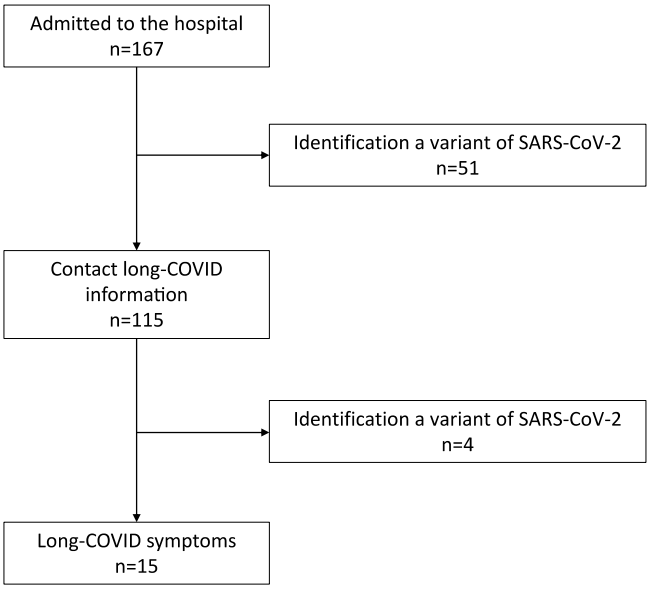

Figure 3. Presentation of Long COVID symptoms across different age groups.