



Original Research

Long COVID-19 Effects (Chronic Covid-19 Syndrome) in Nepalese Cohort Recovered from SARS-CoV-2 Infection

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Keywords:

COVID-19, long COVID-19, post-
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symptoms, long COVID-19 Nepal

Abstract:

Background:

Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological virus for COVID-19 infection. It was first identified in Wuhan, PRC, in December 2019. After this, the highly contagious virus spread globally and is responsible for the ongoing pandemic. Patients infected with COVID-19 present with a wide range of symptoms among which, fever, anosmia, ageusia, cough, headache, fatigue, and dyspnoea are the common ones. Although most of the patients with COVID-19 infection recover completely, a considerable number of infected people have persistent symptoms even after the initial phase of infection. The main objective of this study is to assess the long COVID-19 effects and to associate it with different variables.

Methods:

This single-center retrospective cohort study includes all GWT pensioners, their immediate family members, and all GWT staff who had COVID-19 infection confirmed by RT-PCR from January 2020 to December 2021, and whose signs and symptoms persisted or did not return to normal beyond two weeks from the disease onset. The structured survey questionnaire was used to collect the necessary information on COVID-19 symptoms and their effects on them. The data collected was initially recorded in Microsoft Excel and later analyzed statistically using Statistical Package for Social Science (SPSS).

Result:

Of the 300 COVID-19 patients, 77% (n=231) had long COVID-19 symptoms. The mean age was 66 ± 11.4 years and 50.3% were female. The most common symptoms during acute COVID-19 infection was fever, myalgia, cough, decrease appetite, loss of taste and smell etc. Majority of patient had 2 symptoms (22.7%). The most prevalent long COVID-19 symptoms were fatigue (57%), hair loss, (24%), dyspnea (15.6%), cough (15.3%) and weight loss (13.3%). On systemwise classification of long COVID-19 symptoms, the most commonly affected system were the general system followed by the respiratory system, dermatological symptoms, neuro-psychiatric system, ENT and gastrointestinal system. There was a significant statistical association ($P < 0.05$) between the presence of long COVID-19 symptoms with gender (more likely in female), age group (more likely in the younger age group) and mode of isolation (more likely in hospitalized patients).

Conclusion:

This study confirms the high prevalence of long COVID-19 symptoms in COVID-19-recovered patients.

Introduction:

Over the past three and half years, more than 767 million confirmed COVID-19 cases have been reported around the world. Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological virus for COVID-19 infection. It was first identified in Wuhan, PRC, in December 2019. After this, the highly contagious virus spread globally and is responsible for the ongoing pandemic. Patients infected with COVID-19 present with a wide range of symptoms among which, fever, anosmia, ageusia, cough, headache, fatigue, and dyspnea are the common ones. Many infected individuals remain asymptomatic however, they can still transmit the virus, which probably explains the reason for its rapid worldwide spread. Although most of the patients with COVID-19 infection recover completely, a considerable number of infected people have persistent symptoms even after the initial phase of infection (1). There are many terms used by clinicians around the world for these post-COVID-19 effects such as “long haul COVID-19”, Long term COVID-19 (1), Post COVID-19 syndrome (2). Nevertheless, according to the CDC, patients who have had COVID-19 infection but do not recover completely over the period of 4 weeks are said to belong to the late sequelae of COVID-19 (2). Whereas NICE guidelines recommend the use of the term post-COVID-19 for only those individuals who have had positive symptoms beyond 12 weeks of infection (3). However, some studies emphasize that persisting symptoms beyond 2 weeks of COVID-19 infection are called long-term COVID-19 effects (4,5). Several studies have reported the presence of persistent symptoms following acute infection with COVID-19. According to the literature, one in seven COVID-19 patients remain still symptomatic at 12 weeks (6). Post-COVID-19 symptoms present with a variety of clinical manifestations, some of the most common are fatigue, headache, attention disorder, hair loss, etc (4). Some of these symptoms are severe enough to harm the patient's ability to work and perform daily tasks. This study aims to report results from a survey of Gurkha veterans, their immediate family members, and Gurkha Welfare

Trust staff, investigating the multi-system symptoms of post-COVID-19 effects in them with illness onset from January 2020 to December 2021.

Material and Methods:

This single-center retrospective cohort study includes all GWT pensioners, their immediate family members, and all GWT staff who had COVID-19 infection and whose signs and symptoms persisted or did not return to normal beyond two weeks from the disease onset. A list of 500 Patients was extracted on the basis of estimated COVID-19-positive reported cases as per our electronic medical record. We excluded the following patients:

- Age > 90 years.
- Unreliable clinical History.
- Those who were deceased.
- Those who refused to participate.
- Those who were unable to be contacted.

The remaining patients were contacted by telephone and in a clinic by trained doctors and were asked to answer the structured survey questionnaire that was used to collect the necessary information on COVID-19 symptoms and their effects on them. The questionnaire consisted of general patient information, comorbidities, vaccination status during COVID-19 infection, chief complaint instigating COVID-19 test, the severity of COVID-19 based on the requirement of hospital admission, O₂ requirement, ICU admission and requirement of a mechanical ventilator, presence or absence and duration of persisting symptoms and system-wise review of prolonged/persisting symptoms if any, which includes general, respiratory and cardiovascular, neuro-psychiatric, ENT, gastrointestinal, dermatological and any other specific problems.

Collected data were initially recorded in Microsoft Excel and later analyzed statistically using Statistical Package for Social Science (SPSS). Descriptive analysis was done using frequency. Mean and standard deviation were used for continuous variables whereas categorical variables were analyzed using percentages. The chi-square

test was used to associate different variables. A P-value less than 0.05 was considered statistically significant. This study has been ethically approved

by Nepal Health Research Council (Regd. 50-2022).

Table 1. Baseline characteristics of post-COVID-19 patients

Baseline Characteristics		Frequency n (%)
Gender	Male	151 (50.3%)
	Female	149 (49.7%)
Age Group	Age <60 years	85(28.3%%)
	Age >60 year	215 (71.7%)
Comorbidity	Hypertension	213 (71%)
	Diabetes Mellitus	105 (35%)
	COPD	22 (7.3%)
	Thyroid Disorder	38 (12.6%)
	Cardiovascular Disease	18 (6%)
	Chronic Kidney Disease	7 (2.3%)
	Malignancy	4 (1.3%)
	Rheumatoid Arthritis	1 (0.3%)
	None	61 (20.3%)
Vaccination Status	Pre-Vaccination	188 (62.5%)
	Single Dose	63 (21%)
	Double Dose	48 (16%)
	Booster Dose	1 (0.3%)
Diagnostic Test	PCR	300 (100%)

Abbreviations: HTN-Hypertension, DM- Diabetes Mellitus, COPD-Chronic Obstructive Pulmonary Disorder, CKD-Chronic Kidney Disease, CAD-Coronary Artery Disease, RA- Rheumatoid Arthritis

Table 2. Symptoms during COVID-19 illness

Symptoms	Frequency n (%)
Fever	197 (65.6%)
Myalgia	171 (57%)
Cough	142 (49%)
Decrease appetite	135 (45%)
Loss of taste	103 (34.3%)
Loss of smell	93 (31%)
Diarrhoea	25 (8.3%)
Sore throat	19 (6.3%)
Rhinorrhoea	19 (6.3%)
Fatigue	15 (5%)
Routine test	10 (3.3%)
Asymptomatic/ Contact tracing	8 (2.7%)
Headache	3 (1%)
Abdominal pain	2 (0.6%)

Table 3. Number of Long COVID-19 Symptoms

Number of Long COVID-19 symptoms	Frequency n (%)
No Symptoms	69 (23%)
1 Symptoms	65 (21.7%)
2 Symptoms	68 (22.7%)
3 Symptoms	47 (15.7%)
4 Symptoms	27 (9%)
5 Symptoms	15 (5%)
≥ 5 Symptoms	9 (3%)

Table 4. Persistent long COVID-19 symptoms

System-wise Long COVID-19 Symptoms		Frequency n (%)
General Symptoms	Fatigue	171 (57%)
	Weight loss	40 (13.3%)
	Myalgia	10 (3.3%)
	Fever	0
	None	119 (39.6%)
Respiratory/CVS	Dyspnoea	47 (15.6%)
	Cough	46 (15.3%)
	Palpitation	12 (4%)
	Chest tightness	8 (2.6%)
	Chest pain	3 (1%)
	None	202 (67.3%)
Neuro-Psychiatric	Anxiety	23 (7.6%)
	Insomnia	21 (7%)
	Hypersomnia	11 (3.66)
	Dizziness	13 (4.33%)
	Cognitive symptoms	15 (5%)
	Headache	7 (2.33%)
	Depression	2 (0.66%)
	Syncope	0
	None	224 (74.66%)
Gastrointestinal	Loss of appetite	22 (7.3%)
	Diarrhoea	8 (2.6%)
	Constipation	6 (2%)
	Abdominal Pain	1 (0.3%)
	None	266 (88.6%)
	Loss of smell	31 (10.3%)

ENT	Loss of taste	28 (9.3%)
	Rhinorrhoea	3 (1%)
	Sorethroat	1 (0.3%)
	None	253 (84.3%)
Dermatological	Hair loss	72 (24%)
	Cutaneous sign	10 (3.3%)
	Rash	1 (0.3%)
	None	219 (73%)

Table 5. Association of the presence of long COVID-19 symptoms with baseline characteristics

		Long COVID-19 symptoms		P value
		Yes.	No	
Gender	Female	123 (83%)	26 (17%)	0.016*
	Male	108 (72%)	43 (28%)	
Age Group	Age <60 year	73 (86%)	12 (14%)	0.022 *
	Age >60 Year	158 (73%)	57 (27%)	
Vaccination Status	Not vaccinated	143 (76%)	45 (24%)	0.387
	Vaccinated	88 (79%)	24 (21%)	
Comorbidity	Present	180 (75%)	59 (25%)	0.113
	Absent	51 (84%)	10(16%)	
Mode of Isolation	Home	140 (70%)	60 (30%)	0.000*
	Hospital	91 (91%)	9 (9%)	

* $P < 0.05$ = Significant

Result:

During the initial data extraction from the electronic record, a total of 500 patients were evaluated for having COVID-19 infection, of them we could confirm the diagnosis among 424 patients. 94 (22%) patients were deceased. 14 patients were >90 years of age. 16 patients were unreachable. Finally, 300 patients were included in the study cohort.

Of the total 300 patients included in our study, 151 (50.3%) were male and 149 (49.7%) were female. The mean age was 66 ± 11.4 years. Pre-existing comorbidities were present in 239 (79.7%) of the patients, of which HTN 213 (71%), DM 105 (35%), and thyroid disorders 38 (12.6%) were the 3 most

common comorbidities followed by COPD 22 (7.3%), CAD 18 (6%), CKD 7 (2.3%), malignancy 4 (1.3%), and RA 1 (0.3%). 62.5% of the patient had COVID-19 infection pre-vaccination. The diagnostic test done to confirm the disease was PCR (100%) (Table 1). The most common symptoms during COVID-19 infection were fever 197 (65.6%), Myalgia 171 (57%), cough 142 (49%), decreased appetite 135 (45%), loss of taste and smell (103 (34.3%) and 93 (31%)) respectively. 8 (2.7%) were asymptomatic and 10 (3.3%) were COVID-19 positive on routine tests (Table 2). 100 (33.3%) patients required hospital

admission. The mean duration of isolation was 2 weeks (199 (66.3%).

Out of 300 patients, 231 (77%) patients had long COVID-19 symptoms. 65 (21.7%) had 1 symptom, 68 (22.7%) had 2 symptoms, 47 (15.7%) had 3 symptoms, 27 (9%) had 4 symptoms and 15 (5%) had 5 symptoms. 9 (3%) patients had ≥ 5 symptoms (Table 3). On system-wise classification, the most common overall long COVID-19 symptoms are general symptoms 181 (60.4%), respiratory symptoms 98 (32.7%), dermatological symptoms 81 (27%), Neuro-psychiatric 76 (25.3%), ENT symptoms 47 (15.7%) and gastrointestinal symptoms 34 (11.4%) respectively. The most common presenting symptoms were the general symptoms of which fatigue 171(57%) was the commonest presenting general and overall symptom. 98 (32.7%) patients had respiratory symptoms. Dyspnoea and cough (47 (15.6%) and 46 (15.3%)) were the common respiratory symptoms. Anxiety 23 (7.6%), insomnia 21 (7%), and cognitive symptoms 15 (5%) were 3 common neurological symptoms. Of gastrointestinal symptoms, loss of appetite and diarrhoea (22 (7.3%) and 8 (2.6%)) were seen in many patients. Loss of smell and loss of taste (31 (10.3%) and 28 (9.3%)) were common complaints related to ENT. 72 (24%) patients had hair loss which is the most common dermatological complaint and the second most overall long COVID-19 complaint (Table 4). Symptoms wise most common presenting complaints were fatigue, hair loss, dyspnoea, cough, weight loss, and loss of smell and taste. The average duration of general symptoms was 1 month, respiratory/ CVS symptoms were 1 month, neuropsychiatric complaints were 3 months, gastrointestinal symptoms were 1 month, ENT was 1~2 weeks, and dermatological symptoms were 3 months.

There was a significant statistical association ($P<0.05$) between the presence of long COVID-19 symptoms with gender (more likely in females), age group (more likely in the younger age group), and mode of isolation (more likely in hospitalized patients). Out of 188 non-vaccinated patients, 143 had long COVID-19 symptoms, however, there

was no statistically significant association with vaccination status. Likewise, the patients with pre-existing comorbid conditions had more long COVID-19 symptoms than those without comorbidity, but the analysis was not statistically significant (Table 5).

Discussion:

This study population consisted of mostly older age group patients of which 79.5% had pre-existing comorbidities who have been using the medical service before, during, and after the infection. There were almost an equal number of males and females with a slightly higher long COVID-19 prevalence in the female population (83%) in comparison to the male (72%). Alike other studies (7), in our study, the most common symptoms during COVID-19 infections were fever (65.6%), myalgia (57%), cough (49%), decreased appetite (45%), loss of taste and smell (34.3% and 31%). Like other viral illnesses, fever, cough, and myalgia were the 3 most common complaints. The number of long COVID-19 symptoms varied from single to ≥ 5 symptoms. The majority of which had 2 symptoms, 1 symptom, and 3 symptoms (22.7%, 21.7%, and 15.7% respectively). Similar to other various studies, fatigue, dyspnoea, and cough were the most common long COVID-19 complaints (8). However, hair loss, cognitive symptoms, and loss of taste and smell were also commonly reported.

According to Hannah E. David et al, long COVID-19 symptoms occur in 10% of COVID-19-positive patient and more than 200 symptoms have been identified with impacts on multiple organ systems (9). A systematic review and meta-analysis regarding the prevalence of long covid in hospitalized and non-hospitalized populations done by O'Mahoney LL et al, showed 45% of long covid prevalence in COVID-19 Survivor populations (24). However, in our study, 77% of the patient had long COVID-19 symptoms. Besides the acute symptoms after infection, patients and society are also being challenged by the long-term health complications associated with COVID-19, commonly known as long COVID-19 (10). In our study, fatigue was present in 57% of patients as a

general symptom. Similarly, Ceban F et al, reported that fatigue and cognitive impairment are amongst the most common and debilitating symptoms of post-COVID-19 syndrome (11). Sykes DL et al, reported that females were significantly more likely to have residual COVID-19 symptoms including anxiety, fatigue, and myalgia (12) similarly in our study, females were seen having more long COVID-19 symptoms than males. Dyspnoea (15.6%) and cough (15.3%) were the most commonly presented symptoms in our study which is similar to most of the published studies. Anxiety and insomnia are the most commonly reported symptoms in the neuropsychiatric group in our study, which is consistent with a study published by Efsthathiou V et al, where the author discussed depression, anxiety, post-traumatic stress disorder, and sleep disturbance including fatigue as the most commonly reported symptoms (13). 15.7% of patients presented with GI manifestations where the loss of appetite and diarrhea as the most common symptoms. Choudhury A et al, reported that 12% of the patient complained about GI problems where constipation was the most common symptom (14). Loss of smell and loss of taste were the most common ENT problem in our study observed in 10.3% and 9.3% respectively, this result was similar to the study done by Riestra-Ayora et al. which states that olfactory and gustatory dysfunction as one of the most persistent ENT symptoms in COVID-19 patient (21). Hair loss was the second most common problem in our study which was about 24%. Seyfi S et al, reported that hair loss occurs 2–3 months after the stressful condition and is occasionally self-limiting (15).

In our study, there was a statistically significant association between gender, age group and mode of isolation with the presence of long COVID-19 symptoms (Table 5). Regarding gender and age group, the aforementioned findings confirm that mostly, female patients had a higher chance of getting long COVID-19 symptoms (20). In our study, patients aged 60 years and below presented with more long COVID-19 symptoms (86%) compared to patients aged above 60 years (73%) which probably explains that long COVID-19-

related symptoms decline as the age increases, our result is consistent with the study done by-Unim B, Palmieri et al, (22). In addition, the mode of isolation during the acute phase of COVID-19 infection was found to be significantly associated with an increase long COVID-19 symptoms in hospital admitted patients (91%) than in home-isolated patients (70%). This finding is consistent with other studies showing that patients needing hospital admission are at increased risk of developing long COVID-19 symptoms (20). It's believed that patients with long COVID-19 illness may have prolonged multisystem effects requiring support and follow-up. In our study, 77% of the patient had one or more symptoms with the maximum number of patient's symptoms being manageable. One of the noticeable findings in our study was the insignificant association between vaccination status and comorbidity with the presence of long COVID-19 symptoms. It's believed that vaccines against COVID-19 infection prevent long COVID-19 symptoms in patients. Our study shows a higher number of long COVID-19 symptoms among the vaccinated group (79%) than in the non-vaccinated group (76%) although it may be due to the difference in numbers however, it was not statistically significant. There are few recent studies that show the benefit of effective vaccination on long COVID-19 symptoms (16, 19, 23). Whereas other studies (17) have a low level of association between the impact of vaccination with long COVID-19 (17, 18). The controversial association between vaccination and long COVID-19 symptoms could be due to the number of vaccination doses, and vaccination pre/post-COVID-19 infection. However, many studies have clarified that the COVID-19 vaccine is beneficial for patients and might prevent chronic COVID-19 syndrome to some extent. Additionally, the result of our study was not statistically associated with preexisting comorbid conditions and long COVID-19 symptoms. However, there was an increased number of patients with preexisting comorbidity who had long COVID-19 symptoms. In contrast, studies (19, 20) showed a strong association between long COVID-19 and preexisting comorbidities.

Limitations:

The study has various limitations. It is a single-center study with a relatively small sample size conducted with telephone interviews with many patients. The inclusion of COVID-19 patients during the first and second waves only. Possibility of undetected pre-COVID-19 abnormalities in our study populations. Miscommunication and misinformation between the interviewer and interviewee could be potential biases. The findings are also limited by memory bias, time lag, and patients reporting ability.

Conclusion:

This study confirms the high prevalence of long COVID-19 symptoms in COVID-19-recovered patients. Hence, it's important for all patients presenting with prolonged symptoms post-COVID-19 infection should be ruled out initially for other causes unless proven otherwise, or else could be coined as Long COVID-19. It is important to perform a comprehensive assessment for early detection and proper management.

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Conflict of interest

No potential conflict of interest was disclosed by authors.

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