

CLINICAL SYMPTOMS CHANGES IN POST-COVID-19 MILD AND MODERATE PATIENTS AT NATIONAL HOSPITAL FOR TROPICAL DISEASE

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Patients recovering from SARS-CoV-2 infection may still have persistent symptoms. There is a need for studies on many different groups to have an overview of the clinical manifestations after recovery.

Objectives: Describe the clinical symptoms persist in patients and compare the difference in those symptoms at 3 and 6 months after recovery in patients with mild and moderate COVID-19 infection at Department of Internal Medicine, National Hospital for Tropical Diseases from October 2021 to October 2022.

Methods: Descriptive prospective study on 166 patients with SARS-CoV-2 RT-PCR positive, with mild and moderate severity, and met the criteria to be cured for discharge according to the Vietnam Ministry of Health's COVID-19 Diagnosis and Treatment Guidelines.

Results: Common clinical manifestations at 3 month post infection were: cough (50%), fatigue (31.9%), sore throat (29.7%); 6 months post infection were: hair loss (9%), cough (6.6%), muscle and joint pain (1.8%). The number and severity of clinical manifestations in the 6-month post-discharge period were fewer and milder than in the 3-month post-discharge.

Conclusion: The number and severity of clinical manifestations increase in 3-month post-discharge but significantly decrease in 6-month post-discharge.

Keywords: *Clinical symptoms, persistent symptoms, post COVID-19 infection, mild and moderate COVID-19 patients.*

INTRODUCTION

COVID-19 causes many long-term symptoms in many body systems. Some studies show that a significant portion of patients, possibly up to 87.5%, who recover from acute SARS-CoV-2 infection still have persistent symptoms such as difficulty breathing, cough, and pain. muscles, fatigue and headaches^{1,2}. The concept of prolonged symptoms after recovery from COVID-19 and the duration of those symptoms are still different between studies and treatment units for COVID-19 patients. Reports also show that even the group infected with SARS-CoV-2 with no symptoms or mild symptoms still

has persistent manifestations after recovery³. This shows the serious disease burden that COVID-19 causes. However, the COVID-19 epidemic has just appeared and many related issues are not yet fully understood, especially the condition of patients after recovery and discharge from the hospital. This creates an urgent need for diverse studies, conducted on many different groups of subjects, in many different locations to have a more general overview of the manifestations of patients after recovery.

Objectives: Describe the clinical symptoms that persist in the patient at 3 and 6 months after recovery; and compare the difference in clinical symptoms at 3 and 6 months after recovery in mild and moderate COVID-19 patients treated at the Department of Internal Medicine, National Hospital of Tropical Diseases from October 2021 to October 2022.

SUBJECTS AND METHOD

Subjects: Patients with SARS-CoV-2 by RT-PCR positive, had mild and moderate disease severity, and

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was cured to be discharged according to the Guidelines for Diagnosis and Treatment of COVID-19 of Vietnam Ministry of Health of issued with Decision No. 4689/QĐ-BYT dated October 6, 2021.

Methods: Descriptive prospective study.

Sample size and sampling method: entire sample size selection, all patients who met the criteria and agreed to participate in the study were enrolled.

Data collection: Use a pre-designed questionnaires suitable to the research objectives, collect information on demographic characteristics, underlying diseases, clinical symptoms to determine the classification of disease severity during the patient's hospital stay

from the medical record. Information about clinical symptoms after 3 months and 6 months after recovery will be interviewed patient directly via phone according to a pre-designed questionnaires. The researcher is the person who directly calls the patient to interview. Limit errors by applying the same set of assessment tools, with the same researcher evaluating the same patient at two assessment times: 3 months and 6 months after recovery.

Ethical: Descriptive study, without performing any intervention on the patient, was approved by the Scientific Council of the National Hospital for Tropical Diseases.

RESULTS

Number of persistence clinical symptoms over time

Table 1. Number of persistence clinical symptoms over time

Number of persistence clinical symptom	On discharge (n = 166)		After 3 months (n = 166)		After 6 months (n = 166)	
	n	%	n	%	n	%
0	97	58.4	21	12.7	107	64.5
1	64	38.6	38	22.9	50	30.1
2	3	1.8	37	22.3	9	5.4
3	2	1.2	27	16.3	0	0
4	0	0	16	9.6	0	0
≥ 5	0	0	27	16.3	0	0

Comments: At discharge, all patients had a maximum of 3 clinical symptoms. However, 3 months after discharge, up to 38.9% of patients had at least 3 or more symptoms. After discharge 6 months, all patients only had a maximum of 2 symptoms.

The persistence clinical symptoms

Table 2. The persistence clinical symptoms

Clinical symptom	On discharge (n = 166)		After 3 months (n = 166)		After 6 months (n = 166)	
	n	%	n	%	n	%
Sore throat	3	1.8	49	29.5	2	1.2
Chest pain	0	0	19	11.4	1	0.6
Dyspnea	3	1.8	17	10.2	2	1.2
Palpitations	0	0	5	3.0	2	1.2
Headache	0	0	29	17.5	0	0

Clinical symptom	On discharge (n = 166)		After 3 months (n = 166)		After 6 months (n = 166)	
	n	%	n	%	n	%
Tired	0	0	53	31.9	2	1.2
Fever	0	0	17	10.2	0	0
Loss of taste and smell	3	1.8	11	6.6	0	0
Nausea, vomiting	0	0	2	1.2	0	0
Diarrhea	0	0	9	5.4	0	0
Muscle pain, joint pain	1	0.6	23	13.9	3	1.8
Hair loss	0	0	31	18.7	15	9
Rash	0	0	2	1.2	0	0
Tinnitus	0	0	0	0	0	0
Shortness of breath	0	0	45	27.1	0	0
Reduced memory ability	0	0	17	10.2	11	6.6
Cough	64	38.6	83	50	0	0
Discolored patches on hands and feet	0	0	3	1.8	0	0
Others	2	1.2	62	37.3	30	18.1

Comments: At discharge, only 5 clinical symptoms remained, of which cough was the most common ones (38.6%). 3 months after discharge, there were over 20 clinical symptoms appearing in patients, of which the most common was cough (50%), followed by fatigue (31.9%), burning pain, sore throat (29.5%) and shortness of breath (27.1%). 6 months after discharge, the number of patients with residual clinical symptoms was very low.

Differences in clinical symptoms persist over time

Table 3. Differences in clinical symptoms persist over time

Clinical symptom	On discharge (1) %	After 3 months (2) %	After 6 months (3) %	p (1.2)	p (1.3)	p (2.3)
Sore throat	1.8	29.5	1.2	< 0.01	0.66	< 0.01
Chest pain	0	11.5	1.2	0.02	0.16	0.25
Dyspnea	1.8	10.2	1.2	< 0.01	0.66	< 0.01
Palpitations	0	3.0	0.6	< 0.01	0.32	< 0.01
Headache	0	17.5	0	< 0.01		< 0.01
Tired	0	31.9	1.2	< 0.01	0.15	< 0.01
Fever	0	10.2	0	< 0.01		< 0.01
Loss of taste and smell	1.8	6.6	0	0.03	0.08	< 0.01



Clinical symptom	On discharge (1) %	After 3 months (2) %	After 6 months (3) %	p (1.2)	p (1.3)	p (2.3)
Nausea, vomiting	0	1.2	0			0.16
Diarrhea	0	5.4	0	< 0.01		< 0.01
Muscle pain, joint pain	0.6	13.9	1.8	< 0.01	0.32	< 0.01
Hair loss	0	18.7	9.0			< 0.01
Rash	0	1.2	0			0.16
Tinnitus	0	0	0			
Dizziness	0	0	0			
Hearing loss	0	0	0			
Blurred vision	0	0	0			
Difficulty concentrating	0	0	0			
Reduced memory ability	0	0	0			
Cough	38.6	50.0	6.6	0.03	< 0.01	< 0.01
Insomnia	0	0	0			
Discolored patches on hands and feet	0	1.8	0			0.08
Others	1.2	37.4	18.0	< 0.01	< 0.01	< 0.01

Comments: Most of patients' remaining clinical symptoms at discharge, 3 and 6 months after discharge were statistically significant different with $p < 0.05$.

Change in severity of clinical symptoms

Table 4. Change in severity of clinical symptoms

Clinical symptom	After 3 months (n = 166)		After 6 months (n = 166)	
	n	%	n	%
The severity of symptoms varies	90	54.2	144	86.7
The severity of symptoms increase over time	4	0.02	12	0.07
The severity of symptoms decrease over time	86	51.8	133	80.1
Symptoms worsen with exertion	88	53.0	111	66.9
Symptoms subside with rest	88	53.0	117	70.0

Comments: The severity of remaining symptoms changes over time, most of which decrease over time, especially clearly decrease after 6 months.

General health status of post COVID-19 patients

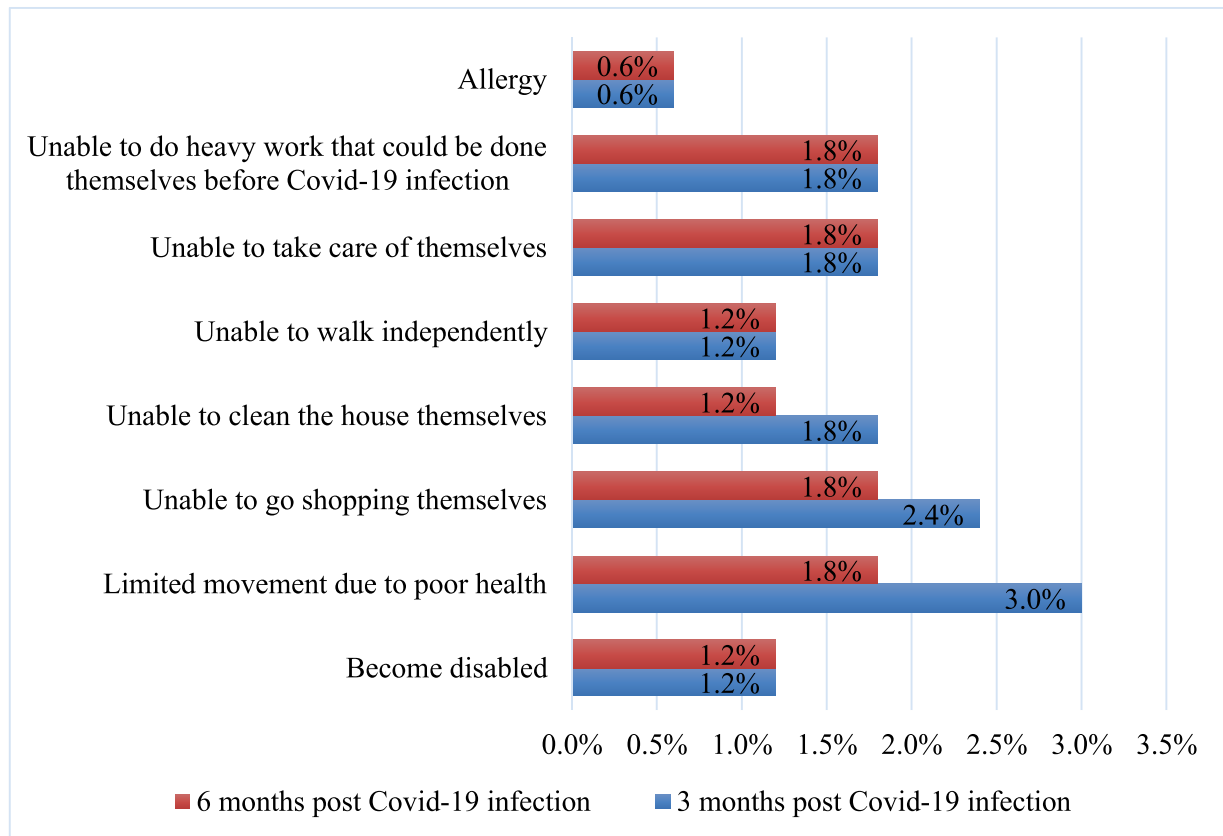


Figure 1. General health status of post COVID-19 patients

Comments: The number of patients with a clear decline in health post COVID-19 infection is very low (all < 3%), in which, decline in health in 3 months after discharge accounts for a higher rate than in the 6 month after discharge (limited movement due to poor health has a rate of 3% and 1,8%, respectively).

DISCUSSIONS

At discharge, all patients only had a maximum of 3 clinical symptoms. However, 3 months after discharge, up to 38.9% of patients had at least 3 or more symptoms. At 6 months after discharge, all patients only had a maximum of 2 symptoms. Most of the differences in remaining clinical symptoms in patients at the time of discharge, 3 months after discharge and 6 months after discharge were statistically significant with $p < 0.05$. For remaining symptoms, the severity of symptoms changes over time, most of which will decrease over time, especially clearly decrease after discharge 6 months. The number of patients with a clear decline in health after COVID-19 infection is very low (all below 3%). Symptoms of health deterioration in the 3 months after discharge account for a higher

proportion compare to 6 months after discharge (limited movement due to poor health has a rate of 3% and 1.8%, respectively). In general, the changes of symptoms over time highlights three distinct patterns that provide a better understanding of the causes and mechanisms of COVID-19 infection. First, some studies show that the incidence of symptoms such as loss of taste or smell, cough, or diarrhea decreases over time. Sivan's study showed that cough rates decreased from 50% to 20% of participants within the first 6 months after symptom onset before reaching a plateau. The same was true for anosmia, with stabilization achieved after 8 months⁴. This development shows that recovery from the acute phase is slower than expected. Currently, most guidelines still consider a 12-week limit to distinguish ongoing symptomatic



COVID-19 (i.e., signs and symptoms of COVID-19 for 4 to 12 weeks) from postpartum syndrome. COVID-19. As for other symptoms, some studies have shown that their prevalence increases over time. For example, the incidence of hair loss increased over time with 8% and 15% of participants reporting it after 2 months and 1 year, respectively. Late onset of symptoms, especially alopecia, has been reported in other studies and requires further investigation⁵. Finally, symptoms that show no change in prevalence over time may be caused by mechanisms that do not change rapidly over time, such as ataxia or post-traumatic stress disorder, or due to a combination of recovery from acute illness and late-onset symptoms that appear as a result of COVID-19 infection³.

CONCLUSIONS

The number and severity of clinical manifestations in the 6-month post-discharge period were fewer and milder than in the 3-month post-discharge. The difference is statistically significant.

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