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Post COVID-19 persistent symptoms and functional status in COVID-19 survivors: a multi-center study

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Abstract

Background Post COVID symptoms are a series of chronic symptoms that patients may experience after resolution of acute COVID-19. Different post-COVID-19 condition phenotypes might exist, although exact causes, management, and outcomes are not known.

Aim To assess the functional status among post-COVID-19 survivors and identify the associated socio-demographic, clinical, and laboratory risk factors of the poor functional status among those cases and to identify the most common persistent symptoms among post-COVID-19 survivors after discharge. This was a cross-sectional study conducted on 150 recovered cases who had been infected with COVID-19 as confirmed by swab during hospitalization and being interviewed regarding functional status 6 months post-hospital discharge. Cases were divided into two groups: the decreased functional status group ($n = 74$) and the non-decreased functional status group ($n = 76$).

Results The present study indicated statistically significant differences between the studied groups; receiving the influenza vaccine was significantly associated with keeping the pre-COVID functional status ($p = 0.02$). The reduced functional status group had a significantly more severe disease course, prolonged hospital as well as ICU stay ($p < 0.001$), and worse CT findings than the normal functional status group ($p = 0.004$). Long-term symptoms such as headache, mood changes, insomnia, hearing problems, dry eyes, breathlessness, and chest tightness were significantly more prevalent among those who reported limitations in their functional status ($p < 0.001$). There were significantly higher CRP, serum ferritin, and D-dimer in the reduced functional status group.

Conclusion The present study highlights that most COVID-19 recovered cases have different degrees of functional limitations ranging from null to severe based on the PCFS scale. These limitations were affected by periodic influenza vaccination, ICU admission, and length of hospital stay. Some laboratory parameters were associated with reduced functionality: CRP, D-dimer, and serum ferritin. Psychological/neurological symptoms and breathlessness were significantly associated with reduced PCFS. This calls for public health action and necessitates widespread health education of post-COVID-19 health consequences.

Keywords Long-term symptoms, Functional limitations, Post-COVID recovered cases

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Introduction

COVID-19 is a new infectious disease caused by the new strain of severe acute respiratory syndrome coronavirus, SARS-CoV-2 [1]. The first outbreak reported was in December 2019, in Wuhan, China, as pneumonia of

unknown etiology linked to a seafood market exposure [2].

The most common symptoms reported are fever, cough or chest tightness, and dyspnea. Most cases are reported to experience a mild illness course [3].

It is expected that COVID-19 may have a critical long-term effect on the physical, mental, cognitive, and psychological health status of the recovered cases [4].

It is not practical to follow-up all recovered cases from COVID-19 due to the large number of post-COVID-19 survivors who will require strict follow-up and monitoring, as it will place an additional burden on the healthcare systems. We are also unable to predict which patients will experience long-term persistent symptoms after their recovery or foresee which long-term symptoms will require follow-up and further investigations to lessen their effects on the life of recovered cases [5].

Despite the well-established usefulness of socio-demographic characteristics in predicting death from COVID-19, there is controversy on the relationship between the underlying socio-demographics and the functional status limitation in these patients. Despite the established significance of these characteristics in predicting death from COVID-19, Leigh et al. discovered that underlying demographics, with the exception of age and underlying medical disorders, were not associated with functional status dependency in the patients in their study. Therefore, additional research is required to either confirm or rule out these relationships [6].

The most frequently reported PCS symptoms are anxiety, depression, abnormal breathing, abdominal symptoms, chest/throat pain, fatigue, headache, cognitive problems, and myalgia [7].

It is crucial to evaluate and keep track of some of these patients who recover from acute COVID-19 to ascertain the prevalence of various symptoms, such as functional limitations, and to emphasize the effects these symptoms have on all aspects of health. Determining individuals who may be more likely to have long-term symptoms and functional limitations that may require additional follow-up and research is also of the utmost importance. Studies should assess the significant importance of post-hospital discharge follow-up clinics, define the patients' sequelae, and decide which measures in the ICU, the hospital following post-ICU discharge, and subsequently in the community may reduce or treat these effects [4, 8, 9].

We aimed to assess the functional status among post COVID-19 survivors and identify the associated socio-demographic, clinical, and laboratory risk factors of the poor functional status among those cases and to identify the most common persistent symptoms among post-COVID-19 survivors after discharge.

Participants and methods

Study population and sample

A cross-sectional study was conducted. Data collection took place during the period from June 2022 to September 2022. The study population included the previously laboratory-confirmed hospitalized patients who were alive at 1–4 months post-discharge. The sample size was calculated using Open epi, an open-source software for epidemiologic statistics, assuming on the basis of a previous study and 95% confidence limits. The minimum calculated sample size to achieve study objectives was 150. Included patients were diagnosed with SARS-CoV-2 infection by polymerase chain reaction (PCR) test of a nasopharyngeal swap sample during inpatient hospital admission, 4 weeks up to 4 months since the discharge from the hospital, not currently a hospital inpatient aged 18 years or older who agreed to participate in the study.

Study setting

The post-COVID-19 survivors were interviewed in the follow-up clinics in 3 public hospitals or by telephone calls and filled out an Arabic-translated pre-designed interview questionnaire [3].

Case definitions

PCR confirmed the diagnosis of all suspected cases.

Mild cases are those who had oxygen saturation of more than 92% with no need for oxygen supplement or low flow nasal cannula.

Moderate cases had oxygen saturation of less than 92% and required oxygen supplement using face masks or using a non-reservoir oxygen mask.

Severe cases are those who meet any of the following criteria: who had oxygen saturation less than 92% with PaO_2/FIO_2 ratio less than 300, with respiratory rate more than 30 with more than 50% lung infiltration, who required oxygen supply using high flow nasal cannula, noninvasive mechanical ventilation (continuous positive airway pressure).

Critical cases are those who meet any of the following: have respiratory failure, septic shock, or multi-organ dysfunction (MODS) or need invasive mechanical ventilation [10].

Study tool

A validated Arabic questionnaire derived from literature was filled through contacting study participants during their visits to the follow-up clinics or through their telephone numbers to assess the persisting COVID-19 symptoms and assess functional status among these cases. It took an average of 25 min to complete, and it included the following sections.

The pre-COVID-19 grade 1 month prior to the infection was assessed to measure the change in functional status. The assessment of the pre-COVID-19 functional status was preceded by the first assessment of the current functional status as recommended [11].

a. First section on personal and socio-demographic section which consisted questions about age, sex, residence, occupation, smoking status, seasonal influenza vaccination, and the presence of coexisting comorbidity status
b. Second section on persistent COVID-19 symptoms to assess the duration and severity of persistent symptoms among individuals which consisted of 6 sections as follows: (I) General symptoms (fatigue and weakness); (II) Skin and musculoskeletal symptoms (muscle aches [s], joint pain, and skin rash); (III) Psychological and neurological symptoms (headache, mood changes, insomnia, esthesia, and anesthesia); (IV) Special sense symptoms (hearing problems, visual disturbances, dry eyes, loss of smell, and loss of taste); (V) Respiratory system symptoms (cough, shortness of breath, and chest tightness); and (VI) Gastrointestinal symptoms (loss of appetite, nausea, diarrhea, and abdominal pain). For each symptom, the participants were asked to score the severity on a three-point scale (mild, moderate, and severe, scored as 1, 2, and 3, respectively). This section was adapted from a study conducted in Saudi Arabia to assess the post-recovery long-term symptoms among recovered patients [6]
c. The third section focused on a functional status activity (Post-COVID-19 Functional Status (PCFS) scale) which consisted of 6 steps ranging from 0 (no symptoms) to 5 (death, D): grade 0 reflects the absence of any functional limitations; *grade 1* is for patients with some symptoms, which does not limit doing any of the usual activities; grade 2 is reserved for patients who are able to independently perform all usual activities but at a lower intensity, sometimes combined with mild limitations in participation in usual social roles; *grade 3* accounts for moderate functional limitations that force patients to structurally modify usual activities, reflecting the inability to perform certain activities which, therefore, need to be taken over by others. Those patients may require assistance in instrumental activities of daily living; *grade 4* describes those patients with severe functional limitations who require assistance with activities of daily living. This section was derived from [11]

Then, two of the participating researchers extracted clinical admission details from the medical records of those previously hospitalized patients with a laboratory-confirmed COVID-19 diagnosis and who consented to participate in the study. These details include the need for oxygen and its concentration, history of ICU admission, length of ICU stay, length of hospital stay, home treatment as ACE inhibitors, statins and antiplatelets, and laboratory investigations as D-dimer, C-reactive protein, and lactate dehydrogenase.

Data analysis

The collected data was revised, coded, tabulated, and analyzed using the Statistical Package for Social Science (SPSS version 25). Quantitative data was presented as mean and standard deviation. Categorical data was presented as numbers and percentages. Student t test was used to assess the statistical significance of the difference between the two study group means. Mann-Whitney test was used if the quantitative variable was skewed. Chi-square test was used to examine the relationship between two qualitative variables. Linear-by-linear association chi-square test was used if one of the qualitative variables was ordinal. Multivariate analysis was done by binary logistic regression to find out the significant determinants of the decreased functional status of post COVID recovered patients. Factors entered in the model were the significant factors in the bivariate analysis, the factors that were plausibly important that the data set supports, as well as age and gender as they are considered universal confounders. Results were considered statistically significant if the p-value < 0.05.

Results

This cross-sectional study included 150 patients who recovered from COVID-19; the mean ± SD age was 53.85 ± 15.24 years, 57.3% males and 42.7% females. The majority of participating patients (78%) lived in urban areas. More than half of the participants were married, while 28% were widows. 77.3% of the participants were suffering from chronic diseases. Regarding habits of special medical importance, 34% were active smokers, and only 29.3% documented receiving seasonal influenza vaccination.

More than one third (38.7%) were suffering from severe COVID-19, followed by 32% who were suffering from moderate COVID-19 18% who had critical form, and the remaining 11.3% complained of mild form. Re-admission after discharge was done to 18.7% of whom 77.3% needed ICU admission. The median ± IQR of the duration of hospital stay was 7 days, and the median and IQR of the duration of ICU stay was 7 days as shown in Table 1.

Table 1 shows significant differences between the two groups: those with reduced functional status after COVID-19 infection and the other group with stable

Table 1 The comparison between the two groups (those with functional activity limitation and those without) regarding their socio-demographic data and medical history

Demographic characteristics		All patients *N* = 150 (%)	Functional status at 6 months		Test of significance	*p* value
			Not decreased *N* (%)	Decreased *N* (%)		
Age (mean ± SD) range (23–90 years)		53.85 ± 15.24	53.78 ± 15.69	53.92 ± 14.87	0.06[a]	0.96
Gender	Male	86 (57.3)	46 (53.5)	40 (46.5)	0.64[b]	0.42
	Female	64 (42.7)	30 (46.9)	34 (53.1)		
Residence	Urban	117 (78)	60 (51.3)	57 (48.7)	0.08[b]	0.78
	Rural	33 (22)	16 (48.5)	17 (51.5)		
Marital status	Single	19 (12.7)	12 (63.2)	7 (36.8)	1.89[b]	0.39
	Married	86 (57.3)	44 (51.2)	42 (48.8)		
	Widow/divorced	45 (30)	20 (40.4)	25 (59.6)		
Occupation	Do not work	46 (30.7)	21 (45.7)	25 (54.3)	0.67[b]	0.41
	Work	104 (69.3)	55 (52.9)	49 (47.1)		
Smoking status	Nonsmoker	99 (66)	54 (54.5)	45 (45.5)	1.75[b]	0.19
	Current smoker	51 (34)	22 (43.1)	29 (56.9)		
Presence of comorbidities	Yes	116 (77.3)	60 (51.7)	56 (48.3)	0.23[b]	0.63
	No	34 (22.7)	16 (47.1)	18 (52.9)		
Seasonal influenza vaccine	Yes	44 (29.3)	29 (65.9)	15 (34.1)	5.79[b]	0.02*
	No	106 (70.7)	47 (44.3)	59 (55.7)		
Clinical characteristics						
COVID-19 disease severity	Mild	17 (11.3)	13 (76.5)	4 (23.5)	26.54[b]	< 0.001*
	Moderate	48 (32)	35 (72.9)	13 (27.1)		
	Severe	58 (38.7)	22 (37.9)	36 (62.1)		
	Critical	27 (18)	6 (22.2)	21 (77.8)		
Intensive care unit admission	Yes	116 (77.3)	51 (44.7)	63 (55.3)	6.68[b]	0.01*
	No	34 (22.7)	25 (69.4)	11 (30.6)		
Hospital readmission	Yes	28 (18.7)	10 (35.7)	18 (64.3)	3.08[b]	0.08
	No	122 (81.3)	66 (54.1)	56 (45.9)		
Length of ICU stay (median IQR) (in days)		7 (6)	5 (4)	9 (6)	4.298[c]	< 0.001*
Length of hospital stay (median IQR) (in days)		9 (6)	7 (4.04)	11 (7.60)	4.181[c]	< 0.001*

* Significant, [a]Student *t* test, [b]Chi-square test, [c]Mann-Whitney test

functional status after infection. Receiving the influenza vaccine was significantly associated with keeping the pre-COVID functional status ($p = 0.02$). The reduced functional status group had a significantly more severe disease course ($p < 0.001$). They also had more prolonged hospital as well as ICU stay ($p < 0.001$).

Figure 1 shows the change in the functional status of study participants before COVID compared to their status after recovery. A major change occurred in grade (0) which was reduced from 87.3 to 38.7%.

Figure 2 shows a statistically significant difference between the two groups regarding CT scan results. The reduced functional status group had worse CT findings than the normal functional status group ($p = 0.004$).

Table 2 shows that long-term symptoms such as headache, mood changes, insomnia, hearing problems, dry eyes, breathlessness, and chest tightness were significantly more prevalent among those reported limitations in their functional status ($p < 0.001$); however, loss of smell was more prevalent among those without any limitation in their functional activities ($p = 0.02$).

Table 3 shows that the only symptom that was significantly more severe in the reduced functional status group was breathlessness and chest tightness ($p = 0.009$).

The differences in laboratory investigations and treatment modalities offered to both groups were compared in Table 4. There were significantly higher CRP, serum ferritin, and D-dimer in the reduced functional status group ($p = 0.01$, < 0.01 and 0.002 respectively).

Table 5 shows that only two of the independent variables made a statistically significant contribution to the final model; seasonal influenza vaccination and serum ferritin showed the statistically significant affection on PCFS.

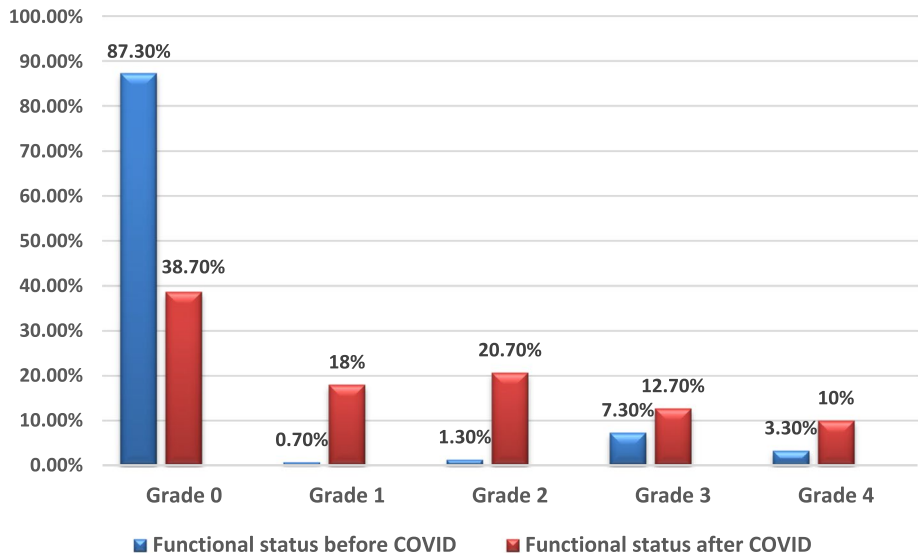

Fig. 1 Functional status before compared to after COVID-19. The change in the functional status of study participants before COVID compared to their status after recovery. A major change occurred in grade (0) which was reduced from 87.3 to 38.7%

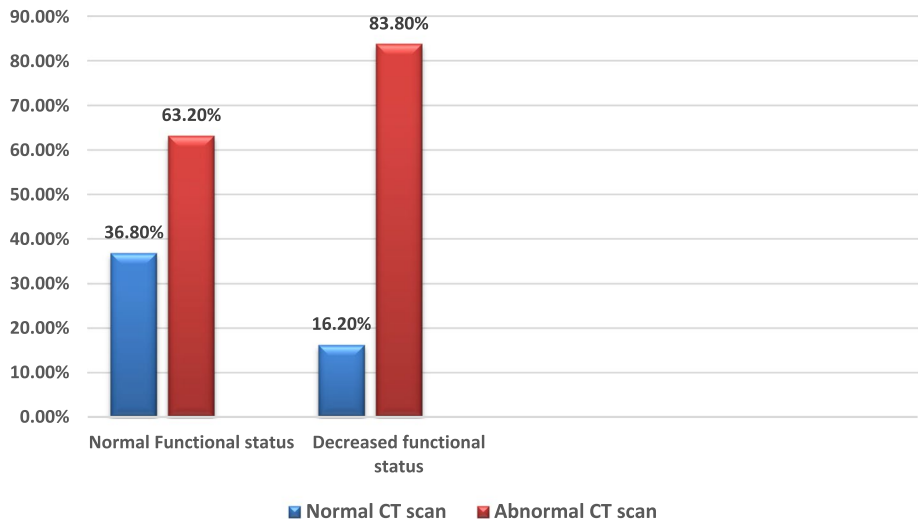

Fig. 2 The comparison between the two groups (those with functional activity limitation and those without) regarding their lung CT scan abnormalities. A statistically significant difference between the two groups regarding CT scan results. The reduced functional status group had worse CT findings than the normal functional status group ($p = 0.004$)

Discussion

The COVID-19 pandemic led to the affection of an enormous proportion of cases with many clinical manifestations, e.g., fever, cough, dyspnea, musculoskeletal disorders like joint pain, GIT disorders, and sleep disorders. There are some reports about patients' functional state after recovery, yet the evidence is still missing. Persistent restrictions on the functional status among convalescent COVID-19 cases were studied in the current study using the recommended PCFS questionnaire [12].

Around 57% of study participants were males which is like in China [13]. Du et al. reviewed patient files in a tumor center in Wuhan from February to March 2020.

COVID-19 critical cases represented 38% of the current study. Critical cases necessitated invasive mechanical ventilation, and it was found that increased COVID severity was significantly associated with reduced functional status. This result agrees with a Danish study [14] that found a long-term affection of cognitive and functional status. They reported this finding in a quarter of

Table 2 The comparison between the two groups (those with functional activity limitation and those without) regarding their long-term symptoms at 6-month follow-up

Persistent symptoms		All patients *N* = 150 (%)	Functional status at 6 months		Chi-square test	*p* value
			Not Decreased	Decreased		
1. General symptoms	Fatigue and weakness	62 (41.3)[a]	28 (45.2)	34 (54.8)	1.28	0.26
2. Skin and musculoskeletal symptoms	Muscle aches	49 (32.7)	27 (55.1)	22 (44.9)	0.57	0.45
	Joint aches	23 (15.3)	8 (34.8)	15 (65.2)	2.74	0.10
	Skin rash	31 (20.7)	16 (51.6)	15 (48.4)	0.01	0.91
3. Psychological and neurological symptoms	Headache	19 (12.7)	4 (21.1)	15 (78.9)	7.63	0.006*
	Mood changes	40 (26.7)	13 (32.5)	27 (67.5)	7.20	0.007*
	Insomnia	31 (20.7)	10 (32.3)	21 (67.7)	5.30	0.02*
	Paresthesia and anesthesia	23 (15.3)	10 (43.5)	13 (56.5)	0.56	0.45
4. Special sense symptoms	Hearing problems	18 (12)	3 (16.7)	15 (83.3)	9.46	0.002*
	Visual disturbance	8 (5.3)	2 (25)	6 (75)	2.23	0.14
	Dry eyes	25 (16.7)	6 (24)	19 (76)	8.54	0.003*
	Loss of smell	20 (13.3)	15 (75)	5 (25)	5.47	0.02*
	Loss of taste	22 (14.7)	15 (68.2)	7 (31.8)	3.16	0.08
5. Respiratory symptoms	Cough days	92 (61.3)[a]	47 (51.1)	45 (48.9)	0.02	0.90
	Breathlessness and chest tightness	101 (67.3)[a]	37 (36.6)	64 (63.4)	24.36	< 0.001*
6. Gastrointestinal *symptoms	Lack of appetite	35 (23.3)	13 (37.1)	22 (62.9)	3.34	0.07
	Nausea	15 (10)	6 (40)	9 (60)	0.76	0.38
	Diarrhea days	73 (48.7)[a]	37 (50.7)	36 (49.3)	0	0.10
	Abdominal pain	23 (15.3)	13 (56.5)	10 (43.5)	0.37	0.54

[*] Significant

[a] Most common persisting symptoms after 6 months

patients surviving intensive care for COVID-19. They also reported that there was a lack of pre-admission patient details of their participants which is the same condition as the current study as well.

But this result disagrees with [15] in Italy who found no significant association between the need for mechanical ventilation and long-term affection of survivors' quality of life. This might be due to different measures of outcome. Additionally, they followed up their study participants for a longer duration (1 year).

Results of the current study show that increased disease severity was inversely associated with survivors' functional status ($p < 0.001$). This result is similar to [16] in Indonesia. The same was found by [17] in their study on Iranian COVID patients. This result was also confirmed by [18] in Cairo, Egypt.

With increased COVID-19 pneumonia severity, the virus infection leads to two sequelae: pulmonary fibroblast activation during the convalescence period and pathological changes like fibroproliferation in the lungs. These changes lead to short- and long-term impacts on PCFS [19].

Receiving seasonal influenza vaccine was significantly associated with better post COVID functional outcomes ($p = 0.02$). This agrees with [12] who performed their study in Assuit, Egypt. Another study [20] found a close result in their study in Mexico. It analyzed the post-COVID survival rates and found that there was a higher mortality rate among the unvaccinated group with the influenza vaccine ($p < 0.001$). There is a high affinity of both influenza and SARS-CoV-2 viruses to the same receptor in the lungs as well as a similar structural protein in both viruses. This may explain this significant association [21, 22].

Previous studies reported that COVID-19 cases from different age groups who required ICU admission had prolonged disability caused by muscle changes, fatigue, and dyspnea. They are at higher risk of developing post-intensive care unit (ICU) syndrome (PICS) [23].

The current study showed a significant reduction in the functional status of patients who had a severe condition and required ICU admission ($p = 0.01$). A similar result was found by Oliveira et al. in their literature review on 15 studies [24]. A study confirmed this finding in Spain. It also found a reduced functional condition with a prolonged hospital stay [8].

Regarding the change in functional status, there was a significant decrease in grade 0 (those without any

Table 3 The comparison between the two groups (those with functional activity limitation and those without) regarding the severity of their persistent symptoms at 6-month follow-up

Persistent symptoms		Degree of severity *N* (%)	Functional status at 6 months *N* (%)		Chi-square test	*p* value
			Not decreased	Decreased		
1. General symptoms	**Fatigue and weakness days**	**Mild**	3 (42.9)	4 (57.1)	0.57	0.75
		Moderate	15 (50)	15 (50)		
		Severe	10 (40)	15 (60)		
2. Skin and musculoskeletal symptoms	**Muscle aches days**	**Mild**	5 (71.4)	2 (28.6)	0.95	0.62
		Moderate	9 (50)	9 (50)		
		Severe	13 (54.2)	11 (45.8)		
	Joint aches days	**Mild**	2 (33.3)	4 (66.7)	0.22	0.89
		Moderate	5 (33.3)	10 (66.7)		
		Severe	1 (50)	1 (50)		
	Skin rash days	**Mild**	11 (52.4)	10 (47.6)	0.02	0.90
		Moderate	5 (50)	5 (50)		
		Severe	0	0		
3. Psychological and neurological symptoms	**Headache days**	**Mild**	2 (33.3)	4 (66.7)	1.13	0.57
		Moderate	2 (18.2)	9 (81.8)		
		Severe	0	2 (100)		
	Mood changes	**Mild**	5 (45.5)	6 (54.5)	3.92	0.14
		Moderate	7 (38.9)	11 (61.1)		
		Severe	1 (9.1)	10 (90.9)		
	Insomnia days	**Mild**	4 (50)	4 (50)	3.54	0.17
		Moderate	6 (33.3)	12 (66.7)		
		Severe	0	5 (100)		
	Paresthesia and anesthesia days	**Mild**	5 (45.5)	6 (54.5)	0.80	0.67
		Moderate	5 (45.5)	6 (54.5)		
		Severe	0	1 (100)		
4. Special sense symptoms	**Hearing problems**	**Mild**	2 (18.2)	9 (81.8)	0.05	0.83
		Moderate	1 (14.3)	6 (85.7)		
		Severe	3 (16.7)	15 (83.3)		
	Visual disturbance	**Mild**	2 (50)	2 (50)	1.50	0.22
		Moderate	0	2 (100)		
		Severe	2 (33.3)	4 (66.7)		
	Dry eye days	**Mild**	4 (30.8)	9 (69.2)	0.85	0.66
		Moderate	2 (18.2)	9 (81.8)		
		Severe	0	1 (100)		
	Loss of smell	**Mild**	1 (100)	0	1.67	0.43
		Moderate	3 (100)	0		
		Severe	11 (68.8)	5 (31.3)		
	Loss of taste	**Mild**	4 (100)	0	2.33	0.31
		Moderate	2 (66.7)	1 (33.3)		
		Severe	9 (60)	6 (40)		
5. Respiratory system symptoms	**Cough days**	**Mild**	16 (66.7)	8 (33.3)	3.21	0.20
		Moderate	15 (44.1)	19 (55.9)		
		Severe	16 (47.1)	18 (52.9)		
	Breathlessness and chest tightness days	**Mild**	10 (62.5)	6 (37.5)	9.34	0.009*
		Moderate	13 (46.4)	15 (53.6)		
		Severe	14 (24.6)	43 (75.4)		

Table 3 (continued)

Persistent symptoms		Degree of severity *N* (%)	Functional status at 6 months *N* (%)		Chi-square test	*p* value
			Not decreased	Decreased		
6. Gastrointestinal system symptoms	**Lack of appetite days**	**Mild**	4 (57.1)	3 (42.9)	2.28	0.32
		Moderate	8 (36.4)	14 (63.6)		
		Severe	1 (16.7)	5 (83.3)		
	Nausea days	**Mild**	2 (33.3)	4 (66.7)	1.11	0.57
		Moderate	4 (50)	4 (50)		
		Severe	0	1 (100)		
	Diarrhea days	**Mild**	14 (50)	14 (50)	0.08	0.96
		Moderate	17 (50)	17 (50)		
		Severe	6 (54.5)	5 (45.5)		
	Abdominal pain	**Mild**	5 (55.6)	4 (44.4)	0.94	0.63
		Moderate	6 (66.7)	3 (33.3)		
		Severe	2 (40)	3 (60)		

Table 4 The comparison between the two groups (those with functional activity limitation and those without) regarding their laboratory investigations and the treatment modalities

	All patients *N* = 150 (mean ± SD)	Functional status at 6 months		*t* test	*p* value
		Not decreased (mean ± SD)	Decreased (mean ± SD)		
Laboratory investigations					
Creatine kinase	241.76 ± 188.66	207.66 ± 160.36	267.90 ± 205.26	1.64	0.10
Direct bilirubin	0.64 ± 0.36	0.66 ± 0.41	0.63 ± 0.31	0.38	0.70
LDH (U/L)	345.33 ± 125.07	311.95 ± 100.22	372.91 ± 138.48	1.60	0.12
ABS neutrophils	3.57 ± 0.91	3.61 ± 0.78	3.55 ± 0.98	0.25	0.80
ABS lymphocytes	0.99 ± 0.28	0.98 ± 0.30	0.99 ± 0.26	0.07	0.95
CRP	66.86 ± 56.16	55.07 ± 51.93	78.66 ± 58.07	2.61	0.01*
Serum ferritin	687.94 ± 463.03	490.30 ± 277.12	879.32 ± 524.76	5.19	< 0.01*
D-dimer	1.81 ± 0.68	1.62 ± 0.63	1.99 ± 0.68	3.16	0.002*
Treatment modalities	***N* = 150 (%)**	***N* (%)**	***N* (%)**	**Chi-square**	***p***
Antiviral	74 (49.3)	53 (71.6)	21 (28.4)	28.33	< 0.001*
Immunosuppressive	14 (9.3)	7 (50)	7 (50)		
Antiviral and immunosuppressive	62 (41.3)	16 (25.8)	46 (74.2)		

*Significant *p* value

limitations at all) from 87.3 to 38.7% ($p < 0.01$). This indicates a significant reduction in patients' status 6 months after COVID infection. This goes in agreement with Kamal et al. in their study in Egypt [7]. Their group of followed up COVID patients underwent a significant reduction in their functional status (grade 0) from 84.7 to 44.3%. A special emphasis is put on ICU admission; there was no significant difference in the PCFS scale between ICU and non-ICU admitted patients before COVID infection, while there was a significant difference in their status after admission (Supplementary Table 1). The same finding was confirmed by Taboada et al.'s study on Spanish patients [8].

The current study found a significant association between CT scan findings and long-term functional impairment ($p = 0.004$). This disagrees with D'Cruz et al.

Table 5 Binary logistic regression showing variables independently affecting the functional status of COVID-19 survivors*

		Beta	*p* value	OR	95% CI for odds ratio	
					Lower	Upper
Age		− 0.027	0.192	0.974	0.935	1.014
Gender		− 0.365	0.508	0.694	0.236	2.044
COVID-19 severity (ref. mild)	Moderate	− 0.283	0.760	0.754	0.123	4.616
	Severe	1.239	0.289	3.452	0.350	34.025
	Critical	0.066	0.963	1.069	0.065	17.698
Seasonal influenza vaccination (ref. no)		− 1.812	0.004	0.163	0.047	0.564
Treatment modalities (ref. antiviral)	Immunosuppressant	− 0.710	0.499	0.491	0.063	3.858
	Immunosuppressant and antiviral	− 0.264	0.791	0.768	0.109	5.388
CRP		− 0.003	0.628	0.997	0.983	1.010
Serum ferritin		0.004	0.006	1.004	1.001	1.007
D-dimer		0.502	0.219	1.651	0.743	3.671

ref (reference category)

* Factors entered in the model were the significant factors in the bivariate analysis and age and gender were not significant. However, they were added because they are considered universal confounders. The used method was the enter method. Significant at *p*-values of less than .05

who concluded the associations of COVID-19 imaging findings at follow-up with functional impairments [25].

The CT scan variable reported in the current study was not based on any type of CT scores and did not specify the type of lesion: ground glass opacities or other lung lesions associated with fibrosis, e.g., reticular changes or changes that may lead to changes in the lung architecture [26]. This may limit the comparability of this variable.

Breathlessness, cough, diarrhea, and fatigue were the most commonly persisting symptoms. This is like a review article done by Gao et al. They reported the persistence of the same symptoms on the long term [27]. This is also similar to a study in Egypt except for diarrhea which was present in only 6.7% of their participants [28]. This difference may be due to different methods of inquiring about diarrhea (number of diarrhea days, frequency, or looseness).

The current study showed that the severity of breathlessness was significantly associated with decreased PCFS. COVID-19 virus has a very high affinity to the angiotensin-converting enzyme-2 (ACE-2) receptor in the lungs leading to lung fibrosis and persistent long-term breathing difficulties. The virus is capable of damaging lung endothelium as well and triggering an inflammatory response leading to lung consolidation. This describes the pathophysiology of lung damage causing long-term pulmonary symptoms [29].

Most of the *psychological and neurological symptoms* were significantly higher in the group with decreased functionality (i.e., headache, insomnia, and mood changes). This result is similar to what Pellitteri found. They followed a group of patients with past COVID infection for 2 and 10 months and found significant changes regarding their sleep quality and mood disturbances. They explained this condition as part of the neuro-homeostatic response to temporary neuronal damage due to the pro-inflammatory state led by the COVID-19 virus. These changes are a result of the yet unclear relationship [30].

Loss of taste and smell were present in 14.7% and 13.3% respectively which is similar to Logue et al. in Washington [31]. But this result disagrees with Kandi et al. in India (5% for both symptoms) [32], Zangrillo et al. in Italy (7.1% for both symptoms) [15], and Pant et al. in Nepal (37.7%, 42.5% respectively) [33]. This big variation may be due to different variants of COVID-19 and different populations with a variable genetic predisposition. Zangrillo et al. specifically studied ICU-admitted patients [15].

C-reactive protein, D-dimer, and serum ferritin were significantly higher in patients with reduced functionality. The same was found by Bahmer et al. in their study on the German population, for CRP and D-dimer [34]. These results also agree with a study done in Egypt by Elgazzar et al. They performed a ROC curve and found them as good to very good predictors of functional status in the post-COVID infection phase (sensitivity from 0.67 to 0.77) [28].

Conclusion and recommendations

According to the PCFS scale, the majority of COVID-19-recovered patients had varying degrees of functional impairments, ranging from null to severe. The duration of hospital stay, ICU admission, and influenza vaccination frequency had an impact on these restrictions. A lower level of functioning was linked to serum ferritin, D-dimer, and CRP. Breathlessness and psychological/neurological symptoms were significantly related to lower PCFS. A simple measure like the PCFS scale must

be incorporated into primary healthcare to determine whether these functional limits require management. Patients and doctors might not be aware that those symptoms are caused by post-COVID sequelae; hence, there needs to be a general health education campaign on the health consequences of post-COVID-19.

Additional research is necessary to clarify the primary causative factors (such as genetic predisposition, treatment strategy, specific drugs, etc.) of functional limitations following COVID-19.

Study limitations

Functional status before COVID-19 infection could not be well-studied. Longer duration of follow-up may be needed to find out which symptoms would persist and become a permanent infirmity (e.g., lung fibrosis).

Abbreviations

SARS-CoV-2	Severe acute respiratory syndrome coronavirus
PCFS	Post-COVID-19 Functional Status
ICU	Intensive care unit
PCR	Polymerase chain reaction
LDH	Lactate dehydrogenase
CRP	C-reactive protein

Supplementary Information

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Additional file 1: Supplementary Table 1. The tool used to measure and categorize these severity scale

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Authors' contributions

Conceptualization: AM, AF; methodology: AM, AF; formal analysis and investigation: AM; writing—original draft preparation: AM, AF, OA; writing—review and editing: AF, AW; funding acquisition: self-funded by authors; supervision: AW, AF. All authors read and approved the final manuscript.

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Faculty of Medicine, Ain Shams University. Administrative approvals from four public hospitals were obtained to conduct the study. Approval of the research ethical committee at the Faculty of Medicine Ain Shams University and informed consent from participants were obtained. The confidentiality of participants' data was assured (FMASU R265/2022).

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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