



Post-COVID-19 syndrome: assessment of short- and long-term post-recovery symptoms in recovered cases in Saudi Arabia

Mohammed A. Garout¹ · Saleh A. K. Saleh^{2,3} · Heba M. Adly¹ · Altaf A. Abdulkhaliq² · Abdullah A. Khafagy¹ · Magda R. Abdeltawab⁴ · Ali A. Rabaan^{5,6,7} · Alfonso J. Rodriguez-Morales^{8,9,10} · Jaffar A. Al-Tawfiq^{11,12,13} · Maher N. Alandijjany^{14,15}

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Abstract

Introduction Recent studies investigated the endurance of symptoms and occurrence of complications three months after SARS-CoV-2 infection. This study aims to examine the prevalence, variation, and severity of continual symptoms in the post-COVID-19 using a single-center questionnaire.

Methods The questionnaire was distributed among population in Saudi Arabia who recovered from COVID-19 between April 1, 2020 and December 31, 2021.

Results A total of 744 participants completed the questionnaire, 318 (42.8%) recovered less than 3 months, 75 (10.1%) recovered 3–6 months, while 351 (47.2%) recovered more than 6 months. About half of the participants 353 (47.5%) had incessant symptoms and of those patients, more than half had two or more symptoms. Common symptoms included fatigue 189 (25.4%), headache 118 (15.9%), and myalgia 63 (8.5%). Of the participants, 189 (21.4%) experienced continual symptoms including anxiety in 98 (13.2%) and depression in 70 (9.5%).

Conclusion The current study showed a high proportion of individuals with long-COVID-19 symptoms. Thus, proper assessment of the individuals in the post-recovery period can guide the patients to the relevant clinics for rehabilitation. Moreover, there is a great importance to decrease COVID-19 infection, populations should be targeted to boost vaccine efficiency.

Keywords COVID-19 · Pandemic · Infection · Coronavirus · Post recovery · Symptoms · Saudi Arabia

Introduction

Globally, as of 4 January 2022, COVID-19-confirmed cases have been recorded in 290,959,019 caes including 5,446,753 deaths, as reported to the WHO, and the recovered cases were 256,200,554 [1]. COVID-19 vaccination uptake of at least one dose has been 58.6% and 9.28 billion doses were dispensed worldwide [2]. On 10 December 2020, the Kingdom of Saudi Arabia (KSA) had authorized the Pfizer/BioNTech COVID-19 vaccine and focused on older citizens and residents and frontline healthcare workers in the initial phase [3]. On 19 February 2022, KSA had achieved at least 25,840,571 (73.12%) vaccine doses, with completed vaccinations of 24,023,925 (67.98%) at rate of 1.22/second or 105,219 each day [2].

Even though the COVID-19 disease has triggered fear ever since the start of the pandemic, the existence of several post-recovery symptoms has attracted additional interest. Many studies revealed that COVID-19 has the potential to cause long-term effects on nearly all systems including respiratory, cardiovascular, gastrointestinal, neurological, and psychiatric manifestations [4]. A significant percentage of patients (87.5%) who had improved after acute infection continued to endure from a diversity of symptoms such as fatigue, dyspnea, cough, myalgia, and headache [5, 6]. Published data indicated that individuals who experienced mild illness or had no apparent symptoms may also suffer from long-term symptoms. The terminology regarding ongoing symptoms after recovery and the resolution of the disease differ among studies and societies' definitions as the Centers for Disease Control and

✉ Jaffar A. Al-Tawfiq
jaffar.tawfiq@jhah.com; jaltawfi@yahoo.com

Extended author information available on the last page of the article

Prevention (CDC) and The National Institute for Health and Care Excellence (NICE) [7, 8]. Continuing symptoms beyond 3 weeks from the disease onset were designated as post-acute COVID-19 [9] and beyond 12 weeks as chronic COVID-19 [10]. The US CDC suggested separating the disease into different categories as: acute COVID-19 (the first 2 weeks from symptom start), post-acute hyperinflammatory illness (between 2 and 4 weeks from symptoms start), and late period symptoms (more than 4 weeks from symptom start) [11].

Few studies were principally included hospitalized patients for acute COVID-19, and investigated the endurance of symptoms and occurrence of complications after SARS-CoV-2 infection and showed that 15–76% of such patients may have persistent symptoms six months after severe illness [12–16]. In addition, one study found that up to 20% of patients had to be re-hospitalized [17], and 80% may need follow-up in primary care centers within 2 months of hospital discharge [18]. Additional studies also showed that post-COVID-19 syndrome is not only present in those requiring hospitalization or in older individuals with comorbidities, but was observed in young and healthy people with mild disease [18, 19] with lack of data on the full spectrum of symptoms of post-COVID-19 [20]. To care for such patients, few countries have set up clinics to check post-recovery symptoms and to enhance the overall knowledge [21–23].

In this study, we examine the prevalence, and severity of persistent symptoms post-COVID-19 and investigate the post-recovery follow-up, and compare these symptoms among the different spectrum of COVID-19 disease.

Materials and methods

Study Design

This study was conducted among recovered COVID-19 patients, between April 1, 2020 and December 31, 2021. The participants declared that they have been diagnosed as COVID-19 by confirmed (SARS-CoV-2) polymerase chain reaction (PCR).

A questionnaire was designed to study the current health status of patients and their continual symptoms in the post-COVID period. As this survey aimed to examine the incidence of post-COVID syndrome, participants who have had COVID-19 at least 2 months before the questionnaire, were included in the survey. The questionnaire was distributed using different social media channels between November 2021 and December 2021. Before completing the questionnaire, all participants were requested

to accept to participate in the study. The study protocol was approved by the Ethics Review Board for Human Studies at the Faculty of Medicine, Umm Al-Qura University (Approval no. HAPO-02-K-012–2022-01-902 in accordance with Saudi National Committee for Bioethics HABO-02-K-012).

Questionnaire design

Basic data information included in the survey were age, gender, chronic diseases status, history of hospitalization (disease severity, extent of hospital stays, necessity for respiratory supports, and necessity for intensive care unit [ICU]), period since symptoms started, occurrence of insistent symptoms by systems. Data about acute COVID-19 were attained from participants' themselves. COVID-19 disease severity was classified as mild to moderate, severe, and critical based on the WHO COVID-19 technical guidelines (30). The symptoms of patients were congregated by systems as follows: general (fatigue, myalgia), respiratory (chest pain, cough, and wheezing), cardiovascular (palpitation), neuropsychiatric (headache, hypersomnia, depression, and anxiety), dermatologic (hair loss), gastrointestinal (diarrhea, and constipation). Participants were asked to score symptoms from 0 (no symptoms) to 10 (extreme symptoms) to assess the level of severity based on the scale of COVID-19 Yorkshire Rehabilitation Screening (C19-YRS). The C19-YRS assesses symptom severity and functional disability performance. The tool has been recommended in England by the National Institute for Health and Care Excellence (NICE) in its guidelines for managing the long-term effects of COVID-19 [24, 25]. The questionnaire has 19 questions about the severity of and impact on function of the following: breathlessness, voice, swallowing, nutrition, mobility, fatigue, personal care, usual activities, pain and discomfort, anxiety, depression, post-traumatic stress disorder, continence, cognition, perceived health status and family views [26]. The scale is used to examine participants' situation for their ongoing symptoms of COVID-19 and to offer management plan for the essential restorations and we can advise the patients to the relevant clinic for more rehabilitation after COVID-19 recovery.

Statistical analysis

All analyses were performed using SPSS V.21 software version 21. Descriptive statistics were described as mean \pm standard deviation (SD) or medians plus with quartiles (25th–75th percentile) for continuous variables that do not have a normal distribution and as frequency and percentages for definite variables. A *t* test was applied in the evaluation of continuous

variables for normally distributed data. The χ^2 test was used for comparing categorical variables in parametric conditions. A *p* value of less than 0.05 was considered statistically significant.

Table 1 Demographic and general characteristics of participants (n = 744)

Characteristics of participants	Value	
Age, years, <i>n</i> (%)	18–29, 138 (18.6%)	
	30–50, 398 (53.5%)	
	≥ 50, 207 (27.9%)	
Gender	Males 366 (49.3%)	
	Females 378 (50.7%)	
Time since diagnosis (months, <i>n</i> , %)	≤ 3 months, 318 (42.8%)	
	≥ 3 months, 75 (10.1%)	
	≥ 6 months, 351 (47.2%)	
Initial symptom severity, <i>n</i> (%)	Asymptomatic 81 (11.1%)	
	Mild to moderate 554 (67.3%)	
	Severe to very severe 160 (21.6%)	
Hospitalization and ICU stay		
	Non-hospitalized, <i>n</i> (%)	677 (91.1%)
	Hospitalized without ICU stay, <i>n</i> (%)	66 (8.9%)
Hospitalized with ICU stay, <i>n</i> (%)	7 (11.1%)	
Comorbidities		
	No comorbidity	459 (61.7%)
	At least one comorbidity	285 (38.3%)

Results

Patients demographic characteristics

A total of 744 participants who recovered from COVID-19 disease completed the study questionnaire, 318 (42.8%) recovered less than 3 months, 75 (10.1%) recovered 3–6 months, while 351 (47.2%) of the patients recovered more than 6 months. Of the total participants, 366 (49.3%) were male, and 378 (50.7%) were females. Of the study population, 398 (53.5%) aged 30–50 years, 207 (27.9%) were above 50 years, while 186 (18.6%) aged 18–29 years (Table 1). Only 66 (8.9%) of the participants were hospitalized, and 82 (11.1%) required ICU admission, and 677 (91.1%) required only home isolation with no oxygen support. Of the patients, 534 (71.8%) had mild-to-moderate COVID-19, 459 (61.7%) declared no comorbidity, 117 (15.8%) had hypertension, 72 (9.8%) had diabetes mellitus, and 34 (4.7%) had heart disease (Figs. 1 and 2).

Characteristics of post-COVID-19 symptoms

Approximately half of the participants 410 (47.5%) had incessant symptoms, and more than half of them had two or more symptoms. Common systemic symptoms included: fatigue 189 (25.4%), headache 118 (15.9%), myalgia 63 (8.5%), and at least one of these symptoms was present in 128 (31.3%) of patients. In general, respiratory symptoms including cough, wheezing and chest pain together were common persistent symptoms in 137 (66.5%) and 51 (6.9%) had subjective feelings of dyspnea. Of the participants, 189

Fig. 1 Clinical characteristics of participants with chronic diseases

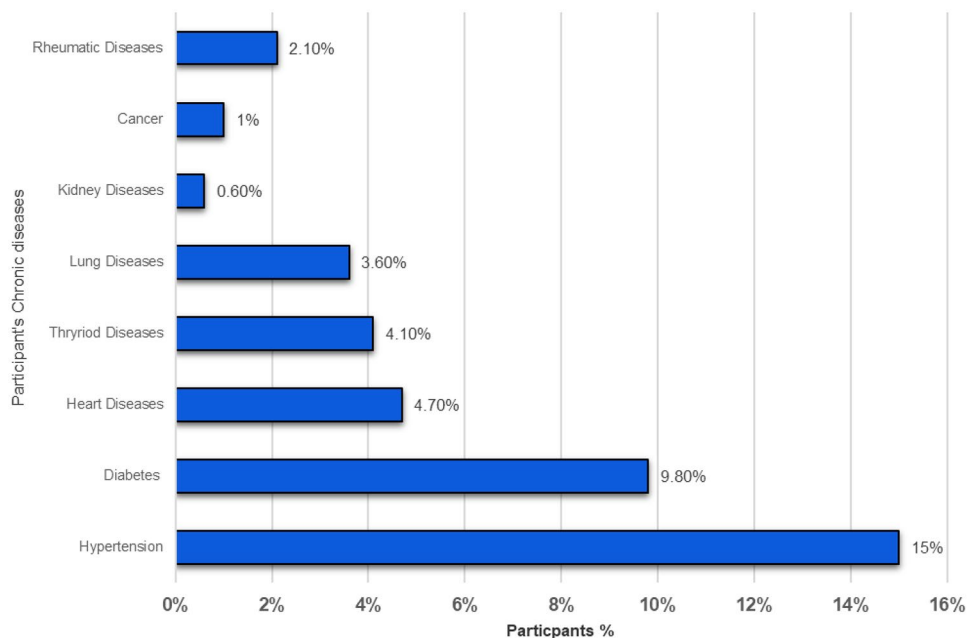
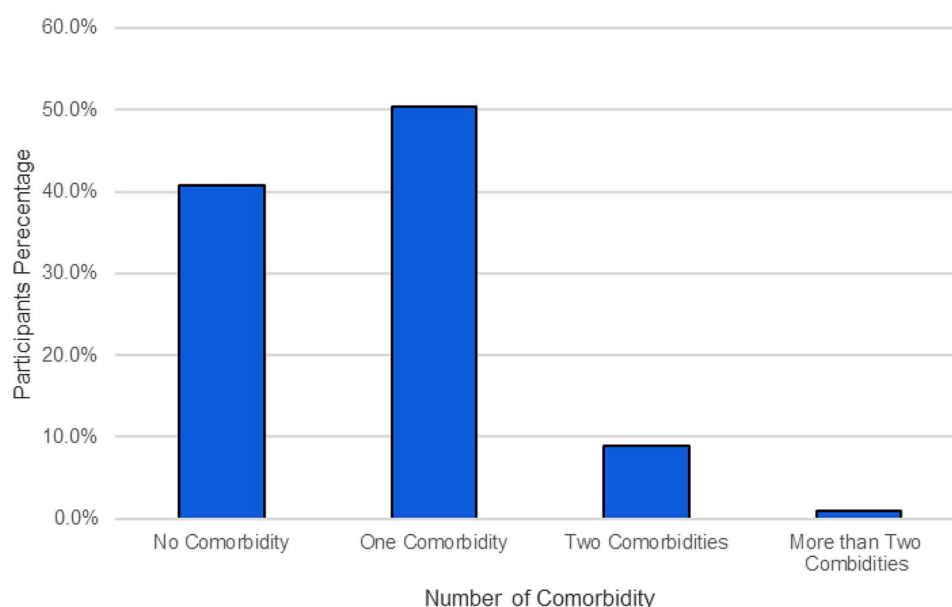


Fig. 2 Number of comorbidities distributed among in the study participants



(21.4%) experienced continual physical symptoms combined with neuropsychiatric symptoms in the form of concentration or memory deficit 79 (10.7%) or headache 118 (15.9%). Anxiety and depression were reported by 98 (13.2%) and 70 (9.5%) of the patients. Hair loss was reported as a recurrent dermatological symptom by 11.5%. On the other hand, 334 (45%) of the patient did not report any of the mentioned post-recovery symptoms (Figs. 2, 3).

Prevalence of post-recovery short- and long-term symptoms

Initial analysis showed a number of associated factors with the development of post-COVID-19 symptoms. A higher ratio of female participants and primarily hospitalized patients stated that they did not fully recover compared to males and non-hospitalized patients, respectively (Table 2). In a multivariable evaluation amongst primarily symptomatic patients, both age > 50 years and the presence of comorbidities correlated with post-COVID-19 symptoms. However, there was no statistical difference in relation to gender, severity of illness or need for hospitalization (Table 2).

Discussion

In this study, we evaluated the incidence and features of post-COVID syndrome in a slightly large number of 744 recovered patients in Saudi Arabia. In a multivariate analysis, hospitalization and presence of comorbidity were independent associated factors with persistent symptoms. It is important to elucidate the prevalence, diversity, and duration

of the post-COVID symptoms that may impact the quality of life, follow-up, and treatment schemes (Fig. 3).

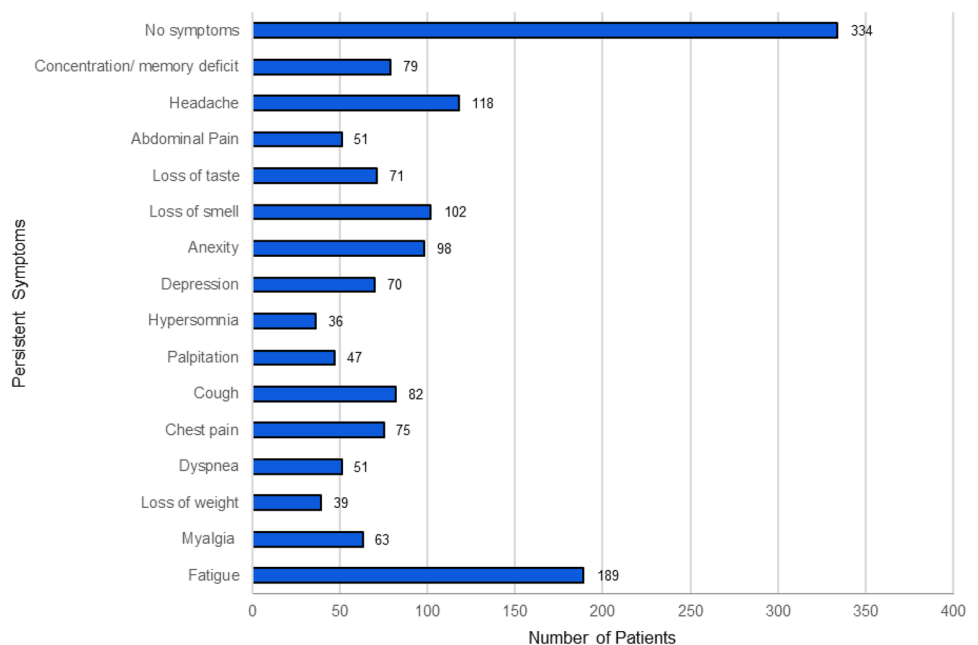
Several studies described persistent symptoms in 13.3% to 96% of patients who recovered from COVID-19 disease [18–20, 27, 28]. The differences in the reported results could be related to differences in the attributes of the study population (inpatients/outpatients, infection severity), study designs (patient self-reporting, questionnaire type, outpatient clinic/inpatients discharged) and the time that had elapsed after infection. A prospective study from Spain stated the occurrence of 50.9% post-COVID syndrome 10–14 weeks after the infection [29]. Another study from the U.K evaluated the electronic medical records of 47,780 hospitalized patients recovering from COVID-19, and showed 33% were re-hospitalized, and about 10% died during the follow-up period of 140 days [30]. Our study included both inpatient and outpatients recovered COVID-19 patients with different levels of severity from mild to severe infection, therefore, our study population signifies nearly the whole spectrum of the COVID-19 illness. However, it is not clear why long-term symptoms continue in certain patients recovered from COVID-19. It is thought that long-term consequences of COVID-19 correlate with the SARS-CoV-2 ability to trigger a substantial provocative response in certain persons [31–33]. The contribution of variants of concerns to the post-COVID-19 syndrome could not be evaluated in this study. However, vaccination provides protection against hospitalization and thus severe cases were decreased even with variants of concerns such as the delta variant [34]. Thus, further studies are needed to elucidate the contribution of the different variants to post-COVID-19 syndrome and the impact of vaccination.

Table 2 Univariate and odd ratio for the development of short- and long-term symptoms post-COVID-19

Short- and long-term symptoms post-COVID-19					
	Present	Absent	<i>p</i> value	Odds Ratio	95% CI
Age, (group range; n (%))					
18–29	59 (42.7)	79 (57.3)	<0.005		
30–50	200 (50.2)	198 (49.7)			
≥ 50	151 (75)	57 (25)		3.547	2.251–5.588
Males, n (%)					
	198, (54.1)	168 (45.9)	>0.05	0.9229	0.6909–1.233
Females, n (%)					
	212 (56)	166 (44)			
Hospitalized, n (%)					
	40 (60.6)	26 (39.4)	>0.05	1.28	0.762–2.161
Non - Hospitalized, n (%)					
	370 (54.7)	307 (45.3)			
Chronic Diseases, n (%)					
	214 (75)	71 (25)	<0.005	4.04	2.921–5.614
no chronic disease, n (%)					
	196 (42.7)	263 (57.3)			
COVID-19 severity level					
Asymptomatic, n (%)					
	41 (50.6)	40 (49.3)	>0.05		
Mild to moderate, n (%)					
	273 (54.3)	230 (45.7)			
Severe to very severe, n (%)					
	96 (60)	64 (40)			

In this study, persistent symptoms did not correlate with severity of illness or gender. Our findings match those from

Fig. 3 COVID-19 persistent symptoms in the study participants



a study conducted in Egypt [35]. In another study, disease severity and comorbidity were risk factors for the persistence of symptoms [36]. Additionally another study reported that age above 65 years and co-morbid diseases were risk factors of persistent symptoms [37]. We also found correlation with age and presence of comorbidities with post-COVID-19 symptoms.

In agreement with our study results, several studies stated fatigue as the most common symptom [18–20, 27]. COVID-19 disease can lead to pulmonary complications such as fibrosis, cough, and bronchiectasis. Long-term dyspnea is one of the feared long-term outcomes of COVID-19 disease [38]. In accordance with our study, Moreno-Pérez et al. assessed 277 patients in follow-up clinic 10–14 weeks after the onset of infection and they observed post-COVID syndrome in almost half of the COVID-19 patients, and < 25% had abnormal radiological changes [29].

Our study showed that the incidence of depression and anxiety appeared in about 9.5% and 13.2%, respectively. These results match those of a meta-analysis that showed the prevalence of depression, anxiety, and insomnia as 15.97%, 15.15%, and 23.87%, respectively [39]. Of the study participants, 10.1% reported hair loss similar to those in one study where 24% reported hair loss on average 110.9 days after disease onset [40].

Cardiac manifestations are also well-defined disorders and clearly foresee mortality between COVID-19 patients [41]. When the pandemic is over, it is estimated that there will be residual lung and cardiac disorders in a significant number of patients. Our study also supports this result as 10–15% of participants claimed that they are suffering from chest pain and palpitation. A study conducted in Saudi Arabia between May and July 2020 among patients discharged from hospital, showed shortness of breath, cough and fatigue in 40.1%, 27.5%, and 29.7%, respectively [42]. Another cohort study, in the same period, using a standardized telephone assessment between 6 weeks and 6 months post-hospital discharge, confirmed that age, dyslipidemia, hypertension, pre-existing lung disease and duration of symptoms were negatively associated with the WHO's five well-being index [43].

We applied C19-YRS tool scale to study the symptoms intensity among COVID-19 patients. Participants were asked to put a score for long-term symptoms as 0 (no problem) to 10 (extreme symptoms). However, most of our study participants reported mild to moderate levels of persistent symptoms with a score of 4 to 6, and patients scored loss of smell and taste as 5–6 and fatigue as 4–5. We think most of the participants have not mentioned symptoms as they believe these were common and do not need to be reported.

The process of post-COVID ailments is yet not well studied although is assumed to be secondary to virus-particular pathophysiological alterations, long-lasting inflammatory

reaction to severe infection and possibly related to post-intensive care illness [44, 45]. Our study was designed to assess patients with different SARS-CoV-2 severity requiring either in-patients or only outpatient care; however, many studies assessed only inpatients after discharged from hospital. A systematic review article reported that clinical characteristics of post-acute COVID-19 infection may appear more than 60 days after the occurrence of infection [46]. A study in the UK, patients with long COVID-19 described persistent multisystem association and substantial disability. In seven months, several patients have not yet recovered (mostly from systemic and neurological symptoms), have not come back to earlier stages of work, and remain with considerable symptoms [18]. A cohort study reported that nearly all COVID-19 patients had a good physical and functional recovery for the period of one-year follow-up and had resumed their previous work and life. The health level in this cohort of COVID-19 patients at twelve months was yet lesser than those in the control population [47]. A meta-analysis of 12 studies and 4828 post-acute COVID-19 syndrome (PCS) showed that persistent symptoms were associated with poor quality of life, tenacious symptoms, and mental health [48]. This suggests that we need more research on PCS patients to understand risk factors and those leading to poor quality of life in order to decrease COVID-19 infection. In addition, populations should be encouraged to receive booster doses of the vaccine and to have better disease control including physical distancing and use of personal protective measures, in the post-vaccination period [49]. To our knowledge, this study explored post-COVID syndrome through spectrum of disease severity from mild to severe in Saudi Arabia. However, the study is based on the patient's self-declaration about their persistent symptoms. Thus, there may be inconsistencies in stating the severity of the patients' symptoms.

Additional study limitations could be attributed to other factors. We had not been able to evaluate the impact of vaccination on the occurrence of such syndrome. However, this is an important point to address in future studies to give additional advantages of vaccination and to decrease hesitancy [50] given the rate of hesitancy across the world [51–54]. One study showed that the risk of having persistent symptoms > 28 days post-vaccination breakthrough infection was associated with an Odd Ratio (OR) of 0.51 in those who received two doses of the vaccine [49]. Thus, it is important to study the effects of vaccination and the contribution of different variants on the development of this syndrome, as these variants may cause different severity of COVID-19 [34, 55].

Conclusion

This study revealed that a significant number of patients with COVID-19 had persistent symptoms for 3 to 6 months after COVID-19 onset, and patients with a mild-to-moderate disease experienced persistent symptoms. Follow-up of these symptoms in the post-recovery time is vital to maintain good life quality.

Author contributions All authors similarly contributed to the article: (1) study conceptualization and design, data analysis and interpretation; (2) investigation, article drafting; and (3) final article review and approval.

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Declarations

Conflict of interest The authors declare that they have no conflict of interests, financial or otherwise.

Ethics approval The study protocol was approved by the Ethics Review Board for Human Studies at the Faculty of Medicine, Umm Al-Qura University. Approval no. HAPO-02-K-012-2022-01-902 in accordance with Saudi National Committee for Bioethics HABO-02-K-012.



Human and animal rights Participants had stated their approval to participate in the study before starting to answer the questionnaire.

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Authors and Affiliations

Mohammed A. Garout¹ · Saleh A. K. Saleh^{2,3}  · Heba M. Adly¹ · Altaf A. Abdulkhaliq² · Abdullah A. Khafagy¹ · Magda R. Abdeltawab⁴ · Ali A. Rabaan^{5,6,7} · Alfonso J. Rodriguez-Morales^{8,9,10} · Jaffar A. Al-Tawfiq^{11,12,13}  · Maher N. Alandiyjany^{14,15}

Mohammed A. Garout
magarout@uqu.edu.sa

Saleh A. K. Saleh
saabdrabou@uqu.edu.sa

Heba M. Adly
hebamadly@hotmail.com; hmhasan@uqu.edu.sa

Altaf A. Abdulkhaliq
aaabdulkhaliq@uqu.edu.sa

Abdullah A. Khafagy
aakhafagy@uqu.edu.sa

Magda R. Abdeltawab
ramadan_magda@yahoo.com

Ali A. Rabaan
arabaan@gmail.com

Alfonso J. Rodriguez-Morales
ajrodriguezmmmd@gmail.com

Maher N. Alandiyjany
mmandiyjany@uqu.edu.sa; maher.najm@bmc.edu.sa

- ¹ Community Medicine and Pilgrims Health Department, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia
- ² Biochemistry Department, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia
- ³ Oncology Diagnostic Unit, Faculty of Medicine, Ain Shams University, Cairo, Egypt
- ⁴ Medical Microbiology and Immunology Department, Ain Shams University, Cairo, Egypt

⁵ Molecular Diagnostic Laboratory, Johns Hopkins Aramco Healthcare, Dhahran 31311, Saudi Arabia

⁶ College of Medicine, Alfaisal University, Riyadh 11533, Saudi Arabia

⁷ Department of Public Health and Nutrition, The University of Haripur, Haripur 22610, Pakistan

⁸ Grupo de Investigación Biomedicina, Faculty of Medicine, Fundación Universitaria Autónoma de las Américas, 660003 Pereira, Risaralda, Colombia

⁹ Clinical Epidemiology and Biostatistics, Universidad Científica del Sur, Lima 4861, Peru

¹⁰ School of Medicine, Universidad Privada Franz Tamayo (UNIFRANZ), 4780 Cochabamba, Bolivia

¹¹ Specialty Internal Medicine and Quality Department, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

¹² Infectious Diseases Division, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA

¹³ Infectious Diseases Division, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

¹⁴ Laboratory Medicine Department, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah 21955, Saudi Arabia

¹⁵ Quality and Development Affairs, Batterjee Medical College, Jeddah 21442, Saudi Arabia