

Assessment of Post-COVID-19 Syndrome and Its Relationship to Age, Sex, and Comorbid Disease in Iraqi Population

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Abstract

Background: Post-coronavirus disease (post-COVID-19 syndrome) is any signs or symptoms that began during COVID-19 infection and persisted for at least 12 weeks after the first onset of infection. **Objective:** The study aimed to assess the post-COVID-19 symptoms in Iraqi patients and evaluate their incidence and relationships with patients' age, sex, comorbid disease, and vaccination status. **Materials and Methods:** This was a cross-sectional study using well-designed questionnaires for recovered COVID-19 patients. The collected data were summarized and analyzed using a specific analytical program. **Results:** About 915 patients participated in the study, male 283 (30.9%) and female 632 (69.1%). About 619 (67.7%) of participants reported at least one post-COVID-19 symptom. Fatigue is the most common postviral symptom which occurs in 365 (39.9%) patients, followed by hair loss 286 (31.3%) and decreases in cognitive functions like forgetfulness 263 (28.7%) and decreased mental performance 248 (27%). The post-COVID-19 syndrome is significantly related to female gender, the severity of COVID-19, and preexisting comorbid diseases. In addition, this study found that the incidence of post-COVID-19 symptoms was significantly reduced after COVID-19 vaccination. **Conclusion:** Post-COVID-19 symptoms affect many patients after healing from acute infection and are mostly related to sex, the severity of coronavirus infection, and associated comorbidities. Follow-up may be required to minimize the effects of post-COVID-19 syndrome on general health and quality of life for affected patients.

Keywords: Comorbidity, COVID-19, female gender, post-COVID-19 syndrome, severity

INTRODUCTION

In December 2019, Wuhan, China, announced the first case of coronavirus disease (COVID-19).^[1] Since then, millions of cases and deaths caused by the disease have been documented globally. The pandemic is characterized by acute respiratory infection and atypical pneumonia caused by a specific virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).^[2]

As the COVID-19 pandemic continues, various symptoms have been reported, including fever, fatigue, muscle ache, shortness of breath, dry cough, headache, gastrointestinal symptoms, rhinorrhea, and others.^[3] Those symptoms arise from affecting many biological systems as well as affecting disease control like diabetes^[4] and increase maternal risks if COVID-19 infection occurs during pregnancy.^[5] Numerous laboratory abnormalities were also reported during COVID-19, including a decrease in lymphocyte counts and an increase in inflammatory

markers, such as high erythrocyte sedimentation rate level, serum ferritin, C-reactive protein, tumor necrosis factor- α and interleukins (IL-1 and IL-6). In addition, COVID-19 may also be associated with severe and life-threatening adverse effects on the respiratory, cardiovascular, renal, and coagulation systems.^[3] Unfortunately, the managing of acute illness does not seem to be the end of the struggle against COVID-19. According to studies, between 40% and 90% of patients experience chronic symptoms following an acute infection, giving rise to the terms "long COVID-19" or "post-COVID-19 syndrome."^[6] The first description

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of post-COVID syndrome by a group of scientists was in 2020.^[7] Later the UK National Health Service defined it as “a set of unexplained signs or symptoms that began during or after the COVID-19 infection and persisted for at least 12 weeks.” Another term is “prolonged COVID-19” which describes the signs and/or symptoms of acute illness that worse or continued for 4–12 weeks,^[2] as shown in Figure 1.

Numerous studies from various parts of the world have demonstrated that COVID-19 has a wide range of long-term impacts on practically all systems, including respiratory, gastrointestinal, cardiovascular, psychiatric, neurological, and dermatological systems.^[8] Therefore, numerous scientists are examining and looking for why and when these symptoms develop and how to treat them. The underline pathophysiology of post-COVID-19 proposed to be related to the affected organ, the severity of the disease, immunologic and inflammatory response,

oxidative stress, and virus-specific factors,^[9] as shown in Figure 2.

COVID-19 infection affects many systems inside the body. SARS-CoV-2 enters the cells primarily by the binding angiotensin-converting enzyme 2 receptor on cell surface, which is widely distributed in most organs. In most patients, the immunological response by macrophage, monocyte, lymphocyte CD4 and CD8 is sufficient for recovery without complications. However, patients with severe life-threatening infections have a SARS-CoV-2 immunological dysregulation, which is accompanied by significant inflammation and high levels of the cytokine's interleukins (IL-1, IL-2, IL-6, and IL-10), which referred to as a “cytokine storm.” Cytokine storms possibly result in multi-organ failure and may lead to symptom persistence. The resulting symptoms may be self-limiting or persistent depending on the immune system's response and autoantibody production.^[2] The exact pathophysiology of

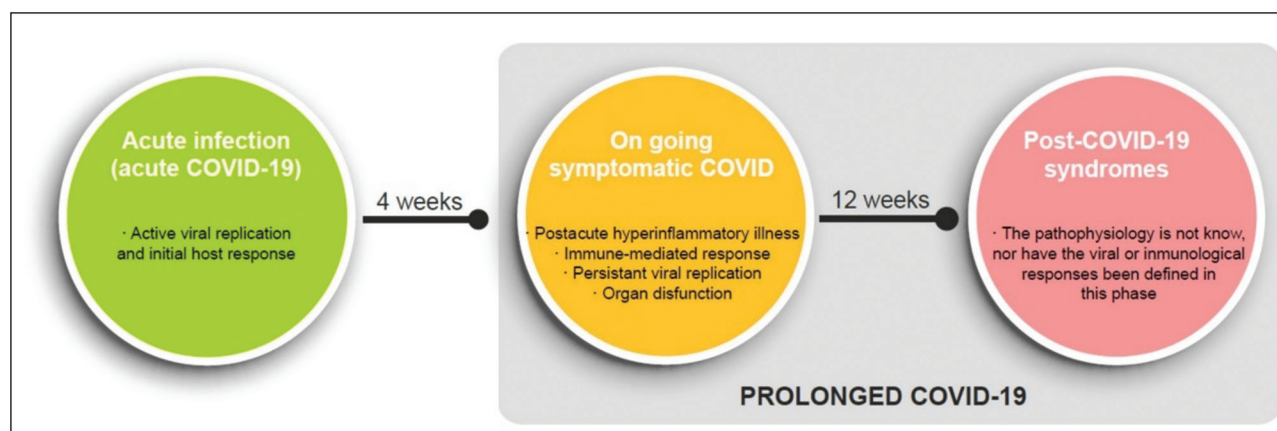


Figure 1: The various evolutionary stages from SARS-CoV-2 infection to post-COVID-19 disease.^[2]

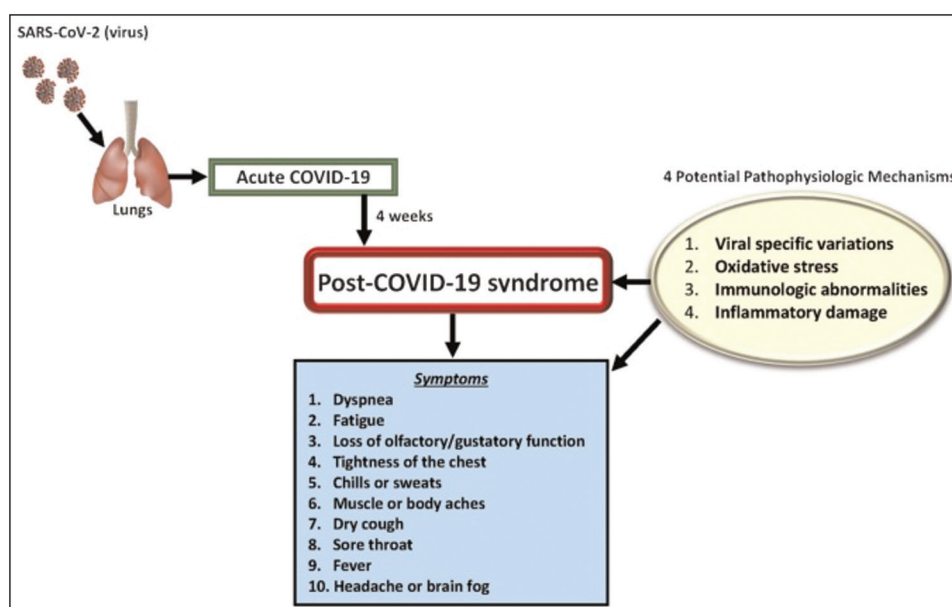


Figure 2: Post-COVID-19 syndrome's potential pathophysiological mechanisms.^[9]

post-COVID syndromes is still mostly unknown, but it is usually related to chronic inflammation.^[7,10]

Previous studies in different countries report various post-COVID symptoms, mainly fatigue, respiratory, and neurological symptoms.^[7,11,12] However, the major concern of post-COVID-19 is the long-term negative impacts on daily functioning and quality of life of COVID-19 survivors.^[13]

We designed a special questionnaire to assess the potential long-term effects of COVID-19. In addition, we studied the correlation between the long-term effects of COVID-19 and comorbidities and the long-term impact of COVID-19 on the mental and physical health of recovered COVID-19 patients.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted on patients who were infected with the coronavirus and gained recovery during the period between February 2022 and June 2022. The ethical approval was obtained from the Ethical Committee of the College of Pharmacy/University of Basra. We created a specific questionnaire to ask patients about their current health and any lingering symptoms they may be experiencing after COVID. This survey aimed to assess the possible long-term effects of COVID-19 infection and the long-term impact of COVID-19 on the mental and physical health of recovered COVID-19 patients. The respondents were asked to confirm their agreement to participate in the study at the start of the questionnaire, and then the questionnaire was filled out online. A total of 915 recovered COVID-19 patients from different age groups participated in the survey.

The questionnaire contained information, such as age, gender, chronic diseases, of coronavirus infection if it occurred before and after taking the vaccine, symptoms experienced by the patient during the period of infection with the coronavirus and the severity of the infection based on WHO guidelines for mild (mild fever, malaise, myalgia, cough, or sore throat), moderate (respiratory symptoms like dyspnea but do not require hospitalization), and severe diseases that require hospitalization or intensive care unit (ICU) admission due to dyspnea, tachypnea, or COVID pneumonia. In addition to the duration of symptoms after recovery and participant thoughts about the long-term effects of COVID-19, “do you think that being infected with the Coronavirus can have far-reaching effects on your psychological or physical health?”

Statistical analysis

All data were analyzed by the SPSS (IBM Corporation, New York, NY) statistical package (Version 19). Chi-square test of independence was applied to find a statistical association. *P* value <0.05 was considered significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to document number EC06 on November 29, 2022 to get this approval.

RESULTS

Demographic data

The present study was performed on 915 Iraqi people previously infected and healed with the COVID-19. The participants' age groups are shown in Table 1. Most of

Table 1: Descriptive criteria of participants included in the study

Parameter	Frequency (%)
Age	
15–25	312 (34.1%)
36–45	251 (27.4%)
46–55	102 (11.1%)
56–65	29 (3.2%)
More than 65	6 (0.7)
Sex	
Male	283 (30.9%)
Female	632 (69.1%)
Comorbid disease	
Hypertension	89 (9.7%)
Diabetes	48 (5.2%)
Asthma	51 (5.6%)
Renal disease	6 (0.7)
Rheumatoid arthritis	54 (5.9%)
Cardiovascular disease	19 (2.1%)
Cancer	1 (0.1%)
No comorbid disease	650 (71%)
Smoking status	
Smoker	112 (12.2%)
Nonsmoker	803 (87.8%)
COVID-19 infection occurs	
Before vaccination	595 (65%)
Postvaccination	177 (19.3%)
Before and after the vaccination	143 (14.1%)
Severity of COVID-19 infection	
Mild	460 (50.3%)
Moderate	416 (45.5%)
Severe	39 (4.3%)
Complaining from post-COVID-19 symptoms	
Yes	619 (67.7%)
No	296 (29.2%)
Duration of post-COVID-19	
1–3 months	269 (29.4%)
3–6 months	56 (6.1%)
More than 6 months	294 (32.1%)

them were middle-aged (<40 years) and most of them were nonsmokers (87.8%). Both sexes were included, but females made up the largest percentage (69.1%). About 650 (71%) of participants have no chronic disease. The remaining subjects have associated comorbidities like hypertension at 89 (9.7%), diabetes at 48 (5.2%), asthma at 51 (5.6%), and rheumatoid arthritis at 4 (5.9%). According to the severity of initial COVID-19 infection, most patients complain of mild infection 460 (50.3%), with moderate 416 (45.5%), and severe infection (who need hospitalization and/or ICU admission) about 39 (4.3%), according to WHO classification. Regarding vaccination, most participants (65%) were infected with COVID-19 prior to vaccination.

Clinical presentations of participants during acute COVID-19 infection

As shown in Table 2, approximately (653, 71.4%) of COVID-19 infections present with fever, fatigue (763, 80.4%), headache (648, 70.8%), sore throat and dry cough (487, 53.2%), difficulty breathing (339, 37%), GIT symptoms (168, 18.4%), and other miscellaneous symptoms (138, 15.4%).

Clinical presentations of post-COVID-19 syndrome

Among 915 participants, about 619 (67.7%) patients report at least one remaining symptom after healing

Table 2: Patients' symptoms during an acute COVID-19 infection

Parameter	Frequency (%)
Fever	653 (71.4%)
Headache	648 (70.8%)
Muscles and joints pain	623 (68.1%)
Vomiting and diarrhea	168 (18.4%)
Fatigue and weakness	736 (80.4%)
Sore throat and dry cough	487 (53.2%)
Difficulty in breathing	339 (37%)
Others	138 (15%)

from the acute COVID-19 virus. These symptoms were variable in duration, ranging from 1 month to more than 6 months, as shown in Table 3. The most frequent residual symptom was fatigue 365 (39.9%), followed by hair loss 286 (31.3%), forgetfulness 263 (28.7%), decrease in mental performance 248 (27%), change in taste or smell 244 (26.7%), depression 218 (23.8%), persistent cough 144 (15.7%), increase frequency of asthmatic attack 124 (13.6%), increase frequency of infection 67 (7.3%), and changes in blood and glucose control 34 (3.7%) and 13 (1.4%), respectively.

Relationships between post-COVID-19 symptoms with age, sex, severity, associated comorbidities, and COVID-19 vaccination.

In Table 4, post-COVID symptoms were assessed regarding different factors like age, sex, smoking, comorbidities, and vaccination. Then the relationship was measured using the chi-square test. There is a nonsignificant relationship between post-COVID-19 syndrome with age and smoking (P value > 0.05). Regarding gender, females were found to be more susceptible to post-COVID-19 syndrome than males [about 466 (73.7%) of females have post-COVID-19 versus 166 (26.3%) who do not have a P -value of >0.001]. In addition, the presence of comorbid disease was significantly related to the occurrence of post-COVID-19 syndrome [195 (73.6%) of patients with comorbidity have post-COVID-19 syndrome versus 70 (26.4%) who do not have a P -value of 0.014].

Regarding the severity of initial coronavirus infection, patients with severe disease have a significantly higher risk of developing post-COVID-19 symptoms after recovery than moderate and mild diseases, 89.7% of patients with severe COVID-19 suffer from post-COVID symptoms, while 78.8% and 55.7% for moderate and mild disease, respectively. Further, the study found that vaccinated people have a lower incidence of developing persistent symptoms after recovery from COVID-19 infection. In Table 5, most of the post-COVID-19 symptoms were found to be lowered after vaccination.

Table 3: The remaining symptoms post-COVID-19 infection

Symptoms	Frequency	Percentage
At least one symptom	619	67.7
Fatigue	365	39.9
Hair loss	286	31.3
Forgetfulness	263	28.7
Decrease in mental performance	248	27
Change in taste or smell	244	26.7
Depression	218	23.8
Persistent cough	144	15.7
Increase the frequency of asthmatic attack	124	13.6
Increased frequency of infection	67	7.3
Change in blood pressure control	34	3.7
Increase in blood glucose level	13	1.4

Table 4: Relation of post-COVID-19 with patients' criteria

	Post-COVID-19 syndrome		Sig. (P-value)*
	Yes	No	
Age			0.152
15–25	222 (71.2%)	90 (28.8%)	
25–35	137 (63.7%)	78 (36.3%)	
35–45	174 (69.3%)	77 (30.7%)	
45–55	67 (65.7%)	35 (34.7%)	
55–65	17 (58.6%)	12 (41.4%)	
More than 65	2 (33.3%)	4 (66.7%)	
Sex			>0.001
Male	153 (54.1%)	130 (45.9%)	
Female	466 (73.7%)	166 (26.3%)	
Comorbidity			0.014
Yes	195 (73.6%)	70 (26.4%)	
No	424 (65.2%)	226 (34.8%)	
Severity			>0.001
Mild	256 (55.7%)	204 (44.3%)	
Moderate	328 (78.8%)	88 (21.2%)	
Severe	35 (89.7%)	4 (10.3%)	
Smoking			0.08
No	561 (68.6%)	257 (31.4%)	
Yes	58 (59.8%)	39 (40.2%)	
COVID-19 occurs			0.001
Before vaccination	419 (70.4%)	176 (29.6%)	
After vaccination	99 (55.9%)	78 (44.1%)	
Before and after vaccination	101 (70.6%)	42 (29.4%)	

*P-value <0.05 is considered significant

Table 5: The relationship between post-COVID-19 infection and vaccination

Post-COVID-19 symptoms	Time of COVID-19 infection regarding COVID-19 vaccination		
	Before vaccination	After vaccination	Before and after vaccination
Fatigue	242 (66.3%)	61 (16.7%)	62 (17.0%)
Hair loss	203 (71.0%)	30 (10.5%)	53 (18.5%)
Forgetfulness	185 (70.3%)	29 (11.0%)	49 (18.6%)
Decrease in mental performance	177 (71.4%)	28 (11.3%)	43 (17.3%)
Change in taste or smell	183 (75.0%)	32 (13.1%)	29 (11.9%)
Depression	144 (66.1%)	32 (14.7%)	42 (19.3%)
Persistent cough	85 (59.0%)	34 (23.6%)	25 (17.4%)
Increase the frequency of asthmatic attacks	183 (64.5%)	32 (12.1%)	29 (23.4%)
Increased frequency of infection	46 (68.7%)	10 (14.9%)	11 (16.4%)
Change in blood pressure control	21 (61.8%)	5 (14.7%)	8 (23.5%)
Increase in blood glucose level	10 (76.9%)	2 (15.4%)	1 (7.7%)

DISCUSSION

The current work aimed to evaluate prevalence and characteristics of post-COVID-19 symptoms in 915 recovered Iraqi patients as the country was hit hard by the pandemic. The present study revealed that 619 (67.7%) patients report at least one persistent symptom post-COVID-19 infection. This result agrees with a cohort study by Sykes *et al.*, which revealed that 80% of hospitalized patients with severe COVID have at least one post-COVID

symptom that persists after recovery.^[14] Another study follows up about 744 recovered Saudi patients and found persistent symptoms in 47.5% of participants.^[15] A study in the USA reported post-COVID symptom in 40% of COVID-19 patients after 8 months of initial illness.^[16] These results may be attributed to differences in study designs, population, inclusion criteria, and/or duration after COVID-19 recovery. The exact etiology of post-COVID syndrome is unknown; however, different

mechanisms are implicated in its pathophysiology which mainly related to prolong inflammation and pathological immune response postinfection which affect multiple systems and account for many of physical and mental symptoms.^[17]

The most frequent symptom in current work is fatigue (39.9%), followed by hair loss (31.3%), forgetfulness (28.7%), decrease in mental performance (27%), a change in taste or smell (26.7%), depression (23.8%), persistent cough (15.7%), and about (13.6%) patients have an increased frequency of asthmatic attacks, as illustrated in Table 3. Fatigue was the most reported persistent symptom in many prospective studies^[8,18,19] and is considered to be multifactorial. Cytokines released during SARS-CoV-2 infection, psychological factors, autoimmunity, and elevated antinuclear antibodies are the main implicated risk factors for post-COVID fatigue.^[20] Among other miscellaneous post-COVID-19 symptom is telogen effluvium (hair loss) which occur in 31.1% of patients with female higher than male. In other studies, hair loss occurs in 25%, 16.5%, and 18.4%,^[8,21,22] respectively, usually in the first 2–3 months after acute infection and is explained by the effect of pro-inflammatory cytokines and microthrombosis on hair follicles.^[17]

Regarding mental function, many symptoms were described by patients postinitial disease like forgetfulness (occur in 28.7% of patients) and a decrease in mental performance (27% of patients). Similar symptoms were reported in other studies, which found that 19% of patients have decreased memorization, about 18% have difficulty concentrating,^[23] and about 34% have memory loss, with 28% concentration disorders.^[24]

A previous study showed that compared to healthy people, COVID-19-infected patients were more susceptible to developing regional abnormalities in the brain that affect memory or change in smell.^[18] In our study, 26.7% of patients still experienced changes in taste or smell and these results agree with another study that showed 22.2% of patients still had olfactory changes 4–6 months post-COVID-19 infection.^[25] Other studies found that the olfactory cortex was believed to be the first specialized area in the central nervous system affected by SARS-CoV-2 and predisposed to the gustatory and olfactory impairment in COVID-19 patients.^[18,26]

Depression was experienced by 23.8% of the patients, which is almost close agreement to the result of Han *et al.* In that study, 23% of COVID-19 survivors had depression 1 year after infection.^[23] Many theories link persistent depression to the direct impacts of viral infection, long-lasting systemic inflammation, the immune response, hospitalization, and ICU admission, corticosteroid medication and social isolation may all play a role in psychological changes associated with COVID-19 infection.^[21,27]

Respiratory symptoms like persistent cough (15.7%) and increased frequency of asthmatic attack (13.6%) was also reported by patients in the current study. In other studies, the prevalence of chronic cough was 2.5%, 4.7%, and 18%,^[28–30] respectively, and probably linked to increase airway hypersensitivity after SARS-CoV-2 infection. Among the other miscellaneous post-COVID-19 symptoms are uncontrolled blood pressure and new-onset hypertension.^[31] Further, COVID-19 may associate with raised blood glucose levels due to many proposed factors like previously undiagnosed diabetes, stress hyperglycemia, steroids, and viral effects on β -cell.^[32,33] Therefore, change in blood pressure and/or blood glucose control are among the post-COVID-19 symptoms that occur in 3.7% and 1.4%, respectively.

An important proportion of the current study is the relationship between occurrence of post-COVID-19 syndrome and multiple patients' criteria [Table 4]. Female gender was more susceptible to post-COVID-19 syndrome than male in this study. This finding agrees with other studies in which female gender are more likely to develop post-COVID-19 symptoms.^[1,23,34,35] It may be due to stronger IgG antibody production in females in the first stages of infection, which could result in a more favorable outcome in women, but may also play a role in maintaining disease manifestations. Hormones may also contribute to the hyperinflammatory status of the acute phase even after recovery.^[34]

An additional finding in this study is that patients presented with the comorbid disease show a high percentage (73.6%) of post-COVID-19 symptoms, in agreement with the study done by Adekunle *et al.*^[36] Persistent symptoms are also more likely in severe cases; about 89% of severe COVID-19 patients have post-COVID-19 symptoms. This finding was in accordance with that of reported by several authors.^[37–40]

Regarding the effect of the vaccine in Table 5, the results show a significant association between nonvaccinated patients and post-COVID-19 symptoms. The vaccine has a good influence on the symptoms as the vaccinated patients showed a much lower percentage of post-COVID-19 symptoms [Table 5] with also the short duration of the symptoms.

This study has strengths of including relatively large number of patients (915) and demonstrates the importance of vaccine as an important factor that lower the incidence of long-term effects of COVID-19 and this might encourage more people to get the vaccine in our country, where many people still refuse vaccination. However, some limitation of this study is the need for a longer follow-up duration and a study of the effects of post-COVID symptom on the functional status of patients.

Finally, more studies are required to assess the long-term inflammatory markers and cytokines levels in patients

with post-COVID-19 syndrome in order to understand the underlying mechanism of this syndrome and predict their future effects.

CONCLUSION

Post-COVID-19 symptoms are common in after recovering from the initial disease. Therefore, there is a need for rehabilitation program and a long-term follow-up and for COVID-19 survivors in order to assess and manage these patients. Female gender, comorbidity, and severity of initial illness are considered important factors that increase the incidence of the long-term effect of COVID-19. Vaccination against SARS-CoV-2 virus significantly lowers the risk of developing post-COVID-19 symptoms.

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Conflicts of interest

There are no conflicts of interest.

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