Clinical and Socio-Demographic Variables Associated With Long COVID-19

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Clinical and Socio-Demographic Variables Associated With Long COVID-19: A Cross-Sectional Study

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Abstract

Considering the importance of long COVID-19 (LC), this study aimed to investigate the relationship between clinical/sociodemographic factors and LC symptoms (LCS). This online cross-sectional study was conducted on 308 people infected with COVID-19 in Alborz, Iran, from April 1 to June 1, 2022. Multivariable logistic regression models were applied to measure the association between the LCS with other variables. Overall, 76.6% of participants had at least one LCS. Results from the multivariate logistic regression analysis showed that females (crude odds ratio [OR] [95% confidence interval (CI)]: 2.725 [1.42, 5.22]), educated persons (3.747 [1.58, 8.84]), people with a higher number of COVID-19 reinfection (2.280 [1.30, 3.97]), having an underlying disease (1.996 [1.01, 3.93]), and COVID-19 severity (3.321 [1.037, 10.635]) had higher odds of LC than others (all $p < .05$). Study findings provide additional clinical/sociodemographic data on risk for LC. These data may inform future research and clinical practice for potential risk identification and early intervention.

Keywords

COVID-19, long-term symptoms, social determinants of health, socioeconomic status

Introduction

During 2 years of the COVID-19 worldwide pandemic, scientific researchers have focused on long-term morbidity from COVID-19. Although the scientific community's understanding of long COVID-19 (LC) is still evolving, and understanding of the diagnoses, phenotypes, and epidemiology is nascent (Bell et al., 2021), LC's health impacts and symptoms have been assessed by a broad range of studies (Aiyegbusi et al., 2021; González-Islas et al., 2022; Nalbandian et al., 2021). It is suggested that more than 20% of people positive for COVID-19 develop post-COVID-19 syndrome (Iqbal et al., 2021).

According to the National Institute for Health and Care Excellence (NICE) guidance, the average recovery time from COVID-19 is 2 to 3 weeks and the long-term effects of COVID-19 are often described as LC. Clinical definitions for COVID-19 at different times include acute COVID-19: signs and symptoms of COVID-19 up to 4 weeks, ongoing symptomatic COVID-19: signs and symptoms of COVID-19 from 4 to 12 weeks; and post-COVID-19 syndrome: signs and symptoms of COVID-19 infection that persist for more than 12 weeks and are not explained by an alternative diagnosis (Shah et al., 2021). The term "long COVID" is commonly used to describe signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more) (NICE, 2021).

Evidence has shown that the most prominent LC symptoms (LCS) were fatigue, dyspnea, muscle/joint pain, headache, cough, chest pain, altered smell/taste, hair loss, cognitive/mental impairments, and diarrhea (Desai et al., 2022; Yong, 2021). Although the mechanisms of long-term complications of COVID-19 infection remain unknown, several pathophysiological mechanisms may be responsible,

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including direct cellular infection, endothelial damage, immune dysregulation, and coagulation (Desai et al., 2022).

Literature has indicated that risk factors of LC may include female sex, more early symptoms, early dyspnea, specific biomarkers (e.g., D-dimer, C-reactive protein, and lymphocyte count), and prior psychiatric disorders (Yong, 2021). Previous studies have shown a higher risk of developing LC with increasing age, female sex, symptom burden, hospitalization during acute COVID-19, presence of comorbidities, smoking, obesity, socioeconomic deprivation, and belonging to an ethnic minority (Carvalho-Schneider et al., 2021; Emecen et al., 2023; Jacobs et al., 2020; Subramanian et al., 2022; Sudre et al., 2021). In addition, a study has indicated that the female sex is a worse predictor of LC, even if the disease is less severe during that phase (García et al., 2022). A prospective cohort study from Iran has shown a significant association between LC and some factors, including age, underlying diseases, acute phase symptoms, weight loss, and history of skin sequel in the acute phase (Larijani et al., 2022).

There is a need for further research into risk factors and socioeconomic determinants related to developing LC for evidence-based service planning and prevention mechanisms, which the NICE guideline has highlighted as a research priority (Thompson et al., 2022). One of the most important things that need more studies in this field is the relationship between LCS and clinical/sociodemographic factors. Therefore, this study aimed to investigate the relationship between these factors and the LCS.

Methods

Design and Participants

We conducted an online cross-sectional study to explore the association between long symptoms of COVID-19 and clinical/sociodemographic factors in Alborz, Iran, from April 1 to June 1, 2022. We used an online survey to collect data from the general population infected with COVID-19 since the beginning of the outbreak of COVID-19 with a positive polymerase chain reaction test, and at least 4 weeks have passed since the onset of their disease. The exclusion criterion was the age <15 and unwillingness to participate in the study. Using convenience sampling, we implemented the survey by posting a link in various social groups through WhatsApp and emails from the general population. A total of 308 participants completed the online survey.

This study protocol was approved by the Ethics Committee of Alborz University of Medical Sciences (IR.ABZUMS.REC.1400.335). Respondent's decision to complete the survey implied consent to participate. At the beginning of the study, respondents were informed that the survey was confidential and anonymous, and their participation was voluntary. They also announced that the survey results would be used for presentations or publications.

Data Collection

Data were completed using a sociodemographic checklist, COVID-19 disease checklist, and socioeconomic status scale (SES). Sociodemographic checklist included questions about age, gender, internationality, education level, marital status, occupation, income, living area, and number of family members, smoking, body mass index (BMI), and the history of underlying disease. COVID-19 disease-related checklist included the onset of the disease, the number of COVID-19 reinfections in a person, the number of COVID-19 vaccines, and the severity of COVID-19 disease (outpatient–hospital admission–intensive care unit [ICU] admission), LCS, and duration of LCS. LCS is defined as the symptoms of COVID-19 that last ≥ 4 weeks (NICE, 2021). LCS in the checklist included cough, dyspnea, fatigue and weakness, headache, hyposmia, hypogeusia, hair loss, sleep disorder, depression, anxiety, memory loss, attention disorder, intolerance to exercise, digestive system problems, chest pain, irregular menstruation, joint pain, and cutaneous signs. SES consisted of six questions, including education, income, economic class, and housing status, which are scored based on a Likert-type scale from 1 to 5, and a total score ranging from 6 to 30. Validity and reliability have been performed in Iran (Eslami et al., 2014).

Statistical Analysis

We used descriptive statistics to analyze survey data using SPSS IBM software, version 20. The demographic characteristics of the study population were summarized using descriptive statistics, mean, standard deviation (*SD*) for continuous variables, and frequency (%) for categorical variables. Univariable and multivariable logistic regression models were applied to measure the association between LC with other variables. Results are presented as crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs). A value of less than 0.05 was considered statistically significant.

Results

A total of 308 people participated in this survey. The majority of participants were female (61%), married (77.6%), bachelor (37.0%), and employed (76.6%). The mean $\pm$ *SD* age of participants was 42.56 ± 11.59 years ranging from 15 to 78 years. The mean $\pm$ *SD* of BMI was 26.54 ± 4.17. Overall, 36.7% of people had a history of underlying disease. Most were hypothyroidism 7.5%, hypertension 6.8%, diabetes 5.2%, and hyperlipidemia 5.2%, respectively. The sociodemographic characteristics of the subjects are shown in Table 1.

76.6% of participants had at least one LCS. The most LCS were fatigue and weakness (43.8%), hair loss (28.2%), and cough (23.7%), respectively. The frequency of LCS is shown in Figure 1.

Table 1. Sociodemographic Characteristics of Subjects.

Variables		No. (%)
Sex	Male	120 (39)
	Female	188 (61)
Educational level	≤Associate degree	88 (28.6)
	Bachelor	114 (37.0)
	<Bachelor	106 (34.4)
Occupational status	Un-unemployed	72 (23.4)
	Employed	236 (76.6)
Income, Rial	≤100,000,000	173 (56.2)
	>100,000,000	135 (43.8)
History of underlying disease	Yes	113 (36.7)
Marital status	Single	69 (22.4)
	Married	239 (77.6)
Smoking	Yes	43 (14.0)
Severity of COVID-19 disease	Outpatients	269 (87.3)
	Hospital admission	37 (12.0)
	ICU admission	2 (0.6)
Long-COVID symptoms	Yes*	236 (76.6)

Note. ICU = Intensive Care Unit.
*Yes (long-term symptoms) is a symptom of COVID-19 lasting ≥4 weeks.

The mean (±*SD*) of the SES score was 14.59 (±3.108). After logistic regression analysis, no significant differences existed between the SES score and LCS of COVID-19 disease ($p = .061$).

Results from the univariate logistic regression analysis showed that females (crude OR [95% CI]: 4.198 [2.40, 7.33], persons who were in bachelor/≤associate degree (3.066 [1.62, 5.79]), >bachelor/≤associate degree (4.20 [2.10, 8.39]), people with a higher number of COVID-19 reinfection during pandemic (2.816 [1.65, 4.80]), smokers (0.452 [0.22, 0.89]), and having the underlying disease (2.033 [1.01, 4.06]) had higher odds of LCS than others (all $p < .05$).

After multivariate logistic regression analysis, females (crude OR [95% CI]: 2.725 [1.42, 5.22]), persons who were in education >bachelor/≤associate degree (3.747 [1.58, 8.84]), people with a higher number of COVID-19 reinfection during pandemic (2.280 [1.30, 3.97]), having the underlying disease (1.996 [1.01, 3.93]), and more severe COVID-19 (3.321 [1.03, 10.63]) had higher odds of LCS than others (all $p < .05$) (Table 2).

Discussion

In the current study, we evaluated the long-term symptoms of COVID-19 and its association with clinical/sociodemographic factors. In our study, 76.6% of participants had at least one LCS. The most LCS were fatigue and weakness (43.8%), hair loss (28.2%), cough (23.7%), and hyposmia (18.5%), respectively. In line with our study, a meta-analysis study demonstrated that 80% of the infected patients with COVID-19 had one or more LCS. The most common symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), dyspnea (24%), and anosmia (21%) (Lopez-Leon et al., 2021). Some LCS were different from our study, which may be due to differences in the study populations, methods, follow-up periods, and sample size. Another study revealed that fatigue, respiratory, and cognitive problems occurred in 51.0, 60.4, and 35.4% of LC cases, respectively (Hanson et al., 2022). In addition, a study in the United Kingdom showed 86% of patients had at least one residual symptom at follow-up. The most long-term symptoms were anxiety, fatigue, and myalgia (Sykes et al., 2021).

Results from the multivariate logistic regression analysis showed that females, persons with higher-level education, people with a higher number of COVID-19 reinfection during the pandemic, persons with hospitalization due to COVID-19 disease and having underlying condition had higher odds of LCSs than others.

In line with our study, Fernandez-de-Las-Penas found that women are more likely to develop symptoms of COVID-19 8 months after contracting the virus than men (Fernández-de-Las-Peñas et al., 2022). In addition, many studies have reported gender as a risk factor associated with post-COVID complications and greater stress after the disease (Iqbal et al., 2021; Mahmoodi et al., 2021). Another study revealed that gender predicts COVID-19 complications such as dyspnea, fatigue, chest pain, and palpitation (Pelà et al., 2022; Yong, 2021). Knowing the different impacts of COVID-19 on men and women is a crucial step to understanding the pathophysiology and its consequences better to promote healthcare interventions. One of the leading causes of these differences is the biological and immunological disparity in the expression of angiotensin-converting enzyme receptors and interleukin-6 production between women and men (Fernández-de-Las-Peñas et al., 2022; Ortona et al., 2021).

According to the present study's results, education level was one of the predictors of LCS after COVID-19. Education is one of the essential socioeconomic factors. Most studies in infectious and non-communicable diseases have suggested the relationship between this factor and health outcomes and have suggested education as an independent factor for long-term complications of infectious diseases (Gupta et al., 2022). Other studies have shown that illiterate or low-educated people have more complications and deaths due to corona than other groups. Delay submitting reports and referring to medical centers is one of the leading causes of complications and deaths in these people. However, the relationship between low socioeconomic status with complications and death from COVID-19 is not specific (Clouston et al., 2021; Sharma et al., 2022). The recent difference in our results may be due to the more reporting and follow-up of people with a higher level of education compared to other groups. In a study, Darvishpour et al. (2016) found that the level of education has a significant relationship with the level of health literacy, and patients with sufficient health literacy seek treatment and control their disease symptoms more than others, and as a result, are more successful (Darvishpour et al., 2016).

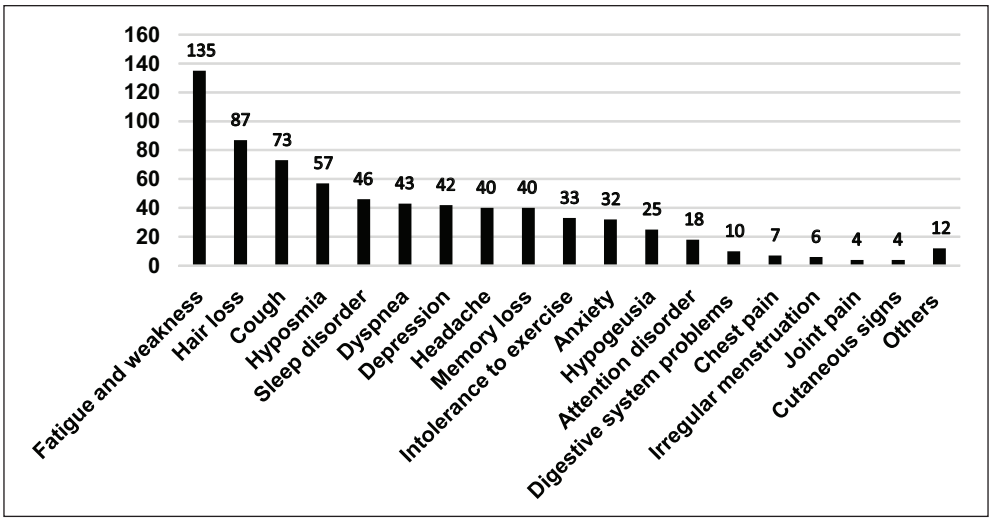

Figure 1. The frequency of long COVID-19 symptoms.

Table 2. Association Between Variables and Long COVID-19 Symptoms: Logistic Regression Analysis.

		Univariate logistic regression		Multivariate logistic regression	
Variables		Crude OR [95% CI]	*p* Value	Adjusted# OR [95% CI]	*p* Value
Sex	Male	1		1	
	Female	4.198 [2.402, 7.336]	.000***	2.725 [1.422, 5.221]	.003**
Age		0.987 [0.965, 1.01]	.543	—	—
Living area	Urban	1		1	
	Rural	0.451 [0.074, 2.751]	.388	—	—
	BMI	0.971 [0.912, 1.033]	.347	—	—
Occupation	Un-unemployed	1		1	
	Employed	0.741 [0.385, 1.425]	.369	—	—
Education	≤Associate degree	1		1	
	Bachelor	3.066 [1.623, 5.793]	.001**	2.089 [0.991, 4.405]	.053
	<Bachelor	4.20 [2.102, 8.391]	.000***	3.747 [1.587, 8.844]	.003**
Marital status	Single	1	1	1	
	Married	1.468 [0.802, 2.685]	.213	—	—
Family number		0.969 [0.778, 1.208]	.782	—	—
Income	≤100,000,000	1		1	
	>100,000,000	1.042 [0.612, 1.775]	.880	—	—
SES		1.085 [0.996, 1.181]	.061	0.972 [0.876, 1.079]	.595
The number of COVID-19 reinfections		2.816 [1.650, 4.806]	.000***	2.280 [1.307, 3.977]	. 004**
Smoking	No	1		1	
	Yes	0.452 [0.228, 0.897]	.023*	0.990 [0.434, 2.258]	.981
Number of COVID-19 vaccine		0.923 [0.600, 1.421]	.717	—	—
Severity of COVID-19	No hospitalization	1		1	
	Hospitalization	2.861 [0.980, 8.357]	.055	3.321 [1.037, 10.635]	.043*
Underlying disease	No	1		1	
	Yes	2.442 [1.323, 4.509]	.004**	1.996 [1.013, 3.933]	.046*

Note. Adjusted# for all variables with $p < .2$ in the univariate model. OR = odds ratio; CI = confidence interval; BMI = body mass index; SES = socioeconomic status scale.
*$p < .05$. **$p < .01$. ***$p < .001$.

In our study, having underlying diseases and the number and severity of COVID infections in a person were one of the factors related to LCS. This finding is consistent with a retrospective cohort study by Ayoubkhani et al. (2021) conducted on COVID-19 patients. They found that the mortality and complications of the COVID-19 disease were higher in patients with a history of hospitalization than in others. However, the available evidence shows many changes in the estimates of the prevalence, incidence and influential factors of the LC due to the differences in the studied populations, survey methods, follow-up periods, and sample size; therefore, conducting more studies in this field is essential.

Limitations

Our study had some limitations: first, asking questions online about disease symptoms will have a high recall bias, which is one of the limitations of our research. Second, because the questionnaire was online, people with a higher socioeconomic level may have more access to participate in the study. Third, Most participants in our study were in the middle age period because older adults do not have enough knowledge of modern communication tools. Fourth, the number of samples in our study who were hospitalized, especially in the ICU, was minimal; further studies must be performed.

Conclusion

This study showed that in addition to the severity and number of reinfections with COVID-19 in a person, some sociodemographic factors, including gender, education, and history of underlying disease, are related to the LC. Therefore, to reduce the disease burden of this pandemic, focusing on these factors can effectively reduce the risks LC. In national policies, governments are advised to be active in other public sectors, such as the Ministry of Education, Ministry of Welfare, and other organizations alongside health organizations. In addition, the private sector and non-governmental organizations should also participate in designing and implementing policies and interventions.

Author Contributions

NG was responsible for the acquisition of data. ZM and NG analyzed and interpreted the patient data. All authors contributed to the concept, design, drafting, and revising the article. All authors critically reviewed content and approved the final version for publication.

Availability of Data and Materials

The datasets used during the current study are available from the corresponding author upon reasonable request.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval and Consent

This study was performed by the latest version of the Declaration of Helsinki and with the approval of the research ethics committee of Alborz University of Medical Sciences (IR.ABZUMS.REC.1400.335). Respondent's decision to complete the survey implied consent to participate. At the beginning of the study, respondents were informed that the survey was confidential and anonymous, and their participation was voluntary. They also reported that the survey results would be used for presentations or publications.

Consent to Publish

Informed consent was obtained from all subjects who participated.

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