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# Long COVID syndrome: psychological and sexual dysfunction among survivors of COVID-19 infection

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**Background:** To explore the neuropsychiatric symptoms, sleep disturbances, and sexual dysfunction in patients with long COVID'syndrome, which can help in building better follow-up strategies for coronavirus disease 2019 (COVID-19) survivors. **Material and methods:** A cross-sectional research was undertaken at the premises of a psychiatry unit at a tertiary care unit in Karachi, Pakistan, between August 2022 and April 2023. All individuals aged 18 years or older, who had a history of contracting COVID-19 infection in the last 12 months presented to the department of Psychiatry with neuropsychiatric symptoms were recruited. Using a predefined questionnaire, data was collected from the participants. A linear logistic regression was used to find the impact of age, sex, hospitalization, and duration of home isolation on the likelihood of persistent neuropsychiatric symptoms or sexual dysfunction.

**Results:** A total of 457 patients were included. It was found that individuals were less likely to experience neuropsychiatric symptoms as age increased (OR = 0.968, 95% CI: 0.949–0.986, P = 0.001). Females were 4.8 times more likely to experience neuropsychiatric symptoms than males, and the association was extremely significant (OR = 4.851, 95% CI: 3.085–7.626, P < 0.0001). An increase in age raised the odds of having sleep disturbances among the survivors by 2.7 times (OR = 2.672, 95% CI: 2.654–2.684, P < 0.0001). The odds of having sleep disturbances were three times more likely in female participants as compared to male participants (OR = 3.00, 95% CI: 1.771–5.094, P < 0.0001).

**Conclusion:** The majority of the COVID-19 survivors are presenting with persistent neuropsychiatric and sexual symptoms in our setting. Therefore, it is necessary to maintain proper follow-up with the survivors of COVID-19 and counsel the patients to inform the family physician if these symptoms persist for longer than a month. Increasing such practices of regular follow-ups with COVID-19 survivors can help in detecting early neuropsychiatric and sexual changes.

Keywords: COVID-19, erectile dysfunction, insomnia, libido, long COVID syndrome, neuropsychiatric symptoms

# Introduction

Coronavirus disease 2019 (COVID-19), which first appeared more than 2 years ago, is still a serious public threat. This burden

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#### HIGHLIGHTS

- It was found that individuals were less likely to experience neuropsychiatric symptoms as age increased (OR = 0.968, 95% CI: 0.949–0.986, *P* = 0.001).
- Females were 4.8 times more likely to experience neuropsychiatric symptoms than males and the association was extremely significant (OR = 4.851, 95% CI: 3.085-7.626, P < 0.0001).
- An increase in age raised the odds of having sleep disturbances among the survivors by 2.7 times (OR = 2.672, 95% CI: 2.654–2.684, *P* < 0.0001).
- The odds of having sleep disturbances were three times more likely in female participants as compared to male participants (OR = 3.00, 95% CI: 1.771–5.094, *P* < 0.0001).

is increased by the fact that a sizable proportion of COVID-19 recovered patients suffer from persistent symptoms that have substantially limited their capacity to function and interfered with their everyday activities<sup>[1,2]</sup>. COVID-19 survivors may develop long-COVID syndrome, which is now emerging as a post-COVID disorder regardless of the age or severity of the initial infection<sup>[2–4]</sup>.

Among COVID-19 survivors, unusual long lasting symptoms including excessive exhaustion, dyspnea, brain fog, anxiety, and mood disturbances can linger for months to years<sup>[5]</sup>. Some other

symptoms of long COVID syndrome may include sexual dysfunction, headaches, and sleep disturbances<sup>[6,7]</sup>. This suggests that the underlying inflammatory pathology continues even after the initial acute symptoms have subsided<sup>[8]</sup>. The immune response to the COVID-19 virus is thought to be predominantly responsible for the emergence of these persistent symptoms, in contrast to the viral infection, presumably via promoting a continuing inflammatory process<sup>[9,10]</sup>.

The frequency with which these symptoms remain has not yet been thoroughly documented, although a systematic review and meta-analysis revealed that the global prevalence of long COVID syndrome was  $0.49\%^{[9]}$ . In Asia (0.51%), the prevalence was highest as compared to Europe (0.44%) and North America  $(0.31\%)^{[9]}$ .

There is a major paucity of literature exploring the epidemiology and symptomatology of long COVID syndrome. Thus, the goal of this study was to explore the persistent neuropsychiatric symptoms, sleep disturbances, and sexual dysfunction among COVID-19 survivors.

#### **Materials and methods**

A cross-sectional research was undertaken at the premises of a psychiatry unit at a tertiary care unit in Karachi, Pakistan, between August 2022 and April 2023. The protocol for the study was registered at Figshare # 10.6084/m9.figshare.23608491 (https://doi.org/10.6084/m9.figshare.23608491.v1). IRB approval was taken for this study as it include human participants. The ethical committee approved the research project, and an approval letter was issued with reference # F.2-81/2022-GENL/238/JPMC. Survivors of COVID-19 who presented to the psychiatry department between the months of August 2021 and July 2022 were requested to visit the department for a follow-up visit. Almost 550 patients were invited to visit the department, out of which 457 accepted the invitation.

All individuals aged 18 years or older who had a history of contracting the COVID-19 infection in the last 12 months and presented to the department of psychiatry with mental health symptoms including sleep disturbances, mood swings, anxiety, et cetera, were recruited. Exclusion criteria included all non-confirmed COVID-19 cases, those with chronic fatigue syndrome or patients with a previous diagnosis of neuropsychiatric illness or erectile dysfunction prior to a COVID-19 diagnosis were excluded from the study. Patient recruitment was based on a nonprobability convenience sampling technique.

The authors determined the sample size using the sample size formula for proportion of disease on OpenEpi software. By keeping the prevalence of long COVID-19 syndrome as reported by Bai *et al.*<sup>[11]</sup> as 69%, a sample size of 328 was determined.

All individuals who presented to the Psychiatry Department with complaints of persistent mental health issues after COVID-19 recovery were enrolled. All participants who gave informed verbal and written consent underwent a short interview, which was conducted by the principal investigator.

A patient was considered recovered from acute COVID-19 if 10 days had passed since symptom onset with an additional three asymptomatic days (no detectable fever or pulmonary symptoms). A patient was labeled with long COVID syndrome if he or she had physical symptoms and/or neuropsychiatric or neurological, and/ or sexual dysfunction that persisted for greater than 12 weeks https://www.england.nhs.uk/coronavirus/wp-content/uploads/ sites/52/2020/10/C0840\_PostCOVID\_assessment\_clinic\_gui dance\_5\_Nov\_2020.pdf - Last Accessed 23/11/20. For the context of this study, the authors mainly focused on three main areas of symptoms: (i) neuropsychiatric symptoms; (ii) sexual dysfunction; and (iii) sleep disturbance.

For the assessment of neuropsychiatric symptoms, sleep disturbances, and sexual dysfunction, the researchers asked direct questions from the patients whether the participant was experiencing any symptoms at the time of data collection or not. For the assessment of depression and anxiety, proper validated scales were used, including the patient health questionnaire (PHQ-9) and generalized anxiety scale (GAD-7)<sup>[12,13]</sup>.

All data were recorded in a predesigned questionnaire at the outpatient department of the psychiatry unit, including the sociodemographics and clinical information related to COVID-19 (i.e. hospitalization, ICU admission, hospitalization, et cetera). The severity of COVID-19 was judged by the need for hospitalization.

The researchers ensured the participants that the data would remain confidential and that no third party would be involved during data analysis. Furthermore, to maintain the anonymity of the participants, no personal identifiers like name, address, or cell phone number were documented. The participants were compensated for their transportation expenses by the department.

For data analysis, IBM SPSS Version 25 was used. Data cleaning was done by removing cases with incomplete form inputs. Secondly, the frequencies and proportions were determined for categorical or binary variables such as sex, levels of education, and persistence of symptoms, among others. Thirdly, for quantitative variables such as age, duration of symptoms, or hospitalization, the mean and SD were determined. Fourthly, binary logistic regression was performed to ascertain the impact of age, sex, home isolation, and duration of isolation on the likelihood that the patient would have neuropsychiatric symptoms or sexual dysfunction. Odds ratios were determined by calculating the inverse log of the regression coefficients. A P-value of <0.05 was taken as the threshold for statistical significance. The data was illustrated using frequency tables. This article has been documented in line with the strengthening the reporting of cohort, cross-sectional, and case-control studies in surgery (STROCSS) criteria<sup>[14]</sup>.

#### **Results**

The sociodemographic and significant clinical history are presented in Table 1. The mean age of patients was  $33.86 \pm 13.58$  years, ranging between 18 and 77 years.

Table 2 shows the neuropsychiatric symptoms and the rate of anxiety and depression among participants. It was found that 146 (32.1%) had anxiety while the rate of depression was 22.6%. The most common symptom was fatigue or lethargy.

Table 3 illustrates the linear regression model for predicting the occurrence of neuropsychiatric symptoms in patients with a history of COVID-19. It was found that individuals were less likely to experience neuropsychiatric symptoms as age increased (OR = 0.968, 95% CI: 0.949-0.986, P = 0.001).

Females were 4.8 times more likely to experience neuropsychiatric symptoms than males and the association was extremely significant (OR = 4.851, 95% CI: 3.085-7.626, P < 0.0001).

Table 1		
Demograph	ics and clinical history of participants.	

Age (years)	33.86 ± 13.58
Sex	
Male	146 (31.9%)
Female	311 (68.1%)
Level of education	
Uneducated	5 (1.1%)
Primary and higher secondary school	76 (16.7%)
Graduate	237 (52%)
Postgraduate	138 (30.3%)
Severity of COVID-19	
Home isolation	379 (82.9%)
Hospitalization	78 (17.1%)
Duration of home isolation	13.64 ± 6.55
Admission to ICU	17 (3.7%)

Hospitalization and intensive care did not significantly correlate with neuropsychiatric symptoms.

An increase in age raised the odds of having sleep disturbances among the survivors by 2.7 times (OR = 2.672, 95% CI: 2.654–2.684, P < 0.0001). The likelihood of sleep disturbances decreased with increased duration of home isolation (OR = 0.967, 95% CI: 0.933–0.997, P < 0.03). The odds of having sleep disturbances were three times more likely in female participants as compared to male participants (OR = 3.00, 95% CI: 1.771–5.094, P < 0.0001) (Table 4).

The frequency of decreased libido was 13.3% in males; erectile dysfunction was 7%, while eight males suffered from premature ejaculation. Menstrual irregularities (18.2%) were the most common reproductive symptom among females, followed by decreased libido (10.5%) and dyspareunia (10.3%) (Table 5).

Age, duration of home isolation, hospitalization, and ICU admission did not increase the odds of having sexual dysfunction among the study population (Table 6).

#### Discussion

The present study's findings are in line with the existing literature. A meta-analysis assessed 19 studies and 11 324 patients for the

# Table 2

Neuropsychiatric symptoms among study population.

Symptoms	N (%)
Anxiety	146 (32.1)
Panic attacks	63 (13.8)
Depression	103 (22.6)
Disturbance in sleep	116 (25.4)
Suicidal ideation	21 (4.6)
Palpitations	80 (17.5)
Vertigo	101 (22.2)
Nervousness	79 (17.3)
Feeling emptiness or hopelessness	55 (12.1)
Nightmares	36 (7.9)
Mood swings	100 (21.9)
Memory lapse	73 (16)
Anger outbursts	51 (11.2)
Loss of smell	238 (52.2)
Loss of taste	220 (48.2)
Malaise	142 (31.1)
Fatigue/lethargy	351 (77)

Та	bl	е	3	

Logistic regression model for predicting occurrence of neuropsychic symptoms in COVID-19 survivors.

Predictors	<i>N</i> /Mean	Odds ratio	95% CI (upper, lower)	Р
Age	33.86 ± 13.58	0.968	(0.949-0.986)	0.001
Duration of home isolation	15.3 ± 9.2	0.943	(0.908–0.98)	0.003
Sex				
Male	146	REF	REF	REF
Female	311	4.851	(3.085-7.626)	< 0.0001
ICU Admission				
No	440	REF	REF	REF
Yes	17	0.000	(0.000-0.000)	0.998
Management				
Home isolation	386	REF	REF	REF
Hospitalized	71	1.399	(0.711–2.75)	0.331

incidence of persistent neuropsychiatric symptoms among patients with a history of COVID- $19^{[15]}$ . Premraj *et al.*<sup>[15]</sup> revealed that the distribution of neurological and neuropsychiatric symptoms encompassed fatigue (37%), cognitive issues (32%), memory lapse (27%), attention disorder (22%), muscle pain (18%), decreased or absence of sense of smell (12%), headache (10%), sleep disturbances (31%), anxiousness (23%), and depression (12%). Another meta-analysis by Badenoch et al.<sup>[16]</sup> showed that the most common neuropsychiatric symptom was sleep disturbance with a cumulative proportion of 27.4%, followed by fatigue (24.4%). The incidence of anxiety was 19.1%. In the present study, the frequency of sleep disturbance, anxiety, and depression were 25.4, 32.1, and 22.6%, respectively. Furthermore, we found that the odds of having neuropsychiatric symptoms and sleep disturbances were 4.8 and 3 times more likely in female participants as compared to male participants, respectively. A study found that females are more susceptible to anxiety, uncertainty, and depression because of higher levels of pathogen disgust sensitivity<sup>[17]</sup>. In contrast, a meta-analysis conducted on COVID-19 patients revealed no discernable difference between females and males in terms of depression, anxiety, and sleep disturbances<sup>[18]</sup>.

Table 4

Logistic regression model for predicting occurrence of sleep
disturbances in COVID-19 survivors.

Predictors	<i>N</i> /Mean	Odds ratio	95% Cl (Upper, Lower)	Р
Age	33.86 ± 13.58	2.672	(2.654-2.684)	< 0.0001
Duration of home isolation	15.3 ± 9.2	0.965	(0.933–0.997)	0.035
Sex				
Male	146	REF	REF	REF
Female	311	3.003	(1.771-5.094)	< 0.0001
ICU Admission				
No	440	REF	REF	REF
Yes	17	0.923	(0.296-2.88)	0.89
Management				
Home isolation	386	REF	REF	REF
Hospitalized	71	1.388	(0.731–2.637)	0.316

Table 5	
Male and fer	nale sexual symptoms among study population.

	N (%)
Male symptoms	
Decreased libido	19 (13.3)
Premature ejaculation	8 (5.6)
Erectile dysfunction	10 (7)
Female symptoms	
Vaginal dryness	20 (6.4)
Change in menstrual cycle	57 (18.2)
Dyspareunia	32 (10.3)
Decreased libido	33 (10.5)

Irreversible tissue damage, such as that of the heart, brain, and lungs, as well as pathological inflammation, may be the cause of long COVID syndrome. Women, early dyspnea, past mental problems, and certain biomarkers (such as D-dimer, C-reactive protein, and total lymphocyte count) may all be interlinked risk factors; however, further exploration is needed to support these claims<sup>[19]</sup>.

Certain comorbidities and pre-existing conditions might also place individuals at a higher risk of long COVID syndrome. A case–control study on migraine patients was conducted by Magdy *et al.*<sup>[20]</sup>, who reported that fatigue (OR = 1.662, 95% CI: 1.064–2.596, P = 0.025), loss or decreases in sensation of smell (OR = 2.06, 95% CI: 1.164–3.645, P = 0.012), depression (OR = 2.259, 95% CI: 1.284–3.975, P = 0.004), anxiety (OR = 3.267, 95% CI: 1.298–3.739, P = 0.003), and headache (OR = 3.148, 95% CI: 1.616–6.136,  $P \le 0.001$ ) were more likely to occur in patients with migraine as compared to controls. However, the study included patients only 3 months after

#### Table 6

Logistic regression model for predictors of sexual symptoms in
male and female participants.

Predictors	<i>N</i> /Mean	Odds ratio	95% CI (Upper, Lower)	P	
Model for female participants					
Age	34.3 <u>+</u> 13.6	1.012	(0.944-1.030)	0.191	
Duration of home	13.8 <u>+</u> 6.2	0.993	(0.955–1.034)	0.742	
isolation					
ICU Admission					
No	303	REF	REF	REF	
Yes	8	2.314	(0.525–10.207)	0.268	
Management					
Home isolation	273	REF	REF	REF	
Hospitalized	38	1.297	(0.591-2.844)	0.517	
Model for male participa	ints				
Age	32.9 <u>+</u> 12.8	1.020	(0.983–1.058)	0.289	
Duration of home	13.4 ± 7.2	1.054	(0.997-1.114)	0.062	
isolation					
ICU Admission					
No	137	REF	REF	REF	
Yes	9	1.781	(0.287-11.060)	0.536	
Management					
Home isolation	113	REF	REF	REF	
Hospitalized	33	0.767	(0.259–2.271)	0.632	

recovering from a severe COVID-19 infection, whereas in our study we included all COVID-19 survivors for the past 12 months.

Sexual dysfunction is one of the many known features of COVID-19 as the disease is known for its hyperinflammation state, which leads to a myriad of symptoms. The possible onset of erectile dysfunction appears to be associated with endothelial dysfunction, preclinical hypogonadism, psychological distress, and poor respiratory blood oxygenation<sup>[20]</sup>. In the present study, we found that the frequency of erectile dysfunction was 7% while eight males suffered from premature ejaculation. Among females, menstrual irregularities, decreased libido, and dyspareunia were the most common sexual and reproductive symptoms. However, our regression model could not find any significant association of sexual dysfunction in either males or females with age, duration of isolation, hospitalization, or ICU admission. There is a major paucity of literature that explores the persisting sexual dysfunction in survivors of COVID-19. A systematic review by Bakr et al.<sup>[21]</sup> explored erectile dysfunction in men during the COVID-19 pandemic. The three articles that the authors assessed revealed an increase in erectile dysfunction during the pandemic. Rates of erectile dysfunction ranged from 32 to 87% among the study populations. Anxiety and depression were both linked with high rates of sexual dysfunction.

This study's strength lies in its comprehensive approach, offering a detailed analysis of the neuropsychiatric symptoms, sleep disturbances, and sexual dysfunction among survivors of COVID-19. By evaluating a significant sample size, our study has shed light on these under-explored and yet crucial aspects of post-COVID recovery. To the best of our knowledge, this is one of the pioneering research projects in Karachi, Pakistan, focusing specifically on long COVID syndrome and its neuropsychiatric implications and sexual dysfunctions.

Our study outcomes are consistent with existing research, confirming the high prevalence of neuropsychiatric symptoms and sleep disturbances among COVID-19 survivors. However, the study expands on previous findings by additionally considering the incidence and factors associated with sexual dysfunction, a less frequently addressed consequence of COVID-19 infection. The difference in the occurrence of these symptoms based on sex, with women being more susceptible to neuropsychiatric symptoms and sleep disturbances, also echoes earlier research. This correlation might be attributable to females having higher levels of pathogen disgust sensitivity, making them more prone to anxiety, uncertainty, and depression.

In terms of sexual dysfunction, the study could not find any significant association with age, duration of isolation, hospitalization, or ICU admission in either males or females. The paucity of literature exploring sexual dysfunction in COVID-19 survivors indicates the need for further research in this area. Given the potential impacts on quality of life and psychological well-being, understanding the underlying causes and potential treatments for these symptoms is crucial.

Our study also encourages the investigation of long COVID syndrome in patients with different comorbidities or pre-existing conditions, as they may have a higher risk. Although our research provided valuable insights into the neuropsychiatric symptoms, sleep disturbances, and sexual dysfunction among COVID-19 survivors, its conclusions are not exhaustive and should be taken as a starting point for more extensive future investigations.

We recognize that our research design, particularly the use of a nonrandomized technique for participant recruitment, may limit the generalizability of our findings. Therefore, we encourage future studies to incorporate randomized participant selection and potentially larger, more diverse populations. Moreover, considering the multiorgan involvement in COVID-19, comprehensive studies covering all potential long-term effects of COVID-19 should be conducted. Furthermore, future research could delve into possible interventions and support strategies for patients experiencing persistent symptoms after recovering from COVID-19.

#### Conclusion

Our study findings revealed that survivors of COVID-19 suffer from a myriad of persistent neuropsychiatric and sexual symptoms. Elder individuals and females were more likely to experience sleep disorders. Furthermore, females had greater odds of experiencing neuropsychiatric symptoms than males. Decreased libido in males and menstrual irregularities in women were the most common sexual symptoms reported. Therefore, it is necessary to maintain proper follow-up with the survivors of COVID-19 and counsel the patients to inform the family physician if these symptoms persist for longer than a month and documenting such practices will aid in the future development of a more systematic follow-up strategies in such cases.

### **Ethical approval**

Jinnah Postgraduate Medical Center, Karachi, 75510. IRB Reference no. NO.F.2-81/2022-GENL/238/JPMC.

#### Consent

Patient privacy was ensured and a written consent was obtained from every study participant.

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None.

# Author contribution

S.A.K.: conceived the topic idea, did study designing and manuscript writing; R.A., S.K., R.R.K., S.U., R.R., H.A., and J.A.H.: manuscript writing and data collection; K.A. and M.A.: data cleaning and statistical analysis; J.K., B.P., and S.B.: manuscript writing and editing; J.A.D.: did proof reading and final approval of the manuscript.

#### **Conflicts of interest disclosure**

The authors declare that they have no conflicts of interest.

# Research registration unique identification number (UIN)

- 1. Name of the registry: not applicable.
- 2. Unique identifying number or registration ID: not applicable.
- 3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

# Guarantor

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#### Data availability statement

None.

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