Neurology Asia 2022; 27(4) : 899 – 908

Post-COVID-19 prolonged neurological symptoms and characteristics: A face-to-face survey study

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Abstract

Background: COVID-19 was declared as a pandemic by World Health Organization on March 11, 2020, and still constitutes a serious health problem affecting millions of people across the world. The evaluation and follow-up of ongoing and/or newly developing neurological involvement after recovery from COVID-19 are important. This study aims to reveal post-COVID-19 neurological symptoms and risk factors for their development. *Methods:* Patients over the age of 18 years who applied to centers, at least 4 weeks after COVID-19 infection and agreed to participate in the study were included in this cross-sectional study between January 20 and March 15, 2021. The patients were evaluated face to face, and their sociodemographic data, medical history, post-COVID-19 neurological symptoms, treatments, and Beck Depression Inventory scores were recorded. All statistical analyses were performed using SPSS 23 for Windows software package (SPSS Inc., Chicago, IL). *Results:* Four hundred patients were included in this study, an average of 108+5.12 days had passed after the onset of COVID-19. The rate of post-COVID-19 neurological involvement was 73.3%, and the top 3 most common symptoms were headache (47%), myalgia (43%), and sleep disturbance (39%). Having depression (OR: 4.54, 95% Cl :1.88-10.96), female gender (OR:2.18, 95% Cl :1.36-3.49), hospitalization (OR: 2.01, 95% Cl :103-3.64), and usage of favipiravir (OR:2.07 95 Cl :1.15-3.72) were determined as independent predictors of developing prolonged neurological symptoms.
Conclusion: The long-term consequences of COVID-19 remain uncertain. It should be remembered that neurological symptoms are very common in post-infectious patients and long-term follow-up may be required in the management of this condition.

Keywords: SARS-CoV-2, post-COVID-19 syndrome, long-term effects, neurological manifestations, neurologic symptoms, neurology

INTRODUCTION

Coronavirus disease-19 (COVID-19), which started in Wuhan, China in December 2019, soon became a global serious health problem declared as a pandemic by World Health Organization (WHO) on March 11, 2020. COVID-19 primarily starts in the respiratory tract and causes severe acute respiratory failure syndrome (SARS). The virus responsible for the disease has been identified as the new beta coronavirus, SARS-CoV-2.[1,2] The disease has a clinical spectrum accompanied by a series of serious signs and symptoms that can involve multiple organs and can lead to a high level of mortality.[1,2] The most common symptoms of COVID-19 include fever, fatigue, dry cough, loss of appetite, dyspnea, myalgia, and headache.[3,4]

COVID-19 targets the angiotensin-converting enzyme 2 (ACE-2) receptor expressed in various tissues.[5-7] In addition to ACE-2 downregulation, SARS-CoV-2 spike glycoproteins are responsible for immune system activation and inflammation, and this process results in endothelial dysfunction and hyper inflammation in distant organs, as well as the respiratory tract.[6,7] Endothelitis and systemic hyper inflammation contribute to the deterioration of the blood-brain barrier, trigger immune cell entry into the central nervous system, and provoke further neuroinflammatory processes.[5-8] Among the possible mechanisms, underlying neurological manifestations are direct viral neuronal damage,

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Date of Submission: 14 October 2021; Date of Acceptance 21 October 2022

https://doi.org/10.54029/2022stz

secondary hyper inflammation, para- and post-infectious inflammatory response, immune-mediated disorders, sepsis, hyperpyrexia, hypoxia, hyper coagulopathy, and systemic effects of the critical disease.[4,9-11]

The neurological clinical manifestation emerging with the neuroinvasive and neurotrophic effect of SARS-CoV-2 has also been shown in many studies conducted on previous coronaviruses, such as SARS-CoV and Middle East Respiratory Syndrome–Related Coronavirus (MERS-CoV).[4,12-15] From a neurobiological perspective, COVID-19 may show post-infectious neurologic clinical symptoms and/or signs.

In previous studies, approximately 35% of patients affected by COVID-19 have been reported to experience neurological symptoms.[3,16] Neurological manifestations show a wide spectrum in the active phase of COVID-19, with the commonly reported being anosmia, ageusia, encephalitis, acute disseminated encephalomyelitis, cerebrovascular diseases, and Guillain-Barré syndrome.[4,16]

In the literature, studies are mainly focused on the early COVID-19 active infection and most are retrospective in design[3,16,17], and there is only limited research on clinical findings in patients who are in the post-infectious recovery state. Recent studies reported the presence of persistent symptoms, such as fatigue, myalgia, dyspnea, arthralgia, chest pain, headache, and autonomic dysfunction, which lasted for at least two months after recovery from COVID-19.[18-20]

There is still no clear terminological definition or approach concerning the symptoms and diseases clustered in the clinical manifestation described as a post-COVID-19 syndrome or long COVID-19.[21] The evaluation and follow-up of ongoing and/or newly developing neurological involvement after recovery from COVID-19 are important. This study aims to reveal post-COVID-19 neurological symptoms and risk factors for their development.

METHODS

Study design and participants

All patients aged over 18 years old and applied to four local Neurology Outpatient Clinics (two centers at city of Ankara, one each center at the city of Yozgat and Tokat) at least four weeks after contracting COVID-19 infection (confirmed by a laboratory test according to the WHO guidelines) between January 20 and March 15, 2021, were invited to the study. Two-hundred-forty-four females and 156 males agreed to participate in this study. All the participant patients were interviewed based on a structured questionnaire form, face to face. The study was approved by local ethic committees.

Data collection

The patients' demographic data, comorbidities, and hospitalization due to COVID-19 disease, types and durations of prolonged neurological symptoms, medications used, and responses to treatments were recorded. All the patients were linguistically competent in responding to the questions directed by the neurology specialist during the interview. The Beck Depression Inventory (BDI) was administered to the patients to evaluate the presence of depression. This instrument consists of a total of 21 items and provides a score between 0 and 63, with a higher score indicating the presence or higher severity of depression. The presence of the neurological symptoms was decided based on the information given by the patient. Tests other than BDI were not used in this study.

Statistical analysis

All statistical analyses were performed using SPSS 23 for Windows software package (SPSS Inc., Chicago, IL). As descriptors, mean ± SD and median (min-max) values were used for quantitative variables and percentages for categorical variables. Mean values were compared using Student's t-test if the normal distribution assumptions were met, and the Mann–Whitney U test otherwise. The relationships between two categorical variables were compared between the groups using the chi-square or Fisher's exact test. The significance level was set at $p < 0.05$. Univariate and multivariate regression models were used to explore risk factors associated with post-COVID-19 prolonged neurological symptoms and odds ratios (OR) with 95% confidence interval (CI) values were estimated.

RESULTS

Analysis of data in with and without prolonged neurological symptoms (PNS) groups

When the patients were enrolled in the study, an average of 108±5.12 days had passed after the onset of COVID-19 infection. Two hundred ninety-three of a total of 400 patients (73.3%) included in the study reported at least

one Prolonged Neurological Symptom (PNS) related to COVID-19 infection (PNS group). The remaining 107 patients did not describe any neurological symptoms (without PNS group). Female/male and hospitalization rates, patients with depression, hypertension, and thyroid disease, and patients who used favipiravir during active infection were higher in the PNS group than without PNS group. However, the rate of smokers was lower in the PNS group than without PNS group (Table 1).

Of the 400 participants, 304 (76.0%) had recovered from COVID-19 at home, 96 (24.0%) had been hospitalized due to COVID-19 infection (4 of 96 cases had required intensive care). Among the 96 participants that had been hospitalized, the mean duration of hospital stay was 8.3 ± 5.1 days. Sixteen (4.0%) participants had contracted the virus between March and June 2020, 92 (23.0%) participants between July and September 2020, 282 (70.5%) between October and December 2020, 10 (2.5%) between January and February 2021.

Analysis of data regarding the characteristics of prolonged neurological symptoms

While 179/293 (61.1%) patients reported that their symptoms had started during active COVID-19 infection, the remaining 114/293 (38.9%) patients stated that their symptoms had started within one month after active infection resolved in the PNS group. The distribution of the post-COVID-19 prolonged neurological symptoms is shown in Table 2. Duration of the symptoms was one month in 33/293 patients (11.3%), 1-3 months in 157/293 patients (53.6%), and ≥3 months in 103/293 (35.1%) patients. The average duration of the symptoms was 108±5 days and the average number of the symptoms was 2.7±1.8. The distribution of the symptoms according to their duration is shown in Figure 1. If patients described an ill-defined feeling of lightheadedness or walking on air, or a sense of disequilibrium without any gait abnormality, since we could not differentiate these three types of sensations, we collected them in the same category as "dizziness/

Table 1: The Demographic and Clinical Characteristics of with PNS and without PNS Group

	Total n (%) N=400	PNS group n (%) N=293	Without PNS group n (%) N=107	p-value
Age (Mean ± SD)	39.9±13.7	40.65±14.9	38.14±12.28	0.181*
Gender F/M	244/156	193/100	51/56	**0.001****
Education (Mean ± SD) years	11.8 ± 4.6	11.4±4.9	12.15±3.9	**0.018***
Hypertension	52 (13.0)	44 (15.0)	8 (7.4)	**0.045****
Diabetes mellitus	42 (10.5)	33 (11.2)	9 (8.4)	0.465**
CAD	27 (6.8)	15 (5.1)	3 (2.8)	0.420***
Thyroid disease	18 (4.5)	25 (8.5)	2 (1.9)	**0.014*****
COPD	21 (5.3)	19 (6.4)	2 (1.9)	0.077***
Hyperlipidemia	5 (1.3)	5 (1.7)	-	0.330***
Autoimmune disease	19 (4.8)	11 (3.7)	8 (7.4)	0.182**
Smoking	85 (21.3)	53 (18.0)	32 (29.9)	**0.019****
Hospitalization	96 (24)	78 (26.6)	18 (16.8)	**0.047****
Favipiravir use	334 (83.5)	251 (85.6)	83 (76.5)	**0.034****
Hydroxychloroquine	123 (30.8)	86 (29.3)	37 (34.5)	0.393**
Antiaggregant/Anticoagulant	192 (48.0)	146 (49.8)	46 (42.6)	0.215**
Antibiotics	118 (29.5)	93 (31.7)	25 (23.3)	0.108**
Vitamin C/D	181 (45.3)	127 (43.3)	54 (50.4)	0.259**
Depression	73 (18.2)	67 (22.8)	6 (5.6)	**< 0.001****

*Mann-Whitney U-test, **Pearson's chi-square test, *** Fisher's exact test; p-value significant at <0.05.
CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease

Table 2: Distribution of post-COVID-19 prolonged neurological symptoms

Symptoms	Total N=293 n (%)	Female n = 244 n (%)	Male n = 156 n (%)	p-value	Depression Yes n = 73 n (%)	Depression No n = 327 n (%)	p-value
Headache	138 (47.0)	94 (38.5)	44 (28.2)	**0.034**	39 (53.4)	99 (30.3)	**<0.001***
Myalgia	125 (42.6)	86 (35.2)	39 (25.0)	**0.031***	30 (41.1)	95 (29.1)	**0.045***
Sleep disorders	115 (39.2)	79 (32.4)	36 (23.1)	**0.045***	36 (49.3)	79 (24.2)	**<0.001***
Dizziness/ Gait disorders	81 (27.6)	53 (21.7)	28 (17.9)	0.360*	27 (37.0)	54 (16.5)	**<0.001***
Paroxysmal vertigo	69 (23.5)	50 (20.5)	19 (12.2)	**0.032***	21 (28.8)	48 (14.7)	**0.004***
Smell disorders	68 (23.2)	53 (21.7)	15 (9.6)	**0.002***	16 (21.9)	52 (15.9)	0.216*
Paresthesia/ dysesthesia	60 (20.4)	37 (15.2)	23 (14.7)	0.909*	15 (20.5)	45 (13.8)	0.142*
Taste disorders	43 (14.6)	30 (12.3)	13 (8.3)	0.212*	10 (13.7)	33 (10.1)	0.368*
Restless legs syndrome (RLS)	38 (12.9)	27 (11.1)	11 (7.1)	0.182*	12 (16.4)	26 (8.0)	**0.025***
Tinnitus	33 (11.2)	21 (8.6)	12 (7.7)	0.746*	13 (17.8)	20 (6.1)	**0.001***
Cognitive difficulties	12 (4.0)	5 (2.0)	7 (4.5)	0.163*	3 (4.1)	9 (2.8)	0.539*

*Pearson's chi-square test, p-value significant at <0.05.

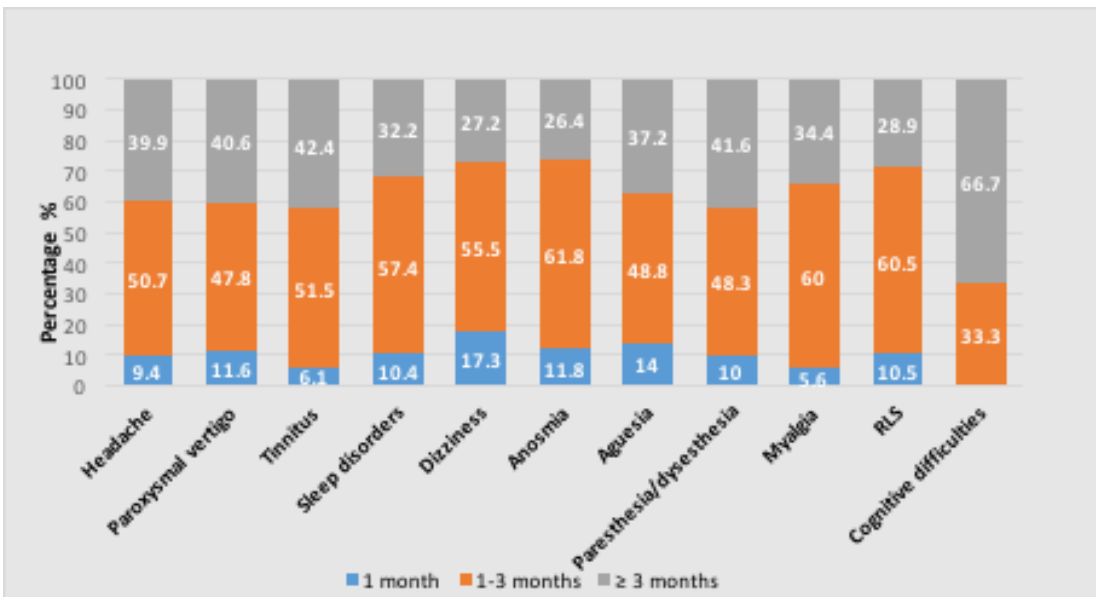

Figure 1. Distribution Of The Symptoms According To Their Duration

gait disorders". If patients described paroxysmal sensations of motion of self or the environment with or without gait abnormality, we used the term "vertigo". Thirty-four of 68 patients who described hyposmia/anosmia had also taste disorders and 34 of 43 patients who had taste disorders had also smell disorders; 34 out of 295 (11.5%) patients with prolonged neurological symptoms had both smell and taste disorders.

The most common treatments applied to the patients for headache were analgesics (98.9%); betahistine (92.3%) or piracetam (7.7%) for vertigo; antidepressants (69.3%) or antipsychotics (30.7%) for sleep disorders, gabapentinoids for paresthesia/dysesthesia (1.6%), myorelaxant or analgesics for myalgia (3.8%), and dopamine agonist for restless legs syndrome (1.6%).

Sub-analyses of data regarding the number of prolonged neurological symptoms by gender and presence of depression in PNS group

While 35.5 % of the patients (104/293) had only one prolonged neurological symptom related to COVID-19 infection, the rest 64.5% had at least two symptoms in the PNS group. The number of post-COVID-19 prolonged neurological symptoms by gender and presence of depression is shown in Table 3. The mean age was 38.8±13.5 and 41.8±13.9 years in female and male patients, respectively; the difference was statistically significant (p=0.026). The mean education level was 8.5±5.4 years in the female and 11.2±5.0 years in male patients (p= 0.543). The mean BDI score of all the patients was 7.7±7.4 with a median value of 6.0 (0.0-31.0). When the BDI score of 15 and above was accepted as the presence of mild to moderate depression, 55 (22.5%) female patients and 18 (11.5%) male patients had depression; the difference was significant, statistically (p=0.044.).

Analysis of data with regression statistics

Univariate analysis showed that female gender, hospitalization and using favipiravir during active infection, not smoking, hypertension, coronary artery disease (CAD), and presence of depression were determined to increase the risk of prolonged neurological symptoms after COVID-19 infection ($p = 0.001$, $p = 0.03$, $p = 0.037$, $p = 0.016$, $p = 0.032$, $p = 0.034$, and $p < 0.001$, respectively). After multivariate regression analysis; female gender, hospitalization and using favipiravir during active Covid-19 infection, and presence of depression were determined as independent predictors of prolonged neurological symptoms after the infection (Only sleep disturbance, myalgia, and restless legs were more common in patients who used favipiravir than those who did not (p=0.017, p=0.035, p=0011, respectively). The

Table 3: Number of post-COVID-19 prolonged neurological symptoms by gender and presence of depression

Number of symptoms	Total n = 293	Female n = 193	Male n = 100	p-value	Depression Yes n = 67	Depression No n = 226	p-value
Mean ± SD Median (min-max)	2.7 ± 1.8 2 (1-9)	2.8 ± 1.9 2 (1-9)	2.5 ± 1.8 2 (1-9)	0.144*	3.3 ± 2.1 3 (1-9)	2.5 ± 1.7 2 (1-9)	**0.003***
	n (%)	n (%)	n (%)	NA	n (%)	n (%)	**NA**
1	104 (35.5)	63 (32.6)	41 (41)		16 (23.9)	88 (38.9)	
2	65 (22.2)	45 (23.3)	20 (20)		13 (19.4)	52 (23)	
3	45 (15.4)	28 (14.5)	17 (17)		11 (16.4)	34 (15)	
4	31 (10.6)	21 (10.9)	10 (10)		11 (16.4)	20 (8.8)	
5	20 (6.8)	16 (8.3)	4 (4)		5 (7.5)	15 (6.6)	
6	16 (5.5)	12 (6.2)	4 (4)		6 (9)	10 (4.4)	
7	5 (1.7)	4 (2.1)	1 (1)		1 (1.5)	4 (1.8)	
8	4 (1.4)	2 (1)	2 (2)		1 (1.5)	3 (1.3)	
9	3 (1)	2 (1)	1 (1)		3 (4.5)	0 (0)	

* Mann-Whitney U-test, **Pearson's chi-square test; p-value significant at <0.05; NA: not applicable

significant differentiating variables for persistent neurological symptoms related to COVID-19 are shown in Table 4 with their calculated ORs.

DISCUSSION

Neurological involvement seen during COVID-19 active infection has frequently been evaluated in studies.[3,21,22] However, there is only limited knowledge and experience concerning the clinical profile of prolonged neurological symptoms associated with COVID-19.[19,20,23-32] In this prospective multicenter study, we documented the neurologic symptoms of our patients that persisted for at least one month using a structured face-to-face standardized questioning.

We found that 293/400 patients (73%) had at least one prolonged neurologic symptom that persisted at least one month or longer after the COVID-19 infection. Prolonged neurological symptoms mostly started during the active COVID-19 infection period (61%), whereas 39% within one month after the infection in our study. More than one prolonged neurological symptom was reported 65% in patients with PNS group and the mean number of reported symptoms was almost three. The top 3 most frequently reported prolonged neurological symptoms were headache (47%), myalgia (43%), and sleep disturbance (39%). Dizziness/gait disorders (28%), paroxysmal vertigo (23.5%), smell disorders (23%), paresthesia/dysesthesia (20%), taste disorder (15%), restless legs syndrome (13%), tinnitus (11%) and cognitive difficulties (4%) were other reported prolonged neurological symptoms by the participants. Combined smell and taste disorders were reported 11.5%. Although the least reported, the longest-lasting symptom was cognitive difficulties, which lasted 3 months or longer in 67% of the patients who have cognitive symptoms. All these symptoms have been reported at different rates during or after COVID-19 infection.[19,20,23-32]

Headache has been reported as among the most common initial manifestations in patients with COVID-19.[17,24,33] As mentioned above, we also found that headache was a more common prolonged neurological symptom and it was striking that headache lasted for at least 3 months or longer in 40% of the patients. This persistent tendency of post-COVID-19 headache is parallel to the findings of some studies in the literature.[23,25] In addition, we found that 67% of the participants with post-COVID-19 headaches required symptomatic treatment, and 72% of them reported benefiting from the treatments in terms of symptom frequency and severity. As the second most common prolonged neurological symptom, we observed myalgia (43%), which continued for more than three months in 34% of these patients. This finding is in agreement with a previous study reporting the presence of treatment-resistant myalgia that lasted for three months

Table 4: Univariate and multivariate odds ratios for having post-COVID-19 prolonged neurological symptoms

	Univariate*			Multivariate**		
	OR	**%95 Cl**	**p-value**	**OR**	**%95 Cl**	**p-value**
Female gender	2.12	1.35-3.32	**0.001**	2.18	1.36-3.49	**0.001**
Favipiravir use	1.87	1.07-3.26	0.340	2.07	1.15-3.72	**0.016**
Hospitalization	1.95	1.09-3.48	0.470	2.00	1.103-3.64	**0.023**
Depression	4.99	2.09-11.88	**<0.001**	4.54	1.88-10.96	**0.001**
CAD	4.89	1.14-21.04	**0.034**			
Hypertension	2.59	1.13-5.94	**0.032**			
Not Smoking	1.93	1116-3.22	**0.016**			

*CI: Confidence interval * Mantel-Heensztel statistics **Binary logistic regression analysis
CAD: Coronary Artery Disease

after the COVID-19 infection.[23] Sleep disorders were also reported among post-COVID-19 symptoms.[23,25,26,32] The third most common post-COVID-19 neurological symptom reported was sleep disturbances and it lasted longer than three months in more than 32% of the patients in our study. However, only 11% of the patients needed medications for sleep disorders.

Rass *et al*. reported that 61% of their patients had neurologic symptoms/signs three months after COVID-19, and, unlike our findings, the main neurological symptom was hyposmia/anosmia in their study population. They reported that although self-reported hyposmia/anosmia was lower with a rate of 17%, it was 45% when assessed by the 16-item Sniffin' Sticks test.[23] Since we did not use any test for evaluating smell disorders, the self-reported hyposmia/anosmia rate was only almost 23%, which was similarly reported by Rass *et al*.[23] We thought if we had also used an objective test for evaluating hyposmia/anosmia in our study, we may have found a higher ratio. Self-reported taste disorders were found in 15% in our study. Self-reported smell disorders and taste disorders were reported 11% and 7%, respectively, in the study by Huang et al, both lower than our findings. However, the median follow-up time was 186 (175-199) days after the symptom onset in that study.[27] Since the mean duration of the symptoms was shorter (108±5 days) in our study, we concluded that both smell and taste disorders would improve in time. Combined self-reported smell and taste disorders were found 11.5% in our study. We thought that the reason for this low rate was also caused by not using objective tests.

The extent of cognitive difficulties included attention deficit, forgetfulness, and difficulty in concentration expressed by the patients in our study. Although cognitive problems were reported at a very low rate in the study, it was remarkable that it lasted at least 3 months or longer in 67% of the patients, which was the highest rate. In general, among the prolonged neurological symptoms mentioned so far, the only prolonged neurological symptom that lasted for at least 3 months or longer in more than half of our patients was cognitive difficulties. Other prolonged neurological symptoms resolved in more than half of the patients within a maximum of 3 months. The presence of a lower rate of cognitive symptoms in our study than the studies evaluating it with objective tests reported so far, reveals the importance of detailed examinations with appropriate cognitive tests.[23,26,32,34]

The hospitalization rate was higher in patients with prolonged neurological symptoms than in patients without PNS in our study (27% vs 17%, respectively). We thought that prolonged neurological symptoms might be more common in patients who had severe enough disease to require hospitalization. Five prolonged neurologic symptoms including headache, myalgia, sleep disorders, paroxysmal vertigo, and smell disorders were more frequent in females than males. Seven prolonged neurologic symptoms including headache, myalgia, sleep disorders, dizziness/gait disturbances, paroxysmal vertigo, restless legs syndrome, and tinnitus were more prevalent in patients with depression than patients without depression. Moreover, patients with depression had a higher mean number of neurological symptoms than those without (3 symptoms vs 2).

When we compare the groups with and without prolonged neurological symptoms, the proportion of female/male and hospitalization, patients with depression, hypertension, and thyroid disease, and patients who used favipiravir during active COVID-19 infection was higher in the PNS group. However, the rate of smokers was lower in with PNS group than without the PNS group. After multiple regression statistics, we found that having depression, female gender, having been hospitalized during active COVID-19 infection, and favipiravir usage during active infection were independent risk factors for having prolonged neurologic symptoms.

Depression, which was present in 18% of all the participants was slightly higher in our study than reported in previous studies.[23,25,29,35] It is known that viral infections have neuropsychiatric consequences, and given the prevalence of COVID-19, it is possible to encounter more and more infection-related neuropsychiatric syndromes.[36-38] In general, depression is a common accompanying symptom in patients with post- COVID-19 syndrome.[25,27] According to our study, depression increases the risk of prolonged neurological symptoms by almost 5 times (OR: 4.5), independently from other factors.

Huang *et al*. reported that at 6 months after COVID-19 symptom onset, most patients had fatigue or muscle weakness, sleep difficulties, and anxiety or depression.[27] Mahmud *et al*. reported that one month after COVID-19, fatigue was the most common symptom, followed by a persistent cough, exertional dyspnea, sleep disorders, adjustment disorders, and headache. The female gender, besides others, was found to be a risk factor for the post-COVID-19 syndrome.[28] Fatigue was

not questioned in our study, however, contrary to previous studies, the headache was the most frequent prolonged neurologic symptom instead of others. Similar to the study by Mahmud *et al*. female gender was an independent risk factor for post-COVID-19 prolonged neurological symptoms, frequency was twice as common in female patients (OR:2.18).

Hospitalization was another independent risk factor for having post-COVID-19 prolonged neurologic symptoms (OR:2) in our study. Since patients with more severe acute COVID-19 infection were hospitalized, we may conclude that having a severe acute COVID-19 infection increases the risk of having post-COVID-19 prolonged neurological symptoms, which is compatible with some previous studies.[27,28]

We found that the use of favipiravir during acute COVID-19 infection also doubled the risk of post-COVID-19 prolonged neurological symptoms (OR:2.07). Sleep disturbance, myalgia, and restless legs were more common in patients who used favipiravir during active infection than those who did not. Favipiravir has a short half-life of 2–5.5 hours.[39] In this case, prolonged neurological symptoms are not expected as a side effect of favipiravir. Patients with more severe infections might have more likely sought medical attention, and therefore, more likely to have been treated with favipiravir.

The strengths of our study are its prospective multicenter design; moreover, the prolonged neurological symptoms were well documented by administering a structured questionnaire form face-to-face. However, there are also weaknesses of our study. The diagnosis of depression, which constitutes the highest risk factor for post-COVID-19 neurological symptoms according to the results, was not made after being examined by a psychiatrist, but only by testing with BDI. Psychiatrists should actively participate in future studies and determine how to approach these patients. If depression is diagnosed and treated early, the risk of post-COVID-19 prolonged neurological symptoms may be reduced. Another limitation of this study is its cross-sectional design. Prospective cohort studies evaluating post-COVID-19 prolonged neurologic symptoms are needed in this field.

We determined smell and taste disorders according to the reports of the patients, objective tests were not used. We could probably get a higher rate with objective tests. As neurologists, we presented cognitive disorders based on the patient's history, we did not use objective tests for cognitive disorders, therefore we detected a low rate compared to other studies.

In conclusion, prolonged neurological symptoms mostly started during the active COVID-19 infection period; the most frequently reported prolonged neurological symptoms was headache and the most common among those which continued for more than three months was cognitive difficulties. Most patients with post-COVID-19 prolonged neurological symptoms had at least two symptoms. Independent risk factors for having prolonged neurologic symptoms were having depression, female gender, having been hospitalized, and favipiravir usage during acute COVID-19 infection. We do not know how long prolonged neurological symptoms will persist and whether there will be any sequelae symptoms. Considering the possibility of persistent neurological symptoms in the post-COVID-19 period, physicians need to increase their knowledge and experience in this area by conducting new studies to better manage this patient group. In addition, if we know the risk factors for post-Covid-19 prolonged neurological symptoms, we can develop strategies to prevent the development of these symptoms over time.

DISCLOSURE

Financial support: None

Conflict of interest: None /Competing interests: The authors declare that they have no conflict of interest.

Ethics approval: This study was approval was granted by the Ethics Committee of Lokman Hekim University, Ankara, Turkey (reference number: 2021005)

Data availability: Data is available upon request from the corresponding author.

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