

Evaluation of the main neurological manifestations in patients from the Post-COVID outpatient clinic of URI Erechim

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Graphical Abstract

Highlights

- Most patients presented neurological symptoms following COVID-19 infection.
- COVID-19 caused short-term neurological effects, without significant deficits in memory or cognition.
- No correlation was observed between orotracheal intubation and cognitive impairment among the analyzed participants.

NEUROLOGICAL SYMPTOMS:



50% OF THE PATIENTS PRESENTED MEMORY LAPSES;



13% SHOWED COGNITIVE DEFICITS ACCORDING TO THE MONTREAL COGNITIVE ASSESSMENT (MOCA);



PATIENTS WHO HAD BEEN INTUBATED EXHIBITED GREATER COGNITIVE IMPAIRMENT COMPARED WITH THE NON-INTUBATED GROUP; HOWEVER, THESE DIFFERENCES WERE NOT STATISTICALLY SIGNIFICANT.



Abstract

The objective of this study was to assess the profile of patients treated at the Post-COVID-19 Rehabilitation Outpatient Clinic of URI Erechim, the neurological manifestations observed, and to correlate patients' symptoms with the need for orotracheal intubation. This is an observational, retrospective, and mixed-methods (qualitative and quantitative) study. Physiotherapy records of patients receiving care at the Post-COVID-19 Rehabilitation Outpatient Clinic, referred by physicians in 2021, were analyzed. The following instruments were employed: the Neurological Manifestations Assessment Questionnaire, the Montreal Cognitive Assessment (MoCA), and the Prospective and Retrospective Memory Questionnaire (PRMQ). Descriptive statistics and MoCA scores were used to compare pre- and post-rehabilitation data using a paired t-test, and to compare intubated and non-intubated participants using a t-test. Values lower than 0.05 were considered statistically significant. Analyses were performed using GraphPad Prism 9.2 software. A total of 16 patients were evaluated; most reported neurological symptoms, with 50% presenting memory lapses and 13% demonstrating cognitive deficits. This study concluded that COVID-19 caused short-term neurological damage, but no significant memory or cognitive impairment was detected in the sample, nor was any association observed between orotracheal intubation and cognitive alterations.

Keywords: Neurological Rehabilitation. COVID-19. Cognitive Deficit. Post-hospitalization.

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INTRODUCTION

The World Health Organization (WHO) identified a new pandemic caused by the outbreak of a novel coronavirus disease (COVID-19), triggered by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)¹. The pandemic has resulted in high global rates of morbidity and mortality².

The SARS-CoV-2 outbreak originated in the city of Wuhan, China, at the end of 2019, initially through zoonotic transmission linked to seafood trade. Human-to-human transmission was crucial for the spread of the outbreak. The disease caused by this virus was named COVID-19 and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020^{3,4}. In addition to respiratory system manifestations, one of the major complications involves the neurological system, including delirium or encephalopathy, stroke, meningoencephalitis, loss of smell (anosmia) and taste (hypogeusia), anxiety, depression, and sleep disorders. Several cases have demonstrated neurological complications even in the absence of respiratory symptoms¹. Moreover, it has been reported that neurological involvement due to SARS-CoV-2 infection is more common in patients with pre-existing neurological conditions⁴.

According to Triana *et al.* (2020)³, previous research assessing the impact of respiratory infections on cognition, memory, and attention demonstrated that such infections are capable of inducing these alterations. This indicates the presence of cognitive decline in patients who have recovered from COVID-19. This evidence is corroborated by a systematic review and meta-analysis of 81 studies evaluating patients 12 weeks or more after COVID-19

diagnosis, identifying fatigue and cognitive impairment as the most frequent long COVID symptoms, associated with significant functional impairment⁵.

In South America, a systematic review⁶ analyzed six studies on neurological and neuropsychiatric manifestations after acute COVID-19 infection (four from Brazil and two from Ecuador): three cohort studies, two case reports, and one cross-sectional study. The main outcomes included new-onset pain, new chronic pain, new headache, chronic daily headache, paresthesia, and various cognitive disorders. Complementing these regional findings, the cohort study by Salci *et al.* (2024)⁷ evaluated Brazilian adults and older adults 12 months after hospital discharge, revealing that long COVID in adults is characterized by a higher prevalence of memory loss, shortness of breath, appetite changes, hair loss, skin spots, itching, fatigue, edema, depression, and anxiety; in older adults, the most prevalent symptoms were memory loss, appetite changes, hair loss, itching, fatigue, edema, depression, and anxiety.

However, evidence remains scarce, revealing significant gaps in knowledge – particularly in Brazil, where few studies have addressed post-COVID neurological sequelae at the outpatient level, especially in populations from southern regions of the country. Therefore, the aim of this study was to assess the profile of patients treated at the Post-COVID-19 Rehabilitation Outpatient Clinic of URI Erechim, to identify the main neurological manifestations during the outpatient phase, and to correlate patients' symptomatology with the need for orotracheal intubation.

METHODOLOGY

This study is characterized as cross-sectional, retrospective, and of a mixed qualitative and quantitative nature. The study population comprised physiotherapy medical records of individuals enrolled in the Cardiopulmonary, Metabolic, and Post-COVID-19 Rehabilitation Outpatient Clinic of the Physical Therapy Teaching Clinic at URI Erechim.

Inclusion criteria consisted of physiotherapy records of individuals affected by COVID-19 who were registered at the Cardiopulmonary, Meta-

bolic, and Post-COVID-19 Rehabilitation Clinic of URI Erechim, including the following analytical parameters: Cognitive Assessment (MoCA), Memory Assessment (PRMQ), and informed consent authorizing the use of physiotherapy record data in an undergraduate thesis. Exclusion criteria included patients without physiotherapy records, incomplete records, and/or those lacking the aforementioned assessments.

For this research, physiotherapy records of individuals referred by physicians and treated at the

Post-COVID-19 Rehabilitation Outpatient Clinic in 2021 were analyzed. The researcher reviewed all physiotherapy assessments and used the following parameters:

The Neurological Manifestations Assessment Questionnaire was developed by the author of this study to identify neurological manifestations reported by participants during or after COVID-19 infection. It was based on the main post-COVID-19 neurological symptoms described in the 2020 literature, and its validity was confirmed through a pilot study.

The Montreal Cognitive Assessment (MoCA) is an instrument used to assess cognition across different domains. The maximum score is 30 points, and scores below 26 indicate cognitive impairment. The Prospective and Retrospective Memory Questionnaire (PRMQ) developed by Smith *et al.*⁸ consists of 16 items referring to memory failures in daily situations, divided into 8 prospective and 8 retrospective memory questions. Each question is followed by a five-point scale: (1) never, (2) rarely, (3) sometimes, (4) frequently, and (5) very frequently. The maximum score of 80 points reflects a high rate of self-reported memory lapses, while the minimum score of 16 points corresponds to a low rate of such lapses. All assessment instruments were routinely applied in the Cardiopulmonary,

Metabolic, and Post-COVID-19 Rehabilitation Program.

Data analysis was performed using descriptive statistics, expressed as relative frequency values. Data normality was verified through the Kolmogorov-Smirnov test. Continuous data were described as mean $\pm$ standard deviation (SD) or median (interquartile range), and categorical data as absolute and relative frequencies. Qualitative variables were analyzed using the chi-square test. All tests adopted a 5% significance level and a 95% confidence interval. Mean MoCA scores were compared between patients who underwent orotracheal intubation and those who did not using the t-test, and pre- and post-intervention comparisons were performed using the paired t-test. Analyses were conducted using GraphPad Prism version 9.2 software.

This study followed the ethical guidelines established by Resolution No. 466, dated December 12, 2012, of the National Health Council of the Brazilian Ministry of Health, which regulates research involving human participants. The protocol was submitted to and approved by the Research Ethics Committee of the Regional Integrated University of Alto Uruguai and the Missions (URI), Erechim Campus, under CAAE no. 53062821.4.0000.5351 and approval no. 5.285.096.

RESULTS

In the present study, physiotherapy records from 16 patients diagnosed with COVID-19 and treated at the Post-COVID Rehabilitation Outpatient Clinic of URI Erechim in 2021 were analyzed. The sample consisted of 25% (n=4) females and 75% (n=12) males, with a mean age of 52 ± 12.51 years.

Regarding hospitalization time, 81% (n=13) of the sample were admitted to the general ward, most of whom remained hospitalized for 7 to 14 days (46%). Furthermore, 69% (n=11) of the participants required intensive care due to the severity of the disease, remaining in the ICU; among these, the majority stayed up to 22 days (46%). Of the patients admitted to the ICU, 44% (n=6) required

orotracheal intubation (OTI).

With respect to neurological manifestations collected through the questionnaire, 10% of the sample presented ageusia and/or hypogeusia (loss or reduction of taste), 20% presented anosmia and/or hyposmia (loss or reduction of smell), 60% reported mental confusion, 70% irritability, 40% headaches, 90% dizziness, 80% memory impairment, and 90% decreased attention. Additionally, other important symptoms were reported by participants: 70% experienced paresthesia in some part of the body, 40% reported loss of sensitivity in a body region, and 100% reported generalized muscle weakness after COVID-19 infection, as shown in Table 1.

Table 1 - Post-COVID-19 neurological manifestations in patients treated at the Cardiopulmonary, Metabolic, and Post-COVID-19 Rehabilitation Outpatient Clinic of the Physical Therapy Teaching Clinic, URI Erechim, 2021 (N=16).

Item	Frequency (%)
Loss or reduction of taste	10
Loss or reduction of smell	20
Muscle weakness	100
Episodes of mental confusion	60
Irritability	70
Headache	40
Dizziness	90
Seizures	0
Memory impairment	80
Reduced attention	90
Loss of sensitivity in some body part	40
Required hospital admission due to COVID-19	90
Required ICU admission	90
Required intubation	50

Regarding the results of the Prospective and Retrospective Memory Questionnaire (PRMQ), it was observed that 50% of the sample reported forgetting something they were about to do, 70% forgot to carry out an activity they had planned, 50% forgot something that had been said shortly before, 50% forgot appointments not written in a planner, 50% forgot to buy something they had intended to purchase, and 50% were unable to recall events that had occurred in

the previous days. Additionally, 40% reported repeating the same things on different occasions, 40% forgot to take something when leaving home, 80% lost items they had just set down, 70% forgot to deliver a message to someone, and 40% forgot to contact a friend or family member again when necessary, as illustrated in the graphs below (Figures 7 to 22). Therefore, it was found that 50% of participants presented memory lapses following COVID-19 infection (Table 2).

Table 2 - Descriptive analysis of PRMQ questionnaire results in patients treated at the Cardiopulmonary, Metabolic, and Post-COVID-19 Rehabilitation Outpatient Clinic of the Physical Therapy Teaching Clinic, URI Erechim, 2021 (N=16).

		%
Q1: Decides to do something in a few minutes and then forgets to do it?	Very Frequently	10%
	Frequently	30%
	Sometimes	50%
	Rarely	10%
Q2: Fails to recognize a place previously visited?	Sometimes	30%
	Rarely	20%
	Never	50%
Q3: Forgets to do something supposed to be done within a few minutes, even when it is right in front of you (e.g., taking a pill or turning off the coffee maker)?	Very Frequently	10%
	Sometimes	70%
	Rarely	20%
Q4: Forgets something that was said a few minutes earlier?	Frequently	10%
	Sometimes	50%
	Rarely	20%
	Never	20%
Q5: Forgets appointments unless reminded by someone or by a note such as a calendar or diary?	Frequently	50%
	Sometimes	30%
	Rarely	20%

to be continued...

...continuation - Table 2.

		%
Q6: Fails to recognize a character in a radio or television program from one scene to the next?	Rarely	60%
	Never	40%
Q7: Forgets to buy something planned, such as a birthday card, even when seeing it in the store?	Sometimes	40%
	Rarely	50%
	Never	10%
Q8: Cannot recall things that happened in the last few days?	Frequently	10%
	Sometimes	10%
	Rarely	50%
	Never	30%
Q9: Repeats the same story to the same person on different occasions?	Sometimes	40%
	Rarely	40%
	Never	20%
Q10: When leaving a room or house, forgets to take something intended to take, even when it is in plain sight?	Frequently	40%
	Sometimes	40%
	Rarely	20%
Q11: Loses something just put down, such as a magazine or a pair of glasses?	Frequently	10%
	Sometimes	80%
	Rarely	10%
Q12: Forgets to deliver a message or hand something to someone when asked?	Frequently	10%
	Sometimes	70%
	Rarely	10%
	Never	10%
Q13: Looks at something without realizing it was seen moments before?	Frequently	10%
	Rarely	50%
	Never	40%
Q14: When trying to contact a friend or relative and failing, forgets to try again later?	Very Frequently	10%
	Sometimes	40%
	Rarely	30%
	Never	20%
Q15: Forgets what was watched on television the previous day?	Frequently	20%
	Sometimes	10%
	Rarely	50%
	Never	20%
Q16: Forgets to tell someone something intended to say a few minutes earlier?	Very Frequently	10%
	Frequently	10%
	Sometimes	20%
	Rarely	50%
	Never	10%

Note: Possible responses were Very Frequently, Frequently, Sometimes, Rarely, and Never. Responses with 0% were not included in the table.

Based on these results, it was found that 50% of the sample presented normal memory function, while 50% showed memory decline. Regarding the cognitive assessment of post-COVID-19 patients,

evaluated in this study using the Montreal Cognitive Assessment (MoCA), 87% (n=14) demonstrated no cognitive impairment, whereas 13% (n=2) exhibited significant cognitive deficits, as shown in Figure 1.

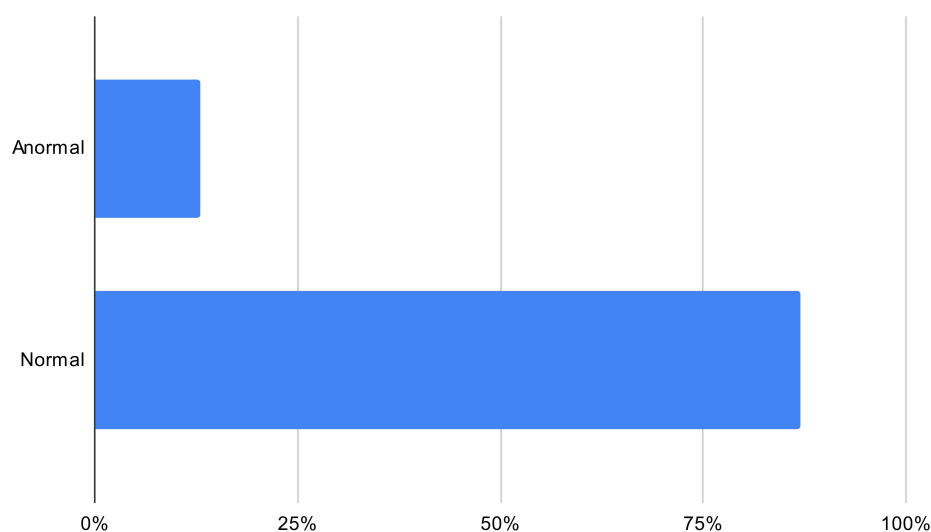


Figure 1 - Cognitive Assessment using the Montreal Cognitive Assessment (MoCA).

A comparison was also performed between the pre-rehabilitation and post-rehabilitation MoCA assessments, in which patients showed an increase in the mean score from 25.88 ± 4.09 to 28.50 ± 4.98 . This result indicates that there was no statistically

significant difference between the pre- and post-assessment ($p = 0.0625$). However, a trend toward improvement was observed, which may not have reached statistical significance due to the small sample size, as shown in Figure 2.

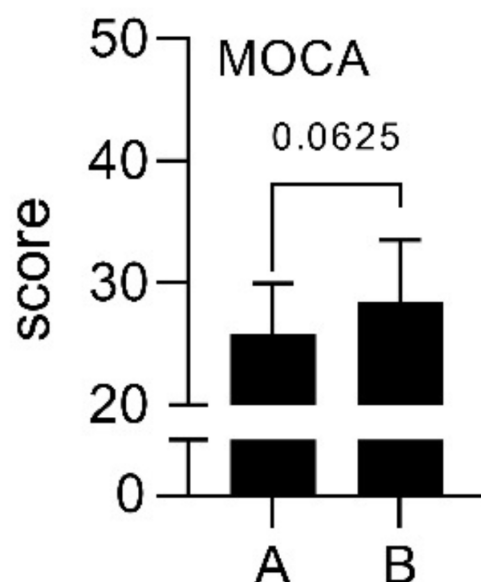


Figure 2 - Comparison between the initial assessment (A) and reassessment (B) of patients' cognition.

Figure 3 shows the correlation between the need for orotracheal intubation (OTI) and the score obtained on the MoCA. The mean score of patients who underwent OTI was 24.67 ± 6.05 , whereas those who were not intubated had a mean

score of 27.00 ± 1.12 ($p = 0.2717$). These findings indicate that intubated patients exhibited greater cognitive decline compared to the non-intubated group; however, the differences were not statistically significant.

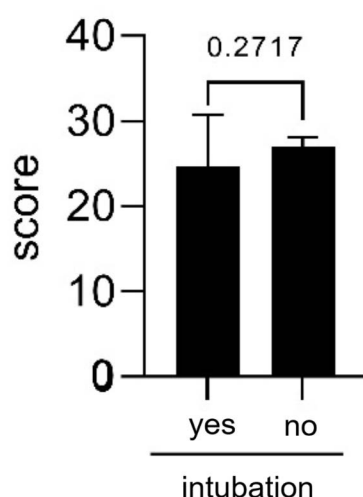


Figure 3 - Relationship between orotracheal intubation (OTI) and the score obtained in the MoCA.

DISCUSSION

The predominance of male participants in this sample may have influenced the prevalence of certain symptoms, as studies indicate that females are more susceptible to post-COVID-19 sequelae. According to Ballering *et al.* (2021)⁹, women exhibit greater pain sensitivity and bodily awareness, leading to an amplified perception of symptoms such as fatigue and chronic pain. This tendency is supported by recent evidence, such as that of Salci *et al.* (2024)⁷, who, in a Brazilian cohort of adults and older adults evaluated 12 months after hospital discharge, observed a higher incidence of neuropsychiatric symptoms among women, including depression and anxiety. Therefore, the predominantly male composition of the present study may have underestimated the prevalence of sensory and emotional symptoms.

Sensory symptoms such as anosmia, ageusia, numbness/tingling, and loss of sensitivity are consistent with well-established pathophysiological mechanisms of SARS-CoV-2 infection. These disturbances are associated with the interaction of the virus with angiotensin-converting enzyme 2 (ACE2) receptors, expressed in pulmonary tissue and in the oral and nasal mucosa, facilitating cellular invasion and local inflammation¹⁰. The low incidence of anosmia and ageusia in this sample, composed predominantly of men over 50 years old, aligns with findings that these symptoms are more common in younger women, as reported by Brandão *et al.* (2021)¹⁰.

Moreover, peripheral neuropathy underlying numbness and tingling is frequent among post-CO-

VID-19 patients, associated with hyperactive immune responses, neurotoxic drug effects, pre-existing risk factors, and nerve compression due to the prone position during ICU stays¹¹. Generalized muscle weakness can be attributed to prolonged immobility: bed rest for seven days can reduce muscle strength by up to 30%, with additional losses of 20% per subsequent week, persisting after discharge¹². This finding supports the generalized muscle weakness reported by all participants in this study, most of whom described it in the upper and lower limb extremities. This highlights the need for early interventions in motor rehabilitation.

In this context, according to Ferreira *et al.* (2021)¹³, several neurological symptoms are related to COVID-19. In the peripheral nervous system (PNS), hypogeusia, hyposmia, generalized weakness, myalgia, and muscle weakness are well described. In the central nervous system (CNS), headache, dizziness, confusion, seizures, delirium, agitation, and coma may occur, potentially leading to stroke. Many of these manifestations were also reported in the present study. Specifically regarding cognitive mechanisms, neuroimmune cells are related to the ability to retain thought and are essential for normal memory function. Symptoms associated with infection are consequences of protective immune responses; thus, COVID-19 infection may cause permanent memory damage¹⁴. Ritchie *et al.* (2020)¹⁵ argue that the hippocampus may be particularly susceptible to coronavirus infections, increasing the likelihood of memory alterations after COVID-19 and exacerbating neurodegenerative

diseases such as Alzheimer's.

Consistent with these findings, Silva *et al.* (2022)¹⁶ evaluated memory in individuals affected by COVID-19 and observed that 58% presented expected or normal memory function, while 25% showed significant memory deficits. In contrast, the present study found a higher percentage of patients with memory impairment. According to neuropsychologist Lívia Stocco Sanches Valentin¹⁷, who evaluated neurological changes through the Mental Plus Game in individuals who had COVID-19, 62.7% exhibited short-term memory alterations, whereas only 26.8% showed long-term memory changes. These manifestations are commonly described as "brain fog," characterized by reduced recent memory, difficulty concentrating, and impaired performance in routine activities¹⁸.

Additionally, Miners *et al.* (2020)¹⁹ noted that it remains unclear whether ischemic injury results from direct or inflammatory effects of COVID-19 on the CNS vasculature or from secondary extracranial cardiorespiratory dysfunction. The authors suggest that the virus may cause long-term neurological problems in many survivors, emphasizing the importance of multidisciplinary follow-up for these individuals.

In the present study, 69% of participants required mechanical ventilation. It is known that impairments in memory, attention, verbal fluency, executive functioning, and information processing speed have been reported in studies involving patients who required mechanical ventilation for other conditions. Neurological problems persisted for one year after hospital discharge in 78% of these patients, and in half of them for more than two years¹⁵. Similarly, Teixeira and Rosa (2024)²⁰ reported that ICU patients under mechanical ventilation may experience cognitive alterations involving memory, attention, and executive function, which tend to be further aggravated in post-COVID-19 patients due to cerebral hypoxia.

These findings reinforce the results of evaluations such as those by Alemanno *et al.* (2021)²¹, who assessed participants using the MoCA and MMSE and observed that 80% exhibited neuropsychological deficits. The group of individuals who underwent ventilation with the aid of a Venturi mask achieved higher scores compared with those subjected to orotracheal intubation. This demonstrates that MoCA scores are not directly related to orotracheal intubation, consistent with the findings of the present study, in which no such correlation was observed.

Furthermore, regarding the multifactorial aspects of ICU hospitalization, Fiani *et al.* (2022)²² reported that patients who remain hospitalized in ICUs may develop long-term cognitive deficits, resulting in new impairments or exacerbation of pre-existing dysfunctions. These deficits are associated with memory, global cognition, attention, and concentration. The authors note that the etiology of these alterations derives from several factors, including hypoxia, glycemic dysregulation, hypotension, and the use of sedatives, as well as in-hospital delirium caused by excessive sedative use and the stressful ICU environment itself. Therefore, it is not possible to assert that the participants of the present study experienced such deficits solely due to COVID-19 infection, since both the ICU environment and sedative use can independently affect cognition and memory.

In light of these findings, the need for multidisciplinary and individualized clinical follow-up for post-COVID-19 patients becomes evident, with an emphasis on cognitive and motor rehabilitation. Early identification and appropriate management of neurological and cognitive deficits are essential to minimize long-term sequelae, improve quality of life, and promote the social and functional reintegration of these individuals. Rehabilitation strategies should include specific interventions targeting muscle weakness, peripheral neuropathies, and cognitive impairments, along with psychological support for the neuropsychiatric symptoms frequently associated with post-COVID conditions.

This study presents several important limitations that should be considered when interpreting the results. The absence of pre-infection cognitive assessments makes it difficult to attribute the observed deficits directly to the effects of the virus. In addition, the small sample size ($n = 16$) and absence of a control group limit the generalizability of the findings. Another relevant point is the use of the Montreal Cognitive Assessment (MoCA), whose validation for the Brazilian population is not yet definitive, potentially introducing bias into the analysis. It is important to emphasize that the MoCA is a cognitive screening tool rather than a definitive diagnostic instrument and may underestimate subtle deficits; thus, future studies should include complementary instruments. Finally, potential biases such as self-report bias in the Prospective and Retrospective Memory Questionnaire (PRMQ) and selection bias due to the limited sample size should also be taken into account.

CONCLUSION

In the present study, severe impairment was observed among patients who experienced prolonged hospitalization in both the ward and the ICU. Participants reported neurological symptoms; however, although there was no statistical significance for memory and cognitive deficits, there was a strong indication of neurological symptoms that justify further research with larger samples and the inclusion of additional assessment instruments to

reach more reliable conclusions. No correlation between orotracheal intubation and cognitive alterations was identified.

The findings of this study highlight the need for healthcare services to incorporate systematic neurological screening protocols for post-COVID-19 patients, ensuring appropriate follow-up and rehabilitation strategies aimed at addressing potential cognitive and neurological sequelae.

CRedit author statement

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All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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