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COGNITIVE DISORDERS IN PATIENTS INFECTED WITH COVID-19: A NARRATIVE REVIEW

TRASTORNOS COGNITIVOS EN PACIENTES INFECTADOS POR COVID-19: UNA REVISIÓN NARRATIVA

TRANSTORNOS COGNITIVOS EM PACIENTES INFECTADOS COM COVID-19: UMA REVISÃO NARRATIVA

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ABSTRACT
Objective: The overactivated immune system due to COVID-19 may be responsible for most of its physiological manifestations, including the neurological ones. **Methods:** The scientific articles were searched by two independent researchers in the MEDLINE (PubMed), LILACS, SciELO, Scopus, Web of Science, and BIREME databases, with no restriction of language, period, or place of publication. To complement and avoid the bias of risk, gray literature was searched in Google Scholar. The narrative review followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The studies included in the research had scored ≥ 6 points in the qualitative protocol proposed by Pithon et al. (2015). **Results:** COVID-19 patients commonly have neurological manifestations. The patients' age was an important risk factor for neuropsychological deficiencies due to COVID-19. Increased fatigability and deficits in concentration, memory, and overall cognitive speed are reported months after hospital discharge. Also, the studies showed that the phase of the disease in which the patient is found directly interferes with the manifestation of the cognitive changes. **Conclusion:** Cognitive changes are frequently found months after hospital discharge in COVID-19 patients. A slower cognitive processing speed and impaired memory may interfere with the patients' daily functioning and their capacity to return to work. Hence, cognitive rehabilitation interventions aiming to increase the processing speed and memory must also be considered for this population.

KEYWORDS: Cognition. COVID-19. SARS-COV-2. Pandemic.

RESUMEN
Objetivo: El sistema inmunológico sobreactivado debido al COVID-19 puede ser responsable de la mayoría de sus manifestaciones fisiológicas, incluidas las neurológicas. **Métodos:** Los artículos científicos fueron buscados por dos investigadores independientes en las bases de datos MEDLINE (PubMed), LILACS, SciELO, Scopus, Web of Science y BIREME, sin restricción de idioma, período o lugar de publicación. Para complementar y evitar el sesgo de riesgo, se buscó literatura gris en Google Scholar. La revisión narrativa siguió las recomendaciones de los elementos de informe preferidos para revisiones sistemáticas y metaanálisis (PRISMA). Los estudios incluidos en la investigación habían obtenido ≥ 6 puntos en el protocolo cualitativo propuesto por Pithon et al. (2015). **Resultados:** Los pacientes con COVID-19 comúnmente tienen manifestaciones neurológicas. La edad de los pacientes fue un factor de riesgo importante para las deficiencias neuropsicológicas debidas al COVID-19. Meses después del alta hospitalaria se informa sobre una mayor fatiga y déficits en la concentración, la

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memoria y la velocidad cognitiva general. Además, los estudios mostraron que la fase de la enfermedad en la que se encuentra el paciente interfiere directamente con la manifestación de los cambios cognitivos. **Conclusión:** Los cambios cognitivos se encuentran con frecuencia meses después del alta hospitalaria en pacientes con COVID-19. Una velocidad de procesamiento cognitivo más lenta y una memoria deteriorada pueden interferir con el funcionamiento diario de los pacientes y su capacidad para volver al trabajo. Por lo tanto, las intervenciones de rehabilitación cognitiva destinadas a aumentar la velocidad de procesamiento y la memoria también deben considerarse para esta población.

PALABRAS CLAVE: Cognición. COVID-19. SARS-COV-2. Pandemia.

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RESUMO

Objetivo: O sistema imunológico superativado devido ao COVID-19 pode ser responsável pela maioria de suas manifestações fisiológicas, incluindo as neurológicas. **Métodos:** Os artigos científicos foram pesquisados por dois pesquisadores independentes nas bases de dados MEDLINE (PubMed), LILACS, SciELO, Scopus, Web of Science e BIREME, sem restrição de idioma, período ou local de publicação. Para complementar e evitar o viés do risco, a literatura cinzenta foi pesquisada no Google Scholar. A revisão narrativa seguiu as recomendações dos itens de relatório preferidos para revisões sistemáticas e meta-análises (PRISMA). Os estudos incluídos na pesquisa tiveram pontuação ≥ 6 pontos no protocolo qualitativo proposto por Pithon et al. (2015). **Resultados:** Os pacientes com COVID-19 comumente apresentam manifestações neurológicas. A idade dos pacientes foi um importante fator de risco para deficiências neuropsicológicas devido ao COVID-19. Fatigabilidade aumentada e déficits de concentração, memória e velocidade cognitiva geral são relatados meses após a alta hospitalar. Além disso, os estudos mostraram que a fase da doença em que o paciente se encontra interfere diretamente na manifestação das alterações cognitivas. **Conclusão:** Alterações cognitivas são frequentemente encontradas meses após a alta hospitalar em pacientes com COVID-19. Uma velocidade de processamento cognitivo mais lenta e memória prejudicada podem interferir com o funcionamento diário dos pacientes e sua capacidade de retornar ao trabalho. Assim, intervenções de reabilitação cognitiva com o objetivo de aumentar a velocidade de processamento e memória também devem ser consideradas para esta população.

PALAVRAS-CHAVE: Cognição. COVID-19. SARS-COV-2. Pandemia.

INTRODUCTION

The disease named 2019 coronavirus (COVID-19) is a respiratory condition caused by the RNA virus. It is known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can result in various syndromes due to long-term effects and variables in the person's body. The diversified changes caused by SARS-CoV-2 are the main reasons why the disease has long-term physiological effects.[1]

On January 30, 2020, the COVID-19 outbreak was classified as a Public Health Emergency of International Concern. COVID-19 infection generally has a range of manifestations, from initial signs and symptoms related to upper respiratory tract infection (such as rhinorrhea and sore throat) to cough, fever, dyspnea, and difficulty breathing.[2] The coronavirus is an important virus that affects mainly the human respiratory system, although it also has a neuroinvasive capacity and can expand from the respiratory tract to the central nervous system (CNS).[3] It is hypothesized in the literature that SARS-CoV-2 is transmitted to the CNS via the hematogenous route, invasion of the olfactory bulb, and retrograde axonal transport.[2]

The overactivated immune system due to COVID-19 is believed to be responsible for most of its physiological manifestations, including the neurological ones. The severe cases of the disease are more prone to manifesting severe neurological syndromes. Another situation to be considered is the endothelial dysfunction caused by SARS-CoV-2, which can occur in different organs of the body, resulting in ischemia/infarction and hemorrhage.[4] Previous observations led to increasing research characterizing the neurological ramifications due to SARS-CoV-2. However, the data on the cognitive effects of the disease have not been fully clarified yet.[1]

Given the above, this research aims to verify scientific evidence of cognitive disorders in patients infected with COVID-19 to answer the following research question: "What are the cognitive disorders present in patients infected with COVID-19?"

METHODS

Protocol

This narrative review, aiming to verify the cognitive disorders in patients infected with COVID-19, was conducted according to the PRISMA recommendations (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[5] The scientific articles were searched by two independent reviewers in the MEDLINE (PubMed), LILACS, SciELO, Scopus, Web of Science, and BIREME databases, with no restriction of language, time, and place of publication. The research was structured and organized in the PICOS framework, which is an acronym standing for Target **P**opulation, **I**ntervention, **C**omparison, **O**utcomes, and **S**tudy. The population of interest or health problem (P) is the patients; the intervention (I) is COVID-19; the comparison (C) is cognitive disorder; the outcome (O) is the impact on patients with COVID-19; and the study (S) comprises cross-sectional and observational studies, case reports, case-control studies, controlled clinical trials, and cohort studies. (**Table 1).**

TABLE 1. Description of the PICOS components.

Acronym	Definition
P	Patients
I	COVID-19
C	Cognitive disorders
O	COVID-19 patients
S	Cross-sectional studies Observational studies Case reports Case-control studies Controlled clinical trials

	Cohort studies

Source: Developed by the authors.

Research strategy

The descriptors were selected based on controlled vocabulary in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) because of their broad use by the scientific community to index articles in the PubMed database. The search strategy combined the following descriptors and Boolean operators: (covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder). The search was concentrated in March 2021. To complement and avoid the bias of risk, gray literature was searched in Google Scholar.

Eligibility criteria

The studies were included with no restriction of language, time, and place of publication. **Table 2** shows the inclusion and exclusion criteria developed for this research. The studies scored 12 in the modified protocol by Pithon et al. (2015),[6] which assesses their quality.

TABLE 2. Summary of the inclusion/exclusion criteria.

Inclusion criteria	
Design	Case reports Case-control studies Controlled clinical trials Cohort studies Screening trials Observational studies
Place	Without restrictions
Language	Without restrictions
Period	Without restrictions
Exclusion criteria	
Design	Letters to the editor Guidelines Literature reviews Systematic reviews Meta-analyses
Studies	Unclear, poorly described, or inadequate studies
Form of publication	Only abstract

Source: Developed by the authors.

Risk of bias

The quality of the methods used in the studies included here was independently assessed by the reviewer (XX), following the PRISMA recommendations (Moher et al., 2015). The assessment gave priority to clearly described information. At this point, the review was blind, masking the names of authors and journals to avoid any potential bias and conflict of interest.

Exclusion criteria

Studies published as letters to the editor, guidelines, literature reviews, narrative reviews, systematic reviews, meta-analyses, and abstracts were excluded, as well as studies not fully available **(Table 2).**

Data analysis

For the eligibility process, the data were extracted from the studies by two researchers with a spreadsheet specifically developed for narrative reviews in Excel® version 16.0 (Microsoft, USA). The extracted data were entered in it by one of the researchers and then checked by another one. The studies were first selected by title; then, the abstracts were analyzed, and only the potentially eligible ones were selected. Based on the abstracts, articles were set apart to be read in full, and those that met all the pre-established criteria were included.

Selection of the studies

Initially, the eligibility reviewer (XXX) was calibrated by XX to conduct the narrative review. After calibrating and answering questions, the titles and abstracts were independently examined, not blind to the names of authors and journals. Those whose title was within the scope but the abstract was unavailable were also obtained and analyzed in full. Studies not within the scope, and the case reports, letters to the editor and/or editorials, literature reviews, indexes, abstracts, systematic reviews, and meta-analyses were excluded. Afterward, the preliminarily eligible studies had their full text obtained and evaluated.

Collected data

After the screening, the text of the selected articles was reviewed and extracted by one of the authors (XXX) supervised by XX, following a standard with the identification of year of publication, place of the research, language of publication, type of study, sample, method, result, and conclusion of the study.

Clinical result

The clinical result of interest consisted in verifying the cognitive disorders in patients infected with COVID-19. Those with a different approach from what had been defined were not included in the sample of this narrative review.

RESULTS

At first, 142 articles were selected, narrowed down to 139 after excluding the duplicate ones. Then, the titles and abstracts were analyzed, and 135 papers were excluded for not being within the scope approached in this research. Hence, four articles were included in the final analysis, as all of them answered the research question **(Figure 1)**. Their study design was cross-sectional.

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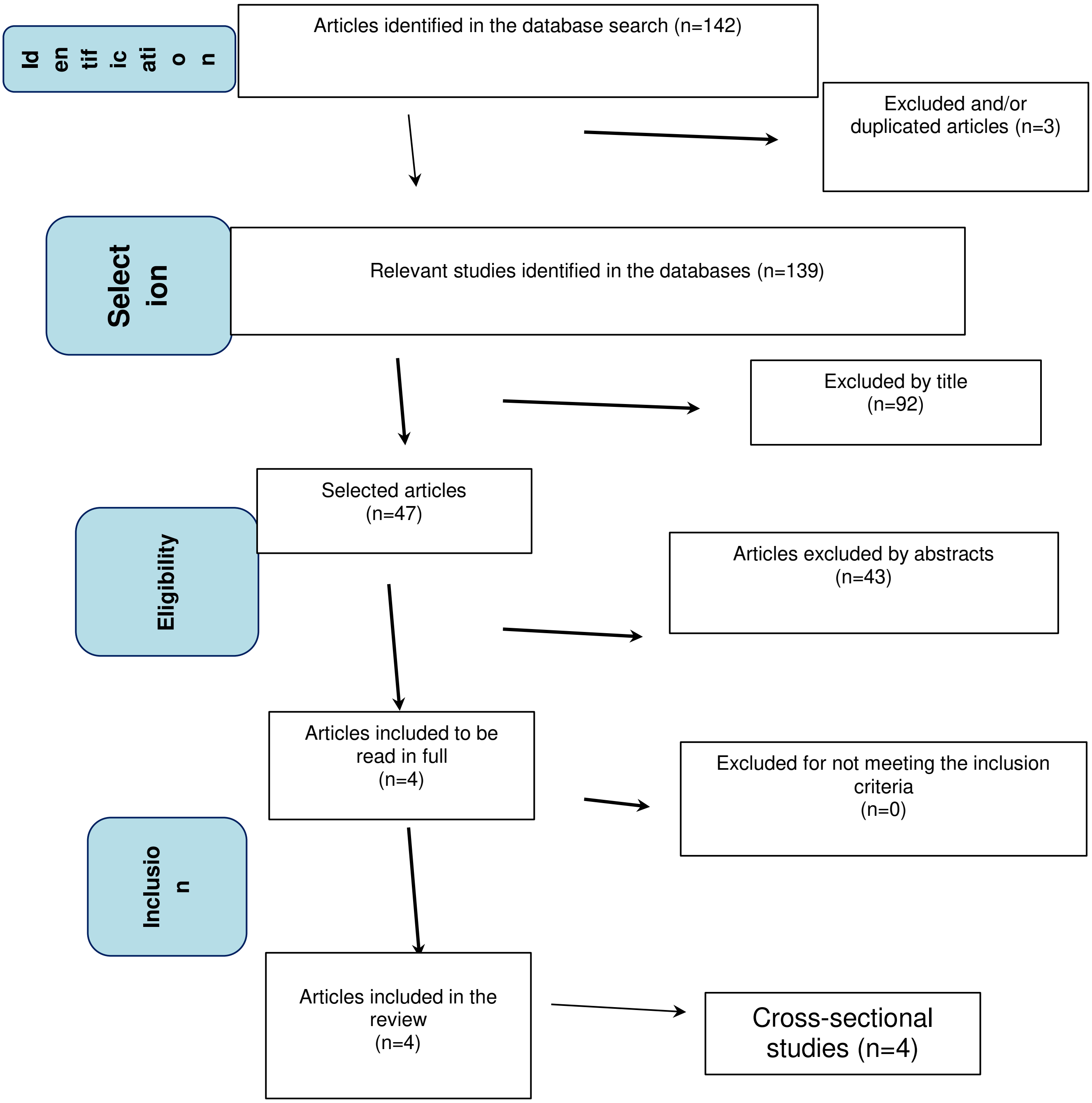
Figure 1. Flowchart of the article search and analysis process



Source: Developed by the authors.

Based on the descriptors selected, the databases were consulted, returning the results made available in **Table 3.**

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TABLE 3. Classification of the references obtained from the PubMed, SciELO, LILACS, Web of Science, Scopus, and BIREME databases.

Descriptors	Total no. of articles	No. of excluded references	Reason for the exclusion	No. of selected articles	Database
(covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder)	83	80	Excluded by title (40) Excluded by abstract (37) Duplicate articles (3)	3	PUBMED
(covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder)	0	0	0	0	LILACS
(covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder)	0	0	0	0	SCIELO
(covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder)	0	0	0	0	SCOPUS
(covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder)	0	0	0	0	WEB OF SCIENCE
(covid 19) and (SARS-CoV-2) and (cognitive function) and (cognitive disorder)	59	58	Excluded by title (52) Excluded by abstract (6)	1	BIREME
Total	142	138	Excluded by title (92) Excluded by abstract (43) Duplicate articles (3)	4	PUBMED, BIREME

Source: Developed by the authors.

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The studies selected for the present research were described in **Table 4.**

TABLE 4. Summary of the included articles.

Author/ Year/ Place of publication	Objective	N	Method	Results	Conclusion
Mao et al., 2020, China	What are the neurological manifestations in COVID-19 patients?	214	The collected data encompassed age, sex, comorbidities (such as hypertension, diabetes, cardiac, cerebrovascular, malignant, or chronic renal disease), and typical symptoms from the onset to hospitalization. The subjective symptoms were provided by the patients who were awake to answer the interview.	In a case series of 214 COVID-19 patients, the neurological symptoms were observed in 36.4% of the patients and were more common in patients with a severe infection (45.5%) based on their respiratory status – including acute cerebrovascular events, impaired awareness, and muscle lesion.	The neurological symptoms manifest in a remarkable proportion of COVID-19 patients.
Zhou et al., 2020, China	To assess the impact of COVID-19 on the cognitive functions of recovered patients and its relationship with inflammatory profiles.	29	Most of the neuropsychological assessments generate function measures in various cognitive domains, including attention, memory, processing speed, executive function, and perception skills. The study included the TMT, SCT, CPT, and DST.	The tests showed differences in the responses of the group with COVID-19, which had lower scores than the control group.	Results indicate a potential cognitive dysfunction in COVID-19 patients. Hence, new studies must investigate the dynamics of long-term cognitive function in COVID-19 patients and its relationship with inflammatory profiles.
Alemanno et al., 2021, Italy	To investigate the impact of COVID-19 on the cognitive functions of patients hospitalized in the COVID-19 Rehabilitation Unit of the San Raffaele Hospital	87	The patients were submitted to MMSE, MoCA, Hamilton Depression Rating Scale, and FIM. The data were divided into 4 groups according to respiratory assistance in the acute phase. The follow-ups were conducted 1 month after hospital discharge.	80% had neuropsychological deficits (MoCA and MMSE), and 40% had mild to moderate depression.	Patients with severe functional impairments had important cognitive and emotional deficits that may have been influenced by the ventilation therapy used. They seem to be mainly related to aging, though, regardless of the FIM scores.

Ferrucci et al., 2021, Italy	To study the occurrence of cognitive changes in hospitalized patients in the months following hospital discharge.	38	The participants were submitted to the neuropsychological assessment within 4 to 5 months from hospital discharge. Clinical variables were collected, such as length of hospital stay, type and duration of oxygen therapy, viral clearance time, comorbidities, and subjective cognitive deficits.	The participants reported a moderate to severe increase in fatigability, forgetfulness, lack of concentration, time taken to perform tasks such as reading/writing documents, and mild to severe difficulties learning new skills or procedures. Also, the patients had deficits in processing speed, delayed verbal memory, and immediate verbal memory.	Cognitive abnormalities are often found in COVID-19 patients months after hospital discharge. The slower cognitive processing speed and impaired memory may interfere with the patients' daily functioning and their capacity to return to work. Increased fatigability and deficits in concentration, memory, and overall cognitive speed are reported months after hospital discharge and may interfere with their work and daily living.

Source: Mao et al., 2020; Zhou et al., 2020; Alemanno et al., 2021; Ferrucci et al., 2021.
Legend: FIM = Functional Independence Measure; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; TMT = Trail Making Test; SCT = Sign Coding Test; CPT = Continuous Performance Test; DST = Digital Span Test.

Study design

The first study[7] was conducted in three centers of a hospital in China. The authors retrospectively analyzed patients diagnosed with COVID-19. A total of 214 hospitalized patients with laboratory confirmation of SARS-CoV-2 were included in the analysis. The collected data encompassed age, sex, comorbidities (such as hypertension, diabetes, cardiac, cerebrovascular, malignant, or chronic renal diseases), and typical symptoms from the onset to hospitalization (including fever, cough, anorexia, diarrhea, sore throat, abdominal pain, symptoms of the nervous system, and laboratory and CT scan findings). The subjective symptoms were provided by the patients who were awake to answer the interview.[7] The neurological manifestations were categorized into groups: CNS manifestations (such as dizziness, headache, impaired awareness, acute cerebrovascular disease, ataxia, and convulsions), peripheral nervous system (PNS) manifestations (such as impaired taste, smell, and eyesight, and nerve pain), and musculoskeletal lesions (Mao et al., 2020). The mean age of the participants was 52.7 years, and 87 patients were men. Of these patients, (38.8%) had at least one of the following underlying disorders: hypertension (23.8%), diabetes (14.0%), cardiac or cerebrovascular disease (7.0%), and malignant disease (6.1%). The most common symptoms at the onset of the disease were fever (61.7%), cough (50.0%), and anorexia (31.8%). A total of 78 patients (36.4%) had nervous system manifestations – CNS (24.8%), PNS (8.9%), and musculoskeletal lesions (10.7%). The most common symptoms reported in patients with CNS manifestations were dizziness (16.8%) and headache (13.1%), whereas in those with PNS symptoms, the most often reported ones were impaired taste (12.6%) and smell (5.1%).[7]

The second study[8] included 29 patients with COVID-19 aged 30 to 64 years, 18 of whom were males and 11, females. The study included neuropsychological tests such as the Trail Making Test (TMT), Sign Coding Test (SCT), Continuous Performance Test (CPT), and Digital Span Test (DST). Both the patients diagnosed with COVID-19 and the healthy control group were submitted to all the tests.

In the third study,[9] 87 patients were included – 62 men, and 25 women. Of these, 31 belonged to Group 1 (five women and 26 men, mean age 61 years), 18 belonged to Group 2 (four women and 14 men, mean age 59 years), 29 were included in Group 3 (14 women and 15 men, mean age 73 years), and nine were included in Group 4 (two women and seven men, mean age 62 years).

The fourth study[10] recruited 38 patients 22 to 74 years old, of whom 27 were men. The patients were hospitalized for SARS-CoV-2 infection. Clinical variables were collected, such as length of stay, type and duration of oxygen therapy, viral clearance time, comorbidities, and subjective cognitive deficits.

Neuropsychological Assessments

The TMT traces visual sweeping and visual movement, reflecting the people's information processing speed. The SCT is used to investigate visual perception, visual sweeping, eye movement, and memory. The CPT measures impulse and continuous and selective attention. And the DST assesses concentration, instantaneous memory, and resistance to information interference.[8]

The analyses of the Montreal Cognitive Assessment (MoCA) scores showed that 74.2% of the patients in Group 1, 94.4% of those in Group 2, 89.6% of those in Group 3, and 77.8% of the ones in Group 4 had some deficit. Group 1 had higher scores than Group 3. Significant differences between these two groups were observed in the subdomains of short-term memory, attention, abstraction, long-term memory, space, and time orientation.[9]

The analysis of the Mini-Mental State Examination (MMSE) showed that 12.9% of the patients in Group 1 had mild to severe deficits; 55.6% of those in Group 2 had mild to moderate deficits; 48.3% of those in Group 3 had mild to severe deficits; and 44.4% of the ones in Group 4 had moderate deficits. Group 1 had higher scores than Group 3. These differences were significant in the domain of attention, calculation, memory, and language.[9]

The participants were submitted to neuropsychological assessment within 4 to 5 months after hospital discharge. Before proceeding to complete neuropsychological assessment, the patients were selected with MoCA. The cognitive functioning was assessed with the Brief Repeatable Battery of Neuropsychological Tests (BRB-NT). Also, the Beck Depression Inventory-II (BDI-II) – to assess whether the depressive symptoms negatively affect cognitive performance – and the Subjective Scale of Damage (SSD) were conducted.[10]

Main findings

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The nervous system manifestations were significantly more common in severe infections than in non-severe ones (45.5% vs. 30.2%). Hence, the authors reported that SARS-CoV-2 can infect the nervous system. In patients with a severe infection, there is a greater neurological involvement, which includes acute cerebrovascular diseases and impaired awareness. Their quick deterioration and or clinical worsening may be associated with a neurological event, such as a stroke, which would contribute to their high mortality rate.[7] The results were based on the four tests they applied. In the CPT, the patients with COVID-19 had a lower score than the control group. Likewise, there was a significant difference in the responses of the COVID-19 patients in the CPT 2 and CPT 3 tests in comparison with the control group.[8]

Approximately 80% of the patients had cognitive deficits in the subacute phase of the disease, and approximately 40% of the patients suffered from mild to moderate depression; these deficits were more significant in older patients. The patients' age proved to be a risk factor for neuropsychological deficiencies due to COVID-19.[9]

Thirty participants answered the SSD. Of these, 50% reported a moderate to high increase in fatigability; 26.7% reported a moderate to severe increase in forgetfulness and incoordination; 23.3% reported a moderate to severe increase in the time taken to perform tasks such as reading/writing documents, and 20% reported moderate to severe difficulties learning new skills or procedures. Also, the scores of 60.5% of the sample were below the normative cutoffs in at least one task of the BRB-NT, approximately 36.8% of the patients had deficits in at least two tasks, 26.3% had deficits in at least three tasks, and 15.8% had deficits in four or more tasks.[10]

Of the total patients, 42.1% had deficits in processing speed, 26.3% had delayed verbal memory deficits, and 10.5% had immediate verbal memory deficits. The long-term visual memory was impaired in 18.4% of the patients, and the short-term visual memory was impaired in 15.8%. Semantic verbal fluency deficits were observed in 7.9% of the patients. The women more often reported a subjective decline in cognitive performance after hospitalization. Participants aged 55 years or above (n = 20) had lower scores than those under 55 years old (n = 18) in all the verbal memory measures.[10]

DISCUSSION

As the number of COVID-19 patients grows all over the world, neurological manifestations have been progressively described. However, no retrospective study has been designed so far to intercept possible neurological manifestations occurring in either the severe hospitalized COVID-19 patients or the mild asymptomatic ones.[11]

In one of the studies included in this review, the participants had deficits in processing speed, delayed verbal memory, immediate verbal memory, and semantic verbal fluency. Other complaints reported by the subjects encompassed moderate to severe increase in fatigability, forgetfulness, lack of concentration, time taken to perform tasks such as reading/writing documents and learning new skills or procedures.[10]

Virus neuroinvasion can take place through various routes in the human body, including transsynaptic transport via infected neurons, entry via the olfactory nerve, infection of the vascular endothelium, or migration of leukocytes through the hematoencephalic barrier. The most common complaints in COVID-19 are anosmia, ageusia, and headache, although other diseases, such as stroke, awareness deficit, convulsion, and encephalopathy, have also been reported. Nonetheless, it is not yet known up to what point the disease affects the CNS, or whether the neurological symptoms are attributable to secondary mechanisms. Therefore, it is necessary to find whether SARS-CoV-2 is neurotropic and contributes to post-infectious neurological complications.[12]

In another study present in this analysis, the patients in the subacute phase of the disease had cognitive deficits, which were more significant in older patients.[9] This corroborates with another study included here,[7] in which the authors report that nervous system manifestations were significantly more common in severe infections. In such patients, there is a greater neurological involvement, including acute cerebrovascular disease and impaired awareness.

There are currently few studies in the literature approaching cognitive sequelae of COVID-19 infection. COVID-19 infection results from a combination of respiratory infection and mechanical ventilation secondary to inadequate oxygenation, the reactivity of the inflammatory system, and an increase in the blood coagulation factors. These can affect the CNS function, resulting in long-term cognitive communication impairment in a proportion of the survivors.[13]

In a study, the overall cognitive deficit was observed in 33.3% of those with a pathological score in the MMSE, with a specific decline in attention, memory, language, and praxis skills. Poor cognitive functioning seems to be linearly associated with ICU length of stay.[14]

Brain vascular disease is emerging as one of the main COVID-19 complications in its severe conditions, thus increasing the risks of lasting brain damage, such as stroke and vascular cognitive deficiency. Many of the metabolic abnormalities that affect COVID-19 patients may also increase their risk of developing dementia – which has comorbidities and risk factors similar to those of COVID-19, including age, sex, hypertension, diabetes, and obesity. These similar comorbidities and mechanisms may also explain the high incidence and increase in mortality rates in people with dementia.[15]

Older adults, particularly those with comorbidities, make up a vulnerable group at greater risk of acquiring the disease and presenting more severe outcomes, including death. Therefore, post-COVID-19 infection follow-up with encompassing cognitive and neuropsychiatric assessments is essential, along with brain imaging, especially for those who developed the severe stage of the disease. It is thus necessary to dismiss long-term sequelae and provide mental health support and cognitive rehabilitation to minimize potential negative effects on the survivors' psychosocial functioning and quality of life.[16]

In another research[8] present in this analysis, the results show that COVID-19 patients had a lower score than the control group in the neuropsychological tests. The careful comparison with the neuropathological findings in people not infected with COVID-19 may be critical to determine whether many findings common to autopsies are substantially more likely in the disease and whether they can represent direct or indirect viral effects.[17] Recognizing and understanding the different comorbidities and their underlying pathological mechanisms are important to improve the clinical handling of COVID-19 patients with neurological manifestations.[18]

CONCLUSION

Cognitive changes are frequently found in patients diagnosed with COVID-19 months after hospital discharge. The slower cognitive processing speed and impaired memory may interfere with the functioning of these patients' quality of life. Hence, cognitive rehabilitation interventions aiming to increase processing speed and memory must also be considered. Therefore, the long-term follow-up of neurological deficits is an essential element, along with the imminently necessary follow-up of the rehabilitation health team.

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