

Cognitive impairment in people with COVID-19 with mild-moderate symptoms in Ecuador

Alejandro Checa*, Eliana Navas, Verónica Valencia, and Jessica Alcívar

Mental Health Unite, Hospital de Especialidades Eugenio Espejo, Quito, Ecuador

Abstract

Background: Complications of COVID-19 can include neurological, psychiatric, psychological, and psychosocial sequelae. Little is known about the consequences of COVID-19 on the cognitive functions of patients in the subacute phase of the disease. **Objective:** The objective of the study was to determine if there is an incidence of cognitive impairment in patients with COVID-19 with mild to moderate symptoms in the remission phase. **Method:** This is a cross-sectional study conducted between April 2021 and August 2021 at the Eugenio Espejo Hospital in Quito, Ecuador. The Montreal Cognitive Assessment test was applied to COVID-19 patients with mild to moderate symptoms. **Results:** A total of 50 subjects were recruited, 88% ($n = 44$) presented cognitive deterioration and only 12% ($n = 6$) showed a normal score. **Conclusions:** In our cohort study, patients with COVID-19 with mild-moderate symptoms are at high risk of cognitive impairment.

Keywords: COVID-19. Cognitive impairment. Mild to moderate.

Deterioro cognitivo en personas con COVID-19 con síntomas leves-moderados en Ecuador

Resumen

Antecedentes: Las complicaciones de COVID-19 pueden incluir secuelas neurológicas, psiquiátricas, psicológicas y psicosociales. Se sabe poco sobre las consecuencias del COVID-19 en las funciones cognitivas de los pacientes en la fase subaguda de la enfermedad. **Objetivo:** Determinar si existe incidencia de deterioro cognitivo en pacientes con COVID-19 con síntomas leves a moderados en la fase de remisión. **Método:** Se trata de un estudio de tipo transversal realizado entre abril de 2021 y agosto de 2021 en el Hospital Eugenio Espejo de Quito, Ecuador. Se aplicó el MoCA test a los pacientes con COVID-19 con síntomas de leve a moderado. **Resultados:** Un total de 50 sujetos fueron reclutados, el 88% ($n = 44$) presentó deterioro cognitivo y apenas el 12% ($n = 6$) evidenció una puntuación normal. **Conclusiones:** En nuestro estudio de cohorte los pacientes con COVID-19 con sintomatología leve-moderada tienen un alto riesgo de presentar deterioro cognitivo.

Palabras clave: COVID-19. Deterioro cognitivo. Leve a moderado.

*Correspondence:

Alejandro Checa
E-mail: alcz_11@yahoo.es

Date of reception: 07-09-2021

Date of acceptance: 14-10-2021

DOI: 10.24875/RMN.21000060

Available online: 08-07-2022

Rev Mex Neuroci. 2022;23(4):126-129

www.revexneurociencia.com

2604-6180 / © 2021 Academia Mexicana de Neurología A.C. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

As the coronavirus disease (COVID-19) pandemic continues to be a multidimensional threat to humanity, more evidence has emerged of the neurological involvement associated with it¹. The neuroinvasive properties of COVID-19 have allowed the hypothesis of several pathogenic mechanisms related to acute and chronic neurological sequelae². Neuroimmune interaction may be important not only in the pathogenesis of neurological manifestations, but also in the implications of systemic hyperinflammation and its consequences at the cognitive level³. While COVID-19 primarily affects the respiratory system, other organs, including the brain, may be involved². In Western clinical studies, relatively mild neurological dysfunction, such as anosmia and dysgeusia, is common, while severe neurological disorders such as stroke and meningoencephalitis are less common⁴. It is unclear how much COVID-19 infection contributes to the incidence of central nervous system damage due to comorbidities in the affected population. Clinically defined cases of acute disseminated encephalomyelitis have been rarely verified, cases of Guillain-Barré syndrome and acute necrotizing encephalopathy have been reported in patients with COVID-19⁵. Common neuropathological findings in patients include microglial activation with microglial nodules in a subset, lymphoid inflammation, acute hypoxic-ischemic changes, and astrogliosis; subacute cerebral infarcts, spontaneous hemorrhage and microthrombi, and occasional infarcts of the anterior pituitary have also been noted⁶. Complications of COVID-19 can include neurological, psychiatric, psychological, and psychosocial sequelae. Little is known about the consequences of COVID-19 on the cognitive functions of patients in the subacute phase of the disease⁷. Much remains to be learned about the effects of direct viral infection of brain cells and whether COVID-19 persists in the long term, contributing to chronic symptoms. More research is needed to understand the causal mechanisms of a probable cognitive deterioration associated with this pathology, so our study proposal focuses on investigating the cognitive profile of the hospitalized patient with COVID-19, which would be an important contribution in the understanding of disease and a better understanding of the interaction of COVID-19 with its human host.

Subjects and methods

This was a cross-sectional study, conducted between April 2021 and August 2021 at the Eugenio Espejo

Hospital in Quito, Ecuador. This hospital has been one of those designated for the care of patients with COVID-19 by the Ministry of Public Health. The study has the approval of the competent entities and the informed consent of all the participants was obtained from patients with mild to moderate COVID-19 infection. That is, patients with a relationship between arterial oxygen pressure and inspired oxygen fraction ($\text{PaO}_2/\text{FiO}_2$) between 201 and 299, in the remission phase of acute symptoms, that is, after 21 days from the beginning of the symptoms were invited to participate in the research; all subjects had a positive polymerase chain reaction test for COVID-19 performed at the institution designated by the Ministry of Public Health of Ecuador. After signing the informed consent, the participants were evaluated using the Montreal Cognitive Assessment (MoCA) test⁸. The test was applied by a neuropsychologist and two resident physicians in psychiatry duly trained for its application. It was considered as a cutoff point < 26 cognitive impairment and ≥ 26 normal. In addition, this test is validated in Spanish in different Latin American countries⁹. Participants with a history of mental, neurological and oncological diseases were excluded in the study; in addition to those who are experiencing reactive mental illness. The age range of the subjects was between 18 and 65 years. The captured data were entered into an electronic database and descriptive statistics, the statistical analysis contemplated a 95% confidence interval, using Chi-square, for which the SPSS version 23 program was used. In all cases, a $p < 0.05$ is significant.

Results

A total of 50 subjects were recruited, mostly men 58% ($n = 29$), of which 86.21% ($n = 25$) had cognitive impairment and only four participants had a normal test. As for the female sex, 90.48% ($n = 19$) showed cognitive deterioration and only 9.52% ($n = 2$) had a normal performance. The participants who were between 51 and 65 years old are 34% ($n = 17$), whereas the subjects between 36 and 50 years old were 46% ($n = 23$) and the remaining 20% ($n = 10$) between 18 and 35 years old. Of the participants between 51 and 65 years old, 82.35% ($n = 14$) presented cognitive deterioration in relation to their counterpart without deterioration 17.64% ($n = 3$), on the other hand, of the group between 36 and 50 years old 95% ($n = 22$) present cognitive deterioration and only one subject presented the normal test, finally, of the participants between 18

and 35 years old, 80% (n = 8) were impaired and 20% (n = 2) it is not.

The patients with university education were 50% (n = 25), of these 88% (n = 23) presented cognitive deterioration. Those with secondary education were 36% (n = 18), of which 83.33% (n = 15) had some degree of deterioration and only 14% (n = 7) had primary education, all showing deterioration cognitive.

Of the sample collected, 88% (n = 44) presented cognitive deterioration and only 12% (n = 6) showed a normal score. Of the 44 subjects with cognitive impairment, 58.81% n = (25) had a score between 20 and 25 in the MoCA test, 34.09% n = (15) had a score between 10 and 19 in the test and in 9.09% n = (4) a score lower than 9 was found.

There was no statistically significant relationship after applying the Chi-square test between cognitive impairment and sex (p = 0.647), nor was there evidence of a relationship between age and cognitive impairment (p = 0.302), in the same way there was no relationship between education and cognitive impairment (p = 0.515).

Discussion

In this study, it has been possible to verify a prevalence of 88% of cognitive impairment in patients treated at the Eugenio Espejo Hospital in Quito, Ecuador, similar incidences can be verified in studies where the same test has been applied in the population under similar conditions¹⁰. In this sense, it is important to mention that most of these patients did not report cognitive alterations and therefore these types of problems go unnoticed.

The sequelae of cognitive disorders are increasingly seen as a major challenge in the COVID-19 pandemic. However, most of the evidence of cognitive alterations after COVID-19 infection and invasion of the virus by the central nervous system comes from severely affected individuals in the acute phase of the disease¹¹ in this study is verified the presence of cognitive impairment in patients with mild and moderate symptoms.

It is believed that direct viral entry and systemic mechanisms such as cytokine storm contribute to neuroinflammation in patients with COVID-19, the etiology of cognitive impairment would be multifactorial, among these factors would be age¹². Age seems to be a risk factor¹³. However, in this study, there seems to be no statistically significant relationship associated with age, which is clinically significant since there is the same incidence in young and old patients.

The clinical presentation of COVID-19 and its long-term effects are still a matter of study, the implications on mental health in the short and long term require clarification¹⁴, it is not clear if the cognitive deterioration persists over time or if there is remission of symptoms. COVID-19 infection can cause long-term effects on immune processes within the CNS by causing microglial dysfunction¹⁵. Our study shows that there is cognitive impairment in the remission phase of symptoms. Therefore, it is necessary to continue investigating relatively recent onset pathology.

Apparently, there are no significant differences in the incidence of cognitive impairment in people with COVID-19 related to sex¹⁶, however studies on the subject are scarce, in any case our data show that there is no difference.

As has been noted, there is a similar prevalence of cognitive impairment in patients with different levels of education, so it does not seem to be a protective factor. No scientific literature could be found in this regard, so data must be taken with caution.

Although it is true that the use of the psychometric instrument could have increased the number of diagnosed patients, we believe that the criteria used allowed us to select the most clinically significant cases. We consider as a serious limitation that it was not possible to increase the sample due to the considerable decrease in diagnosed cases due to vaccination against COVID-19 in Ecuador and there was no control group either. In any case, our data support the fact that there is a high incidence of cognitive impairment in patients with COVID-19 with mild to moderate symptoms in the remission phase.

Conclusions

In our cohort study, patients with COVID-19 with mild to moderate symptoms have a high risk of presenting cognitive impairment, a better understanding of the causal processes and evolution over time is required to develop preventive and therapeutic interventions.

Funding

The authors declare that the research was funded by the Mental Health Unit of the Hospital de Especialidades Eugenio Espejo and no contribution of any kind has been received from any other entity.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

1. Septyaningtrias DE, Susilowati R. Neurological involvement of COVID-19: from neuroinvasion and neuroimmune crosstalk to long-term consequences. *Rev Neurosci.* 2021;32:427-42.
2. Fiscaro F, Di Napoli M, Liberto A, Fanella M, Di Stasio F, Pennisi M, et al. Neurological sequelae in patients with COVID-19: a histopathological perspective. *Int J Environ Res Public Health* 2021;18:1415.
3. Wang SC, Su KP, Pariante CM. The three frontlines against COVID-19: brain, behavior, and immunity. *Brain Behav Immun.* 2021;93:409-14.
4. Lou JJ, Movassaghi M, Gordy D, Olson MG, Zhang T, Khurana MS, et al. Neuropathology of COVID-19 (neuro-COVID): clinicopathological update. *Free Neuropathol.* 2021;2:2.
5. Chen CC, Chiang PC, Chen TH. The biosafety and risk management in preparation and processing of cerebrospinal fluid and other neurological specimens with potential coronavirus infection. *Front Neurol.* 2020;11:613552.
6. Nagu P, Parashar A, Behl T, Mehta V. CNS implications of COVID-19: a comprehensive review. *Rev Neurosci.* 2021;32:219-34.
7. Alemanno F, Houdayer E, Parma A, Spina A, Del Forno A, Scatolini A, et al. COVID-19 cognitive deficits after respiratory assistance in the subacute phase: a COVID-rehabilitation unit experience. *PLoS One.* 2021;16:e0246590.
8. Pedraza OL, Salazar AM, Sierra FA, Soler D, Castro J, Castillo P, et al. Confiabilidad, validez de criterio y discriminante del montreal cognitive assessment (MoCA) test, en un grupo de adultos de Bogotá. *Acta Médica Colombiana.* 2016;41:221-8.
9. Loureiro C, García C, Adana L, Yacelga T, Rodríguez-Lorenzana A, Maruta C. Uso del test de evaluación cognitiva de montreal (MoCA) en América Latina: revisión sistemática. *Rev Neurol.* 2018;66:1-10.
10. Patel R, Savrides I, Cahalan C, Doulatani G, O'Dell MW, Togliola J, et al. Cognitive impairment and functional change in COVID-19 patients undergoing inpatient rehabilitation. *Int J Rehabil Res.* 2021;44:285-8.
11. Borsche M, Reichel D, Fellbrich A, Lixenfeld AS, Rahmüller J, Vollstedt EJ, et al. Persistent cognitive impairment associated with cerebrospinal fluid anti-COVID-19 antibodies six months after mild COVID-19. *Neurol Res Pract.* 2021;3:34.
12. Toniolo S, Scarioni M, Di Lorenzo F, Hort J, Georges J, Tomic S, et al. Dementia and COVID-19, a bidirectional liaison: risk factors, biomarkers, and optimal health care. *J Alzheimers Dis.* 2021;82:883-98.
13. Cristillo V, Pilotto A, Cotti Piccinelli S, Zoppi N, Bonzi G, Gipponi S, et al. Age and subtle cognitive impairment are associated with long-term olfactory dysfunction after COVID-19 infection. *J Am Geriatr Soc.* 2021;69:2778-80.
14. Orrù G, Bertelloni D, Diolaiuti F, Mucci F, Di Giuseppe M, Biella M, et al. Long-COVID syndrome? A study on the persistence of neurological, psychological and physiological symptoms. *Healthcare (Basel).* 2021;9:575.
15. Stefano GB, Büttiker P, Weissenberger S, Martin A, Ptacek R, Kream RM. Editorial: the pathogenesis of long-term neuropsychiatric COVID-19 and the role of microglia, mitochondria, and persistent neuroinflammation: a hypothesis. *Med Sci Monit.* 2021;27:e933015.
16. Korompoki E, Gavriatopoulou M, Hicklen RS, Ntanasis-Stathopoulos I, Kastritis E, Fotiou D, et al. Epidemiology and organ specific sequelae of post-acute COVID19: a narrative review. *J Infect.* 2021;83:1-16.