

NEUROLOGICAL MANIFESTATIONS IN PATIENTS DIAGNOSED BY COVID-19, HOSPITAL DR. PUBLIO ESCOBAR, CHIMBORAZO, ECUADOR, 2023

Maykel Soto Rodríguez

Doctor in Stomatology. Master in Oral
Health & Stomatological Emergencies
Universidad Nacional de Tumbes. Perú
<https://orcid.org/0000-0002-7349-7754>

Víctor Manuel Reyes

Doctor of Science (PhD)
Universidad Nacional de Tumbes. Perú
<https://orcid.org/0000-0002-8336-0444>

Raúl Alfredo Sánchez Ancajima

Doctor of Science (PhD)
Universidad Nacional de Tumbes. Perú
<https://orcid.org/0000-0003-3341-7382>

All content in this magazine is
licensed under a Creative Com-
mons Attribution License. Attri-
bution-Non-Commercial-Non-
Derivatives 4.0 International (CC
BY-NC-ND 4.0).



Abstract: The SARS-CoV-2 virus is responsible for the COVID-19 disease pandemic, this acute phase disease is characterized not only by respiratory symptoms, but the clinical symptoms may be accompanied by multiple systemic symptoms, including neurological manifestations. The objective of the research was to characterize the neurological manifestations present in COVID-19 patients treated at the Dr. Publio Escobar hospital during the period from January 2022 to July 2023. The methodology used was a quantitative, descriptive, cross-sectional approach. The universe of study was 556 adult patients, over 18 years of age, of both sexes, diagnosed with COVID-19 and who presented some neurological manifestation on clinical examination. For the calculation of the sample size, a confidence level of 95% and a margin of error of 5% were taken into consideration, obtaining a sample of 181 patients, the sampling method was the probabilistic simple random type at random. The data collection technique was indirect quantitative and the data collection instruments used were the clinical history and data collection form. The data were processed using the statistical software SPSS version 21.0, and later analyzed using descriptive statistics. The results reveal that the mean age was 56 years, female (69.61%), with a previous history of arterial hypertension (34.81%), with 56.35% of the duration of the disease. The most frequent neurological manifestations were headache (51.93%) and anosmia (24.31%). It is concluded that a large proportion of patients with a confirmed COVID-19 diagnosis in a severe stage present neurological manifestations, so that the greater the degree of evolution of the disease, the greater the neurological sequelae. The increase in morbidity and mortality in patients with neurological manifestations will allow timely decisions to be made that impact

the prevention of patients with COVID-19.

Keywords: Neurological alterations, sensory alterations, COVID-19, neurological manifestations

INTRODUCTION

At the end of December 2019 in the Hubei Province, Wuhan City, China, the new virus called SARS-CoV-2 (Severe Acute Respiratory Syndrome -Coronavirus 2 for its acronym in English) emerged, responsible for the Coronavirus Disease of 2019. (COVID-19). The disease is characterized by respiratory symptoms that can lead to respiratory failure requiring invasive ventilatory support. However, since the start of the pandemic in early 2020, other symptoms have been described in the acute phase of the infection, including neurological, gastrointestinal, renal, and hematological symptoms, among others (Hu B et al., 2020).

Since the start of the COVID-19 pandemic, it was observed that some patients, even though they had overcome the acute phase, presented neurological symptoms, with headache, anosmia, cognitive impairment, insomnia, fatigue and dizziness being more frequently described (Carod-Artal F., 2020). Despite the fact that the virus is a respiratory syndrome, the family of coronaviruses shows a potential neurotropism that can induce late neurological complications such as polyneuropathy, encephalopathy, demyelinating lesions, ischemic stroke, Guillain-Barré syndrome, among other neurological disorders observed in other respiratory epidemics such as the Middle East respiratory syndrome and SARS (Cuevas-García C., 2020).

Due to its high prevalence, severity and magnitude that COVID-19 generates in the population, it could represent a serious public health problem on a global scale in the immediate future (Huarcaya-Victoria., 2020). Various hypotheses have been formulated

about the pathophysiology of neurological manifestations in the context of the acute phase of COVID-19. Some of these mechanisms could be related to systemic inflammation, which in the context of the acute phase of COVID-19 can become so great that it has been defined as a “cytokine storm” (Mehta, P. et al., 2020).

After infection, it cannot be ruled out that some patients may present a sustained inflammatory response and that this may be involved in the persistence of post-COVID neurological symptoms. A recent study has detected elevated levels of proinflammatory cytokines between 3 and 9 months after hospital discharge in patients with persistent symptoms after COVID-19 compared with healthy controls (Ahearn-Ford, S. et al., 2021). Other authors support the existence of autoimmune mechanisms generated against host epitopes in the acute phase of infection (Bhadelia, N. et al., 2021).

METHODOLOGY

It was an epidemiological study with a quantitative methodological approach, descriptive level, cross section. The population consisted of 556 adult patients, over 18 years of age, of both sexes, diagnosed with COVID-19, and who presented some neurological manifestation on clinical examination. To calculate the sample size, a confidence level of 95% and a margin of error of 5% were taken into consideration, obtaining a sample of 181 patients. The sampling method used was the probabilistic one of a simple random type at random. For data collection, the empirical method of observation was used, the technique was indirect quantitative and the data collection instruments were the clinical history and data collection form.

The evaluation of patients with neurological pathologies was carried out by a multidisciplinary team made up of an

internist, a general practitioner on duty and a dentist for monitoring and evaluation of peripheral neurological manifestations that compromised the stomatognathic system. The follow-up of the cases was supported by a neurologist. The inclusion criteria included those patients over 18 years of age, of both sexes, with neurological manifestations of the central nervous system (CNS) such as headache, ischemic or hemorrhagic cerebrovascular attack, encephalitis, meningoencephalitis, acute symptomatic crisis, encephalopathies, others (myelitis, extrapyramidal picture); peripheral nervous system (PNS): involvement of cranial nerves (anosmia, ageusia/hypogeusia, others), polyradiculoneuropathy (Guillain-barré syndrome), musculoskeletal (myalgia symptoms and myopathies, rhabdomyolysis, and others).

Patients with neurological or psychiatric disease, alcohol or drug use, immunosuppressed patients, and those who did not approve their informed consent to participate in the study were excluded. In addition, a history of ischemic cerebrovascular accidents whose focal symptoms were similar to previous lesions were considered. patients with hemorrhagic cerebrovascular accident of aneurysmal etiology, vascular malformation or hemorrhagic contusion, patients with previous neurological sequelae such as: neuromuscular diseases, myopathies, amyotrophic lateral sclerosis (if it is desired to evaluate musculoskeletal symptoms).

The data were processed with the statistical program SPSS version 21.0.1 for Windows (Statistical Package for the Social Sciences; SPSS Inc. Chicago, Illinois, USA), and later analyzed using descriptive statistics. The qualitative and quantitative categorical variables were presented as frequencies with their respective percentages, mean and median. The procedures were followed and the

ethical norms consistent with the Declaration of Helsinki were respected, the data that identified the patients were encrypted to protect their confidentiality and privacy, through informed consent. The research was approved by the institutional Research and Ethics Committee according to resolution No. 042/2023-MSP-DDS06D04-HPE.

RESULTS

The study sample had 181 patients diagnosed with COVID-19, with an average age of 56 years, 161 were over 50 years of age, the age group from 56 to 65 years of age was more frequent with 114 (62.98%); 126 females (69.61%); the most frequent comorbidities: arterial hypertension 63 (34.81%), diabetes mellitus 31 (17.13%) and obesity 18 (9.94%), (Table 1).

Variables	Number	%
Age (X²): 56 years (18-85)		
18-35	2	1,10
36-45	6	3,32
46-55	12	6,63
56-65	114	62,98
66-75	32	17,68
76-85	15	8,29
Gender		
Male	55	30,39
Female	126	69,61
Comorbidities		
Heart disease	7	3,87
Arterial hypertension	63	34,81
Diabetes mellitus type 2	31	17,13
Obesity	18	9,94
Other	20	11,05
None	42	23,20
Total	181	100

Table 1: Description of the sociodemographic and epidemiological characteristics.

Regarding the clinical and paraclinical variables, it is evident that in the examined patients there was a time of illness ≤ 7 days 102 (56.35%); the most frequent presenting symptoms were dyspnea 49 (27.07%), cough 46 (25.42%) and anosmia 44 (24.31%). The serious clinical syndromes on admission to the emergency room were severe pneumonia 94 (51.93%) and adult respiratory distress syndrome 51 (28.18%). The most frequent paraclinical tests performed were the positive molecular RT-PCR test in 92 patients (50.83%), rapid reactive test in 58 patients (32.04%) and suggestive chest X-ray in 25 (13.81%). (table 2).

Variables	No.	%
Duration of the disease		
≤ 7 days	102	56,35
8-14 days	51	28,18
≥ 15 days	28	15,47
Presenting symptoms of COVID-19		
Fever	30	16,57
Dyspnoea	49	27,07
Cough	46	25,42
Anosmia	44	24,31
Diarrhea	12	6,63
Clinical disease syndromes		
Mild pneumonia	26	14,36
Severe pneumonia	94	51,93
Sepsis	6	3,32
Septic shock	4	2,21
Acute Respiratory Distress Syndrome	51	28,18
Paraclinical laboratory tests		
RT-PCR positive	92	50,83
Rapid reactive test	58	32,04
Suggestive chest x-ray	25	13,81
Thorax tomography	6	3,32
Total	181	100

Table 2: Description of the clinical and paraclinical characteristics of the study sample.

* RT-PCR +: Nasopharyngeal swab real-time polymerase chain reaction

Table 3 describes the neurological manifestations in the COVID-19 patients examined. Headache was the most frequent neurological manifestation of the central nervous system 94 (51.93%), both encephalopathies and vascular accidents were not significant in the study. Regarding the neurological manifestations of the peripheral nervous system, anosmia was the most frequent manifestation of the peripheral nervous system with 44 patients (24.31%), followed by myalgia due to musculoskeletal involvement in 27 cases (14.92%), only the 6% of the total cases reported Ageusia/Dysgeusia, as a chemisensory neurological symptom.

Variables	Number	%
Neurological manifestations of the Central Nervous System		
Encephalopathies	2	1,11
Ischemic cerebrovascular accident	1	0,55
Headache	94	51,93
Hemorrhagic cerebrovascular accident	1	0,55
Neurological manifestations of the peripheral nervous system		
Myalgia	27	14,92
Anosmia	44	24,31
Dysgeusia/ ageusia	12	6,63
Total	181	100

Table 3: Description of the associated neurological manifestations in COVID-19 patients.

DISCUSSION

The neurological manifestations occurred in COVID-19 patients with a mean of 56 years of age, with a greater predominance in the age group comprised of 56-65 years (62.98%), the female sex being the most affected (69, 61%), with arterial hypertension (23.20%) as comorbidity. These data are similar to what was reported by previous studies, where the mean age ranged from 55 years, female sex (59.34%

and arterial hypertension was the most frequent comorbidity (21.3%) (Romero Sánchez CM et al.,2020), (Luigetti M et al.,2020).

Regarding the time of onset of COVID-19, the results showed that 56.35% transited with an average of less than 7 days of clinical course. The most frequent symptoms were dyspnea, cough and anosmia, behaving similarly with 27.07%, 25.42% and 24.31% respectively. Regarding the diagnostic tests for COVID-19, half of the patients underwent the RT-PCR molecular test with 50.83%.

Regarding the results of the clinical course of the disease and the diagnostic test carried out, it coincides with the study carried out by Zubair et al where the duration of the symptoms presented less than 7 days (58.45%), as well as the RT-test. PCR was the most used diagnostic test in their study (59.14%). However, the figures for the symptoms of the appearance of COVID-19 and the presence of clinical syndromes associated with COVID-19 do not agree with that described in the study where dyspnea was the most frequent symptom with 60.21%, and severe type pneumonia occurred in 45.35% (Zubair AS et al., 2020).

The neurological manifestations have a wide spectrum of presentation, ranging from a headache and alterations in the sense of taste or smell to cerebrovascular disease. Since the beginning of the pandemic, various pathological processes due to coronavirus have been published and one of them is neurological manifestations. It has been shown that the SARS-CoV-2 virus can invade and penetrate the central nervous system by various mechanisms of neuroinvasion. In a series of 43 postmortem cases, neuropathological changes in patients infected with the virus were studied in 53% where viral particles were detected in the brain (Matschke et al., 2020).

However, in another case series of 18 autopsies of patients who presented neurological symptoms with COVID-19, the

neuropathological examination failed to detect the virus due to neither the molecular RT-PCR test nor the immunohistochemical technique, revealing that the samples only showed changes due to hypoxia (Solomon IH et al., 2020).

On the other hand, research carried out previously reveals an association of neurological manifestations both at the central and peripheral level in patients infected with the SARS-CoV-2 virus, where 35% of the patients present at least some symptoms (Ahmed MU et al., 2020). The first report made since the pandemic began was the one described by Mao et al. In China, in said series, 36% presented some neurological manifestation, a percentage similar to that reported in the international literature (Mao L et al., 2020).

In the present study, most of the patients presented headache as a central neurological symptom and a quarter of the population studied reported anosmia as a peripheral neurological manifestation. The incidence of smell disorders according to the literature ranges from 4.9 to 85.6% (Wang Z et al., 2020). The most common is anosmia, similar to what was identified in this study; The incidence of headache is reported from 0.6 to 70.3% (Wang D et al., 2020). In the current study, headache was the most frequent symptom of the central type (51.93%).

Despite the fact that in the present study the cases that presented encephalopathies and vascular accidents were not significant, it is worth noting that the literature reports that these central neurological manifestations due to SARS-COV-2 virus infection are due to multiple factors such as administration of induced steroids as part of the COVID-19 treatment protocol, sustained hypoxia in patients, multi-organ failure and systemic hyperinflammation (Aghagoli G et al., 2021).

In the case of ischemic and hemorrhagic cerebrovascular diseases, they share similar risk factors with severe coronavirus infection

(arterial hypertension, metabolic syndrome, dyslipidemia, sedentary lifestyle). The mechanism of vascular damage is intense inflammation at the level of the arterial endothelium, generating signs of endothelitis at the level of the central nervous system, producing said manifestations (Paterson RW et al., 2020).

As limitations of the study, it is declared that a small group of patients with mild-moderate COVID-19 is presented compared to the number of patients who are part of the severe and severe stages of the disease, due to the fact that the database was developed only with the clinical histories of the patients who were hospitalized, and this population is more likely to have significant comorbidities, which could alter the statistical relationship of this group of severity in relation to comorbidities. It must also be taken into consideration, that symptoms and signs that are complex to interpret are covered and there is a possibility that the symptoms precede the disease and during the period of infection it exacerbates or changes in some quality and the patient refers it.

CONCLUSIONS

The COVID-19 pandemic has caused an increasing morbidity and mortality, with this investigation it was possible to describe the different neurological manifestations in COVID-19 patients in the hospital institution under study, obtaining that the average age was 56 years, the fourth Part of the patients were female with the presence of arterial hypertension as a previous health history. Half of the sample had symptoms lasting less than 7 days and presented severe pneumonia as an associated syndrome. A quarter of the patients presented dyspnea, cough and anosmia. The most frequent neurological manifestations were headache and anosmia.

REFERENCES

- Aghagoli G, Gallo Marin B, Katchur NJ, Chaves-Sell F, Asaad WF, Murphy SA.(2021). Neurological involvement in COVID-19 and potential mechanisms: A review. *Neurocrit Care*; 34(3):1062-71. doi: 10.1007/s12028-020-01049-4.
- Ahearn-Ford, S. et al. (2021). Long-term disruption of cytokine signalling networks is evident in patients who required hospitalization for SARS-CoV-2 infection. *Allergy*; 76: 2910–2913.
- Ahmed MU, Hanif M, Ali MJ, Haider MA, Kherani D, Memon GM, Karim AH, Sattar A.(2020). Neurological Manifestations of COVID-19 (SARS-CoV-2): A Review. *Front Neurol*; 11:518. doi: 10.3389/fneur.2020.00518.
- Bhadelia, N. et al.(2021).Distinct Autoimmune Antibody Signatures Between Hospitalized Acute COVID-19 Patients, SARS-CoV-2 Convalescent Individuals, and Unexposed Pre-Pandemic Controls. medRxiv 2021.01.21.21249176 doi:10.1101/2021.01.21.21249176.
- Carod-Artal FJ. Complicaciones neurológicas por coronavirus y COVID-19. (2020). *Rev Neurol*;70 (9):311–22.
- Cuevas-García C, Calderón-Vallejo A, Berrón-Ruiz L.(2020). La neurología de COVID-19. *Rev Alerg Mex*;67(4):338–49.
- Huacaya-Victoria J.(2020). Consideraciones sobre la salud mental en la pandemia de COVID-19. *Rev Peru Med Exp Salud Publica*;37(2):327–334.
- Hu B, Guo, H, Zhou, P. & Shi, Z.-L.(2021). Characteristics of SARS-CoV-2 and COVID-19. *Nat. Rev. Microbiol*; 19: 141–154.
- Luigetti M, Iorio R, Bentivoglio AR, Tricoli L, Riso V, Marotta J, et al.(2020). Assessment of neurological manifestations in hospitalized patients with COVID-19. *Eur J Neurol [Internet]*. [Citado 25/08/2023];27(11):2322-8. Disponible en: <https://onlinelibrary.wiley.com/doi/10.1111/ene.14444>
- Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. (2020).Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol*;77(6):683.
- Matschke J, Lütgehetmann M, Hagel Ch, Spherhake JP, Schröder AS, Edler C, et al. (2020). Neuropathology of patients with COVID-19 in Germany: a post-mortem case series. *Lancet Neurol*; 19(11):919–29. doi: 10.1016/S1474-4422(20)30308-2.
- Mehta, P. et al. COVID-19. (2020). Consider cytokine storm syndromes and immunosuppression. *Lancet*; 395: 1033–1034.
- Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, et al.(2020). The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings. *Brain*; 143(10):3104–20. doi: 10.1093/brain/awaa240
- Romero Sánchez CM, Díaz Maroto I, Fernández Díaz E, Sánchez Larsen Á, Layos Romero A, García García J, et al.(2020). Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOV registry. *Neurology [Internet]*. [Citado 25/08/2023];95(8):e1060-70. Disponible en: <https://n.neurology.org/content/95/8/e1060>
- Solomon IH, Normandin E, Bhattacharyya S, Mukerji SS, Keller K, Ali AS, et al. (2020). Neuropathological features of Covid-19. *N Engl J Med*; 383(10):989–92. doi: 10.1056/NEJMc2019373.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al.(2020).Clinical Characteristics of 138 Hospitalized Patients With 2019 NovelCoronavirus–Infected Pneumonia in Wuhan, China. *JAMA [Internet]*. [Citado 25/08/2023];323(11):1061. Disponible en: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7042881/>
- Wang Z, Yang B, Li Q, Wen L, Zhang R.(2020). Clinical Features of 69 Cases With Coronavirus Disease 2019 in Wuhan, China.*Clin Infect Dis [Internet]*. [Citado 25/08/2023];71(15):769-77. Disponible en: <https://academic.oup.com/cid/article/71/15/769/5807944>
- Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. (2020). Neuropathogenesis and Neurologic Manifestations of the Coronaviruses in the Age of Coronavirus Disease 2019. *JAMA Neurol*; 77(8):1018–27.