Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 7 Issue 12 December 2023

Research Article

Neurological Implications in Elderly COVID-19 Patients Hospitalized in Mexico

Marisol Silva Vera[1]*, María de Jesús Jiménez González[1], Marcela Ortega Jiménez[1] and Jorge Alejandro Morales Treviño[2]

[1]University of Guanajuato, Division of Health Sciences and Engineering, Celaya- Salvatierra Campus, Guanajuato, Mexico

[2]Mexican Social Security Institute, Regional General Hospital No. 58, Internal Medicine Service. Leon, Guanajuato, Mexico

***Corresponding Author:** Marisol Silva Vera, University of Guanajuato, Division of Health Sciences and Engineering, Celaya- Salvatierra Campus, Guanajuato, Mexico.

DOI: 10.31080/ASMS.2023.07.1716

Received: November 02, 2023

Published: November 27, 2023

Abstract

Introduction: The COVID-19 disease can have distinct phases, including a replicative phase of the virus, a phase of lung involvement and an adaptive immune response phase. Some patients may have an excessive inflammatory response, known as a "cytokine storm," which can cause tissue damage and clinical worsening. Older adults are at higher risk of developing severe forms of the disease. Some of the neurological manifestations associated with COVID-19 infection in older adults include central nervous system alterations, neurovascular symptoms, and neuromuscular symptoms, such as muscle weakness and joint pain.

Objective: Identify the neurological manifestations in older adults hospitalized for COVID-19.

Materials and Methods: A quantitative, cross-sectional, non-experimental study, which was carried out in 840 hospitalized elderly adults, from 60 to 95 years of age. The sample selection was non-random and the patients were grouped according to the National Institute of Respiratory Diseases (INER) Classification. Neurological symptoms were evaluated and the Confusion Assessment Method (CAM) algorithm was used to identify delirium. Patients with a history of neurological disease and cognitive impairment were excluded.

Results: Neurological manifestations of the CNS occurred in 92.9% of patients. The most common CNS symptoms were headache (85.2%) and dizziness (29.4%). CNS manifestations were more common in older adults with a consolidating tomographic pattern. In patients with PNS manifestations, the most common symptoms were deterioration of taste (52.7%) and deterioration of smell (28.4%), vision deterioration showed significant differences between groups ($p \leq 0.05$). The deterioration of taste occurred more frequently in patients with a consolidation tomographic pattern, while the deterioration of smell was more frequent in the Reticular pattern. Regarding the symptoms of the musculoskeletal system, the most common manifestations were asthenia and adynamic, occurring in 100% of the patients.

Conclusions: Our patients presented manifestations of the central nervous system, the peripheral nervous system, and the musculoskeletal system. Clinicians should consider SARS-CoV-2 infection as a differential diagnosis when seeing patients with these neurological manifestations to avoid late or misdiagnosis and prevent transmission.

Keywords: Older Adult; Covid-19; Neurological Manifestations; SARS-CoV-2

Introduction

The SARS-CoV-2 virus, which causes the COVID-19 disease, emerged as a health threat in December 2019 and this led the World Health Organization to declare a pandemic in March 2020 [1]. Many patients hospitalized with COVID-19 develop delirium; The pathophysiology of COVID-19 most frequently causes respiratory symptoms of variable severity. Several studies state that patients develop neurological manifestations that include delirium, altered mental status, anosmia, ageusia, paresis, cognitive alterations, and encephalitis [2], therefore not only affecting the brain stem but also other structures of the brain.

Emerging interventions used to treat patients with covid-19 have forgotten mental health care and delirium prevention. The treatment of neurological disorders can be extremely difficult, due to the extreme isolation and distancing from human contact, especially in older people. Neurological manifestations can be a presentation of direct invasion of the central nervous system (CNS), induced by inflammatory mediators, organ failure, side effect of sedatives, prolonged mechanical ventilation time, environmental factors, and social isolation [3].

In the literature there is evidence of the ability of some coronaviruses to cause CNS [4] infection in humans; SARS-CoV-2 particles were identified in the brains of infected patients [5]. Several authors have suggested the possibility that SARS-CoV-2 may cause encephalitis [6, 7]. This theory has gained relevance after the presence of SARS-CoV-2 in the cerebrospinal fluid was reported [8].

Headache is a common early symptom in COVID-19 [9], it is the first symptom reported in patients [10]; The most common headache associated with COVID-19 is bifrontal or holocephalic [11], with a sensation of pressure and a daily frequency. Several studies have identified common migraine-related symptoms, such as light sensitivity [12], sound sensitivity [13], and gastrointestinal upset [14]. In most cases, a COVID-19-related headache lasts about three days and usually doesn´t last more than two weeks. Other studies have reported headache and dizziness as the most common symptom [15].

It is suggested that COVID-19 may increace the seizure threshold in patients with an existing seizure disorder [16], not only worsens seizure control in patients with previously controlled seizures but may also trigger new-onset seizures in patients with no known history of seizures [17]. Hypoxia, fever, severe metabolic or electrolyte disturbances secondary to COVID-19 can trigger seizures [18].

Seizures may be the initial presentation of COVID-19 and patients may not have any respiratory symptoms [19]. Some patients reported ataxia, while others reported ataxia and tremor [20]. The incidence of acute ischemic stroke among COVID-19 patients is estimated to be 2.3%; The prevalence of acute cerebrovascular diseases in hospitalized COVID-19 patients with severe infection reaches 6% [21].

Anosmia represents up to 40% of cases infected by SARS-CoV-2. Several studies conducted in China, South Korea, France, Italy, Iran, the United Kingdom, and the United States have reported similar associations, with anosmia frequently combined with hypogeusia or ageusia [22]. This suggests that the virus may directly affect odor processing mechanisms.

In the peripheral nervous system (PNS), inflammatory events in muscles and nerves have been reported. These disorders are likely related to a systemic inflammatory response [23]. Symmetrical sensory-motor axonal myopathies and neuropathies have been reported. The degree of muscle injury can also influence the patient's prognosis [24].

Myalgia is a common symptom seen in patients with COVID-19. The prevalence of myalgia varies widely across studies, ranging from 3.36% to over 64% [25]. It has been proposed that generalized inflammation and cytokine storm could be the pathophysiological background of myalgia. Currently, it is unclear whether the muscle manifestation of COVID-19 is due to nonspecific systemic inflammation or direct invasion of muscles [26].

Delirium may be a primary manifestation and the only presenting symptom of COVID-19 without overt respiratory symptoms [27]. Delirium is identified as a complication of COVID-19 [28], and various researchers affirm that the presence of comorbidities during SARS-CoV-2 infection can facilitate the appearance of an acute confusional state [29-31]. Therefore, the aim is to identify the neurological manifestations of older adults with atypical pneumonia hospitalized for COVID-19 at the Regional

General Hospital No. 58 of the Mexican Social Security Institute of León, Guanajuato.

Materials and Methods

A cross-sectional study and descriptive was conducted elderly adults were included, who attended the internal medicine area clinic of the Regional General Hospital No. 58, in León, Guanajuato, México. The participants were selected using a simple random technique based on the availability of patients. Eight hundred and forty hospitalized patients with laboratory confirmation of SARS-CoV-2, aged 60 to 95 years, were included in the analysis. Before enrollment, informed consent was obtained from patients. Lung involvement was evaluated using the National Institute of Respiratory Diseases (INER) scale; patients were grouped into three categories, according to the percentage of lung tissue affected in each lobe; ground-glass opacities, reticular pattern, and consolidation.

All patients were questioned about neurological symptoms at the level of the CNS, PNS and musculoskeletal manifestations; In addition, the Confusion Assessment Method (CAM) diagnostic algorithm was applied to identify suspected delirium.

Neurological manifestations were classified into 3 categories: central nervous system (CNS) manifestations (dizziness, headache, seizures, vertigo, altered state of consciousness, ataxia, and Acute cerebrovascular disease), manifestations of the peripheral nervous system (PNS) (impaired taste, impaired smell, impaired vision and nerve pain) and manifestations of skeletal muscle injury (myalgia, myositis, asthenia and adynamic). Delirium was assessed by Confusion Assessment Method (CAM).

The exclusion criteria were older adults with a history of previous neurological disease and/or previous diagnosis of cognitive impairment, as well as uremic, hepatic, and/or metabolic encephalopathy. Older adults treated with biological therapy, chemotherapy, HIV, and transplant patients were also excluded.

SARS-CoV-2 infection was confirmed by real-time reverse transcription-polymerase chain reaction assay using a SARS-CoV-2 nucleic acid detection kit according to the manufacturer's protocol (Shanghai bio -germ Medical Technology Co). Chest CT scans were performed a Siemens brand multidetector tomograph Somatom Scope Power model with sixteen slices (detectors), manufactured in October 2015, with serial number 749172194. It has the following specifications: collimation of 16 x 0.6 mm, scanning time of 50 s, length of 705.2 mm scan, 1 s rotation time, 130 kV tube settings, eighty mAs, and 0.5 mSv effective dose. Workstations with high image quality BARCO brand screens, PACS Webrx system awarded by Company Mexicana de Radioecology (CMR) with software for precision image analysis.

The study was conducted in accordance with the principles of the Declaration of Helsinki. This study was approved and written informed consent was waived by the Ethics Committee of the Delegation of the Mexican Social Security Institute.

Results

Neurological symptoms and manifestations can affect three different systems: the central nervous system (CNS), the peripheral nervous system (PNS) and the musculoskeletal system. A total of 840 hospitalized older adults with a confirmed SARS-CoV-2 diagnosis were included. The average for age was 65.9 years. 88.3% of older adults had at least one comorbidity present at the time of confirmed SARS-CoV-2 diagnosis and 46.8% were men. According to National Institute of Respiratory Diseases (INER) scale, 167 patients had polished glass, 300 patients had Reticular pattern, while 373 had a consolidation pattern. Patients with a consolidation pattern were significantly older and showed a higher frequency of comorbidities. Neurological manifestations of the CNS occurred in 92.9% of patients. The most common CNS symptoms were headache (85.2%) and dizziness (29.4%). CNS manifestations were more common in older adults with a consolidating tomographic pattern. Nine patients with cerebrovascular disease died from hypoxia. (Table 1).

In patients with PNS manifestations, the most common symptoms were deterioration of taste (52.7%) and deterioration of smell (28.4%), vision deterioration showed significant differences between groups ($p \leq 0.05$) (Table 2). The deterioration of taste occurred more frequently in patients with a consolidation

Variable	Polished glass n = 167	Reticular pattern n = 300	Consolidation n = 373	p
Dizziness	53	49	145	*p < 0.05.
Headache	67	306	343	ns
Seizures	0	9	58	*p < 0.05.
Vertigo	46	38	44	ns
Alteration of consciousness	0	3	85	*p < 0.05.
Ataxia	1	0	0	ns
Acute cerebrovascular disease	0	1	9	ns

Table 1: Manifestations of the Central Nervous System.

The data is expressed as Frequencies. *p < 0.05.

Variable	Polished glass n = 167	Reticular pattern n = 300	Consolidation n = 373	p
Deterioration of taste	86	9	348	ns
Smell impairment	85	106	48	ns
Vision impairment	0	5	83	*p < 0.05.
Neuropathic pain	18	35	3	ns

Table 2: Manifestations of the Peripheral Nervous System.

The data is expressed as Frequencies. *p < 0.05.

tomographic pattern, while the deterioration of smell was more frequent in the Reticular pattern. Regarding the symptoms of the musculoskeletal system, the most common manifestations were asthenia and adynamic, occurring in 100% of the patients (Table 3).

Variable	Polished glass n = 167	Reticular pattern n = 300	Consolidation n = 373	p
Myalgia	167	300	373	ns
Myositis	93	NA	NA	ns
Asthenia	167	300	373	ns
Adynamia	167	300	373	ns

Tabla 3: Manifestations of Injury to Skeletal Muscles.

The data is expressed as Frequencies. *p < 0.05.

Discussion

SARS-CoV-2 presents different mechanisms that facilitate its entry and damage to the CNS, the Systemic hematogenous dissemination or neuronal dissemination, activating astrocytes and microglia. These two possible neurotropic mechanisms of SARS-CoV-2 involve the compromise of the blood-brain barrier, resulting in the death of neuronal cells due to viremia, on the one hand, and the entry of SARS-CoV-2 through the olfactory bulb and its subsequent transport to neurons [32]. There is evidence that suggests that the hematogenous and neuronal pathways can be used to invade the CNS. Various viruses can also infect and migrate through peripheral nerves to reach the CNS. Our patients presented manifestations of the central nervous system, the peripheral nervous system, and the musculoskeletal system.

Ground-glass opacities, consolidation, and reticular pattern are common features seen on computed tomography (CT) scans of patients with COVID-19 [33]. The tomographic pattern of consolidation was the most frequently observed. Tomographic patterns may be associated with COVID-19 progression and prognoses [34]. The literature suggests that the neurological manifestations of COVID-19 can occur before, during and after respiratory involvement [35]; in this study, neurological signs and symptoms were only evaluated during hospitalization for COVID-19.

Anosmia and ageusia were the most common symptoms reported by patients. Taste and smell disorders are common PNS neurological symptoms of COVID-19, which appear to develop in the early stages of the disease [36]. The olfactory epithelium is vulnerable to SARS-CoV-2 since it expresses ACE2, and this explains the appearance of symptoms from very early stages. Disorders of taste and smell can therefore be considered diagnostic markers.

Myalgia is a common symptom observed in the patients studied [37]. Myalgia is explained by generalized inflammation and cytokine storm [38]. At present, it is still unknown whether the muscular manifestation of COVID-19 is due to non-specific systemic inflammation or direct invasion of muscle fibers [39]. Elevated levels of lactate dehydrogenase and creatine kinase can be observed in patients with severe COVID-19 disease [40], however they were not quantified in the study.

We hope that this article allows healthcare professionals to be aware of the neurological manifestations of COVID-19. Further studies are warranted to identify of neurological manifestations, complications of COVID-19 and the pathophysiological mechanisms. The current literature on COVID-19-associated neuropathological alterations and direct neurotropism is limited.

Conclusion

This study presents the first detailed report on the neurological manifestations observed in hospitalized patients with COVID-19. The patients studied presented various neurological manifestations that affected the central nervous system, the peripheral nervous system and skeletal muscles. Patients with severe infection were older adults with pathologies such as systemic hypertension and type 2 diabetes mellitus, and they were uncontrolled at the time of evaluation. Patients with severe infection were more likely to develop neurological manifestations, such as acute cerebrovascular disease, delirium, and seizures.

Most neurological manifestations occurred in the initial stage of the disease, with a median time to hospital admission of 1-2 days. Some patients without typical COVID-19 symptoms presented to the hospital with only a neurological manifestation as their presenting symptom and were admitted to the general emergency area. It is important to pay attention to neurological manifestations in patients with COVID-19, especially those with severe infection, as they may contribute to their death. Additionally, clinicians should consider SARS-CoV-2 infection as a differential diagnosis when seeing patients with these neurological manifestations to avoid late or misdiagnosis and prevent transmission.

Acknowledgements

This study was supported by Universidad de Guanajuato.

Conflict of Interest

The authors declare no conflict of interest.

Bibliography

1. World Health Organization WHO Director-General's opening remarks at the media briefing on COVID-19. Published March 11 (2020).

2. Helms J., *et al*. "Neurologic features in severe SARS-CoV-2 infection". *The New England Journal of Medicine* 382.23 (2020): 2267-2268.

3. Battaglini D., *et al*. "Neurological manifestations of severe SARS-CoV-2 infection: potential mechanisms and implications of individualized mechanical ventilation settings". *Frontiers in Neurology* 11 (2020): 845.

4. Lau KK., *et al*. "Possible central nervous system infection by SARS coronavirus". *Emerging Infectious Diseases* 10.2 (2004): 342-344.

5. Gu J., *et al*. "Multiple organ infection and the pathogenesis of SARS". *Journal of Experimental Medicine* 202.3 (2005): 415-424.

6. Nilsson A., *et al*. "Fatal encephalitis associated with coronavirus OC43 in an immunocompromised child". *Infectious Diseases (Lond)* 52.6 (2020): 419-422.

7. Steardo L., *et al*. "Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19". *Acta Physiology (Oxf)* 229.3 (2020): e13473.

8. Moriguchi T., *et al*. "A first case of meningitis/encephalitis associated with SARS-Coronavirus-2". *International Journal of Infectious Diseases* 94 (2020): 55-58.

9. López JT., *et al*. "Phenotypic characterization of acute headache attributed to SARS-CoV-2: an ICHD-3 validation study on 106 hospitalized patients". *Cephalalgia* 40 (2020): 1432-1442.

10. Magdy R., *et al*. "Characteristics of headache attributed to COVID-19 infection and predictors of its frequency and intensity: a cross sectional study". *Cephalalgia* 40 (2020): 1422-1431.

11. Sahin BE., *et al*. "Patterns of COVID-19-related headache: a cross-sectional study". *Clinical Neurology and Neurosurgery* 219 (2022): 107339.

12. Toptan T., *et al*. "Case series of headache characteristics in COVID-19: headache can be an isolated symptom". *Headache* 60 (2020): 1788-1792.

13. García-Azorín D., *et al*. "Post-COVID-19 persistent headache: a multicentric 9-months follow-up study of 905 patients". *Cephalalgia* 42 (2022): 804-809.

14. Chen N., *et al*. "Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study". *Lancet* 395.10223 (2020): 507-513.

15. Mao L., *et al*. "Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China". *JAMA Neurolgy* 77.6 (2020): 1-9.

16. Abdulsalam MA., *et al*. "Generalized status epilepticus as a possible manifestation of COVID-19". *Acta Neurologica Scandinavica* 142.4 (2020): 297-298.

17. Elgamasy S., *et al*. "First case of focal epilepsy associated with SARS-coronavirus-2". *Journal of Medical Virology* 92.10 (2020): 2238-2242.

18. Asadi-Pooya AA. "Seizures associated with coronavirus infections". *Seizure* 79 (2020): 49-52.

19. Lyons S., *et al*. "Seizure with CSF lymphocytosis as a presenting feature of COVID-19 in an otherwise healthy young man". *Seizure* 80 (2020): 113-114.

20. Balestrino R., *et al*. "Onset of Covid-19 with impaired consciousness and ataxia: a case report". *Journal of Neurology* 267.10 (2020): 2797-2798.

21. Favas TT., *et al*. "Neurological manifestations of COVID-19: a systematic review and meta-analysis of proportions". *Neurology Science* 41.12 (2020): 3437-3470.

22. Xu H., *et al*. "High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa". *International Journal of Oral Science* 12.1 (2020): 1-5.

23. Bocci T., *et al*. "Critical illness neuropathy in severe COVID-19: a case series". *Neurology Science* 42 (2021): 4893-4898.

24. Tsai ST., *et al*. "The Neurologic Manifestations of Coronavirus Disease 2019 Pandemic: A Systemic Review". *Frontiers in Neurology* 11 (2020): 498.

25. Lippi G., *et al*. "Myalgia may not be associated with severity of coronavirus disease 2019 (COVID-19)". *World Journal of Emergency Medicine* 11.3 (2020): 193-194.

26. Yang X., *et al*. "Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study". *Lancet Respiratory Medicine* 8.5 (2020): 475-481.

27. Butt I., *et al*. "Prolonged confusional state as first manifestation of COVID-19". *Annals of Clinical and Translational Neurology* 7.8 (2020): 1450-1452.

28. Beach SR., *et al*. "Delirium in COVID-19: a case series and exploration of potential mechanisms for central nervous system involvement". *General Hospital Psychiatry* 65 (2020): 47-53.

29. Pinzon RT., *et al*. "Neurologic Characteristics in Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis". *Frontiers in Neurology* 11 (2020): 565.

30. Wang D., *et al*. "Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China". *JAMA* 325.11 (2021): 1113.

31. Chen T., *et al*. "Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study". *BMJ 368* (2020): m1295.

32. Priyal Sehgal V., *et al*. "Review of Neurological Manifestations of SARS-CoV-2". *Cureus* 15.4 (2023): e38194.

33. Karimian M and Azami M. "Chest computed tomography scan findings of coronavirus disease 2019 (COVID-19) patients: a comprehensive systematic review and meta-analysis". *Polish Journal of Radiology* 86 (2021): e31-e49.

34. Corapli M., *et al*. "Frequency of typical and atypical computed tomography findings of COVID-19 and their effect on hospitalization". *Northern Clinics Of Istanbul* 8.6 (2021): 554-561.

35. Keyhanian K., *et al*. "SARS-CoV-2 and nervous system: From pathogenesis to clinical manifestation". *Journal of Neuroimmunology* 350 (2020): 577436.

36. Brann DH., *et al*. "Non-neuronal expression of SARS-CoV-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19-associated anosmia". *Science Advances* (2020).

37. Favas TT., *et al*. "Neurological manifestations of COVID-19: a systematic review and meta-analysis of proportions". *Neurology Sciences* 41.12 (2020): 3437-3470.

38. Jiang X., *et al*. "Towards an artificial intelligence framework for data-driven prediction of coronavirus clinical severity". *Computers, Materials and Continua* 62.3 (2020): 537-551.

39. Lippi G., *et al*. "Myalgia may not be associated with severity of coronavirus disease 2019 (COVID-19)". *World Journal of Emergency Medicine* 11.3 (2020): 193-194.

40. Huang C., *et al*. "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China". *Lancet* 395.10223 (2020): 497-506.