Review article

Post-COVID 19 neurological syndrome: Implications for sequelae's treatment

William Camargo-Martínez [a], Ivan Lozada-Martínez [a,b,c,*], Angie Escobar-Collazos [a], Aura Navarro-Coronado [a], Luis Moscote-Salazar [a,b,c], Alfonso Pacheco-Hernández [b], Tariq Janjua [d], Pilar Bosque-Varela [e]

[a] Medical and Surgical Research Center, School of Medicine, University of Cartagena, Cartagena, Colombia
[b] Colombian Clinical Research Group in Neurocritical Care, School of Medicine, University of Cartagena, Cartagena, Colombia
[c] Latin American Council of Neurocritical Care, Cartagena, Colombia
[d] Intensive Care, Regions Hospital, 640 Jackson St, Saint Paul, MN, USA
[e] Department of Neurology, Christian Doppler Klinik, Paracelsus Medical University of Salzburg, Austria

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ABSTRACT

Study design
Literature review.
Objectives: Describe the implications of post-COVID syndrome due to neurological sequelae including treatment and the differences that may exist between this group of patients and those who present these events not associated with COVID-19.
Methods: A non-systematic review of the literature was carried out in PubMed and Science Direct databases, using the keywords "Post-acute COVID-19 syndrome"; "Neurological complications"; "Neurologic Manifestations" "COVID-19″ and "Rehabilitation", as well as synonyms, which were combined with the operators "AND" and "OR".
Results: The COVID-19 viral caustive agent, SARS-CoV-2, has a high affinity for human angiotensin-converting enzyme 2 receptor on type II pneumocytes. This receptor is also expressed in neurons and glial cells. Based on the foregoing and other not so clear mechanisms, it is stated that SARS-CoV-2 has tropism for the nervous system, being evident through the neurological manifestations observed in patients with mild, moderate and severe phenotype of the disease such as anosmia, ageusia, headache, cerebrovascular accidents, Guillain-Barré syndrome, seizures, and encephalopathy. This can generate severe sequelae and even fatal outcomes in those affected.
Conclusions: Neurological complications caused by COVID-19 are frequent and represent a risk that compromises the functional capacity and the life of patients. The suspicion of these conditions, the strict control of metabolic alterations and cardiovascular risk factors, the effective and safe treatment of these entities, are a current challenge throughout the pandemic. The rehabilitation process in these patients is a challenge. This is due to the limitations generated by multi-organ damage, as well as risk of brain death.

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1. Introduction

The COVID-19 infectious agent, SARS-CoV-2, has a high affinity for human angiotensin-converting enzyme 2 (ACE2) receptor. This receptor is also expressed in neurons and glial cells, which could explain the reported neurological manifestations, such as olfactory neuropathy (anosmia), peripheral neuropathy and brain disorders.

In post-mortem studies, viral particles have been found in the cerebrospinal fluid and cytoplasm of neocortex and hypothalamus neurons, as well as neuronal degeneration and necrosis, edema, glial cell hyperplasia, and cellular infiltrates. A study with murine models showed that the dissemination path of SARS-CoV-2 into central nervous system is through the olfactory bulb, spreading to other adjacent areas and generating severe perivascular inflammation and meningitis [1]. It has been suggested that in cured patients, SARS-CoV-2 remains latent in the central nervous system for a long time, being able to reactivate and trigger neurological

* Corresponding author at: Medical and Surgical Research Center, School of Medicine, University of Cartagena, Cartagena, Colombia.
E-mail address: ilozadam@unicartagena.edu.co (I. Lozada-Martínez).

complications [1]. Currently, Post-COVID Syndrome can include symptoms related to residual inflammation, organ damage, impact on pre-existing health conditions or non-specific effects due to hospitalization or prolonged ventilation (post-intensive care syndrome) [2]. In this sense, it is pertinent to pay attention to new research aimed at evaluating prognostic markers, such as markers of inflammation in peripheral blood, such as the neutrophil–lymphocyte ratio, C-reactive protein, D-dimer, or serum ferritin, which seek to predict morbidity and mortality [3].

The most frequently reported neurological manifestations are anosmia, ageusia, and headache. However, case series and observational studies show data on a large number of patients who develop cerebrovascular accidents (CVD), Guillain-Barré syndrome (GBS), de novo status epilepticus, and encephalopathy [4]. The neurological complications that more frequently cause severe sequelae will require neurorehabilitation to try to recover the lost functional capacity. However, since COVID-19 is a multisystemic disease that considerably affects organs such as lungs and heart, the rehabilitation process is not equivalent in comparison to other groups of patients who develop neurological complications due to other causes, which is why the neurorehabilitation approach is more complex [5]. Rehabilitation encompasses many sequelae, and the rehabilitation team in a specialized center can treat many sequelae simultaneously, however, in regions where resources are limited and there are no specialized neurorehabilitation centers and multidisciplinary teams, it is a challenge to prioritize the rehabilitation of one organ over another [6]. On the other hand, pandemic statistics highlight the need for careful and continuous follow-up of all patients with COVID-19, even those considered asymptomatic, with regular screening for probable long-term persistent neurological sequelae. Such cases also require rapid lines of communication between primary care physicians and neurologists via direct email or telephone communications through neurology registrars at least once to properly document and study these cases [6]. In this context, the objective of this manuscript is to describe key aspects of neurological complications due to COVID-19 with post-COVID syndrome, focused on the nervous system, and the elements that must be taken into account during evaluation and neurorehabilitation of those with neurological complications.

2. Methods

A non-systematic review of the literature was carried out in PubMed and Science Direct databases, using the keywords "Post-acute COVID-19 syndrome"; "Neurological complications"; "Neurologic Manifestations" "COVID-19″ and "Rehabilitation", as well as synonyms, which were combined with the operators "AND" and "OR". The search date was carried out until January 2021. Systematic reviews, case series and case reports were included. The only exclusion criterion was the unavailability of the full text. Finally, 18 studies were included that met the inclusion criteria for the specific description of cases (Table 1), as well as review articles and letters to the editor for the description of the pathological mechanisms of neurological complications. The articles including are all in English.

3. Stroke

Various studies have found a relationship between COVID-19 and stroke. Correia et al. [7], carried out a systematic review, which included a total of 409 patients diagnosed with COVID-19 that presented with neurological manifestations. They found that 6 (1.4%) patients had acute cerebrovascular disease [7]. Likewise, Fraiman et al. [8] characterized a population of 275 patients with COVID-19 that presented with cerebrovascular disease, mostly ischemic

stroke (82%) [8]. In this group, great vessel disease was the most frequent cause (47%), the mean age was 64.16 ± 14.73 years (range 27–92 years), and 54% were men. The results described are short-term and mainly related to the hospitalization phase for acute treatment, 129 (65.48%) patients survived or remained critically ill, while 68 (34.52%) died [8]. SARS-CoV-2 can cause stroke by various mechanisms, such as invasion of vessel wall that provokes coagulopathy due to endothelial inflammation, myocardial damage that precipitates the formation of clots, or destabilization of a pre-existing atheroma plaque [8]. In patients with stroke and COVID-19 infection the reported mortality is 39%, much higher than stroke patients without COVID-19 infection [9]. The coexistence of COVID-19 infection and cerebrovascular accident considerably increases the risk of developing kidney failure, either due to the use of contrast in a hemodynamically unstable patient, or to multisystemic failure secondary to COVID-19 itself, which increases the risk of dying [9]. There is limited data on the usage of intravenous thrombolysis in cases of severe infection, so it is preferable to evaluate the coagulation profile in detail before making a decision regarding this intervention, especially in patients with neurovascular or cardiometabolic diseases such as heart failure, Diabetes Mellitus, arterial hypertension, arteriovenous malformations or asymptomatic aneurysms, where it is necessary to establish the risk–benefit ratio [10]. Most of the patients that develop this complication present with catastrophic brain involvement (multi-vessel or massive stroke), generating a very high risk of loss of total functional capacity or death, especially, patients that express the severe COVID-19 illness, who are on mechanical ventilation for long periods, complicating the neurorehabilitation and decreasing the probability of recovering functional capacity [10].

These factors represent a challenge for the neurology multidisciplinary team, critical care, neurorehabilitation, among others. It is essential to carry out a complete evaluation in stroke patients that eventually will go to the rehabilitation area, since it must be determined the short, medium and long term prognosis. Even though early initiation of neurorehabilitation is crucial, it is not prudent to start until the patient's health status stabilizes, with the objective of avoiding possible relapses during of rehabilitation. More recently, Wijeratne et al. [11] recommend administration of immunomodulatory hormones, like melatonin, and curcumin to help the neurorehabilitation interventions, based on the demostrated share pathobiology of the neurological impact in acute ischemic stroke and COVID-19, as well as manifestations like fatigue, infection, dyspnea and muscle weakness and neuropsychiatric manifestations as impaired thinking, depression and anxiety. However, better quality studies are needed to support this intervention [11].

We suggest that these patients should be treated by a multidisciplinary team, which depending on the patient's abilities, strictly monitoring vital signs when motor exercises are being executed, as well as balance training, gait training (all these with or without external stimuli) and exercises with an intensity according to the recovery period, with a progressive nature and focused on the affected brain region [12].

4. Guillain-Barre syndrome

In a systematic review carried out by Whittaker et al. [13], 2504 COVID-19 patients were evaluated, in this study 11 cases of Guillain-Barré syndrome were reported (0.4%). Despite smaller proportion, these patients have long-term permanent neurological sequelae or even have fatal outcomes. In this sense, there is a lot of interest in the association of COVID-19 and the development of Guillain-Barre syndrome, which in almost all cases, occurs during the acute phase of the infection [14]. The manifestation of this

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Table 1
Recent evidence summary of COVID-19 cases with neurological complications.

Author	Study type	Complication	Study population	Age	Description	Outcome
Beyrouti et al. (2020) [25]	Case series	Stroke	6	64 years olds	A man with respiratory failure due to COVID-19 is admitted to intensive care unit. 15 days after onset of symptoms the patient developed left upper monoparesis. The magnetic resonance imaging confirmed intradural left vertebral artery occlusion and acute left posterior inferior cerebellar artery territory infarction with petechial hemorrhage. D-dimer values were > 80,000 μg/L. On day 22, he developed acute bilateral incoordination and right homonymous hemianopia, due to extensive acute posterior cerebral artery territory.	Not specified
				53 years olds	A woman anticoagulated due to valvular atrial fibrillation, arrived 24 days after the onset of COVID-19 symptoms due to sudden confusion, incoordination, and drowsiness. Brain tomography confirmed acute large left cerebellar and right parietal-occipital infarcts. D-dimer values were 7750 μg/L and the INR was 3.6 at the time of stroke symptoms.	Death
				85 years olds	A man who arrived 10 days after the onset of COVID-19 symptoms with dysarthria and right hemiparesis. He had a history of atrial fibrillation, hypertension, and ischemic heart disease. Brain CT showed occlusion and infarction of the left posterior cerebral artery. D-dimer values were 16,100 μg/L.	Not specified
				61 years olds	Hypertensive man, with a history of stroke and high body mass index, presented dysarthria and left hemiparesis. Brain magnetic resonance imaging showed an acute the right striatum infarct. D-dimer values were 27,190 μg/L.	Not specified
				83 years olds	Hypertensive male, diabetic, with a history of ischemic heart disease, heavy smoking and alcohol consumption, presented dysarthria and left hemiparesis 15 days after the onset of COVID-19 symptoms. CT angiography showed thrombotic occlusion of a proximal M2 branch of the right middle cerebral artery. An infarct in the right insular area was shown. D-dimer values were 19,450 μg/L.	Not specified
				73 years olds	Male presented dysphasia and right hemiparesis, 8 days after the onset of COVID-19 symptoms. Brain MRI showed a thrombus in the basilar artery, bilateral P2 segment stenosis, and multiple acute infarcts (right thalamus, left pons, right occipital lobe, and right cerebellar hemisphere).	Not specified
Zhai et al. (2020) [26]	Case report	Stroke	1	79 years olds	A man presented right monoparesis for a day and mild cough for one week. Runs of speech were not fluent with tongue deviation. Brain CT showed lacunar infarction.	Mild impairment on speech fluency
Avula et al. (2020) [27]	Case series	Stroke	4	73 years olds	Hypertensive man, with dyslipidemia and carotid stenosis, was admitted with fever, respiratory distress and altered mental status. The cerebral tomography showed a large acute infarct of the left middle cerebral artery territory.	Not specified
				83 years olds	A woman with a history of urinary tract infection, hypertension, hyperlipidemia, diabetes mellitus type 2 and neuropathy. She presented with facial paralysis and slurred speech, NIHSS scale of 2. Later, the patient's facial paralysis progressed to left hemiparesis. NIHSS scale of 16. Brain tomography showed moderate hypodensity in the right frontal lobe representing acute infarct.	Death
				80 years olds	A woman with a history of hypertension was brought to the emergency department due to altered mental status and left hemiparesis. Brain tomography scan showed acute right middle cerebral artery infarction. Later on, she presented acute kidney injury and a progressive increase of oxygen requirements.	Death
				88 years olds	A woman with a history of hypertension, chronic kidney disease, and hyperlipidemia, arrived at the emergency department with transient 15-minute episode of right arm weakness and speech impairment. D-dimer values of 3442 ng/L. Magnetic resonance imaging showed an acute infarction in the left medial temporal lobe. Magnetic resonance angiogram revealed mild stenosis of the right M1 segment.	Not specified
Zhao et al. (2020) [28]	Case report	Stroke	1	60 years olds	A man with hypertension, developed dyspnea and dizziness, progressing to facial paralysis and left hemiparesis. Brain MRI showed an acute cerebral infarction and large blood vessels occlusion.	Not specified
Al Saiegh et al. (2020) [29]	Case series	Stroke	2	31 years olds	A man presented severe headache and loss of consciousness a week after onset of COVID-19 symptoms. cerebral angiogram that showed a right-sided ruptured dissecting posterior–inferior cerebellar artery aneurysm that was treated with a flow-diverting stent. Later he did not show focal neurological deficit, but he did show confusion, with gradual improvement.	Confusion
				62 years olds	A woman presented right hemiparesis and acute onset aphasia. In the CT angiogram revealed a left middle cerebral artery occlusion, which was then treated. Days later, she returned with altered mental status, and a brain tomography scan confirmed a hemorrhagic stroke with midline shift and obstructive hydrocephalus that required decompressive hemicraniectomy.	Not specified

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Table 1 (*continued*)

Author	Study type	Complication	Study population	Age	Description	Outcome
Giri et al. (2020) [30]	Case report	Encephalopathy - Stroke	1	68 years olds	A man with no relevant past medical history, was admitted to intensive care unit due to respiratory distress. Brain tomography scan ruled out cerebrovascular disease; however, he remained encephalopathic, unable to be extubated. Brain MRI showed numerous small areas of restricted diffusion throughout the centrum semiovale, consistent with a small acute infarct. Acute infarction was also found adjacent to the frontal horn.	Not specified
Ordoñez et al. (2020) [31]	Case report	Encephalopathy	1	46 years olds	A man with a history of diabetes mellitus and arterial hypertension, was intubated in intensive care unit for respiratory distress and general deterioration. When extubated, he presented disorientation, psychomotor agitation, and detachment with the environment. Magnetic resonance imaging with contrast revealed hyperintense subcortical images, as well as in occipital and frontal (bilaterally) white matter in T2 and FLAIR sequence. Hypointense lesions on T1, without diffusion restriction, without enhancement after contrast.	Weakness in lower extremities
Hallal-Peche et al. (2020) [32]	Case series	Encephalopathy	7	77 years olds	A woman with a history of transient ischemic stroke. She was admitted to intensive care unit due to respiratory distress and required intubation. After two days with sedation, she developed clonic head and buccal movements. Her EEG revealed a burst-suppression pattern probably induced by drugs (Propofol, Diazepam). Weakness was registered in all 4 limbs and the electromyogram revealed moderate motor and axonal polyneuropathy.	Discharged in stable condition
				65 years olds	A man with no relevant past medical history, presented fever, cough, and dyspnea. He required intubation in critical care due to respiratory distress. On day 13 of his stay, he was still unconscious with discreet anisocoria. The EEG showed an alpha coma pattern with generalized activity of invariant 11 Hz and amplitude of 10–20 μV, not reactive to passive opening and closing of the eyes, or to painful stimuli.	Death
				78 years olds	A man with a history of moderate chronic thrombocytopenia, heart transplant and chronic kidney disease. After onset of COVID-19 symptoms, he presented acute confusional state. The EEG showed signs of diffuse cortical involvement compatible with a mild degree of encephalopathy, with a probable toxic-metabolic origin.	Death
				79 years olds	A woman with a history of stroke, atrial fibrillation and myelodysplastic syndrome. Despite being in supportive therapy for COVID-19, she presented a rapid deterioration of her general condition and a decreased state of consciousness. The EEG showed slow and polymorphous background activity (3–4 Hz), interspersed with paroxysms of acute-slow wave of high persistence, compatible with encephalopathy with generalized ictal activity.	Death
				69 years olds	A woman with a history of hepatitis C and chronic kidney disease on hemodialysis, developed acute confusional state after respiratory symptoms of COVID-19. The EEG showed a posterior alpha rhythm of 9 Hz reactive to the opening and closing of the eyes, and outbreaks of polymorphic slow waves (3–4 Hz) of moderate persistence and short duration (2–3 s) located in the bilateral frontotemporal region with right dominance. Due to the suspicion of a toxic-metabolic origin, several drugs were withdrawn with progressive improvement.	Discharged in stable condition
				75 years olds	A man with type I respiratory failure secondary to pneumonia. On the day 22 of hospitalization, he presented cardiorespiratory arrest, and required 30 min of resuscitation maneuvers. He was admitted to critical care unit to be intubated, and on day 31, without sedation, he presented absence of brain stem reflexes, irregular breathing, and non-reactive pupils.	Death
				53 years olds	A man with respiratory failure due to COVID-19, required 15 L/min of oxygenation or through a reservoir nasal cannula and suffered three cardiorespiratory arrests. On day 12 of hospital stay, after 24 h without sedation, he persisted with 3 points on the Glasgow scale in a context of renal failure. The EEG showed a theta coma pattern (6–7 Hz and low amplitude) without topographic differentiation and was not reactive to pain or passive opening or closing of the eyes.	Not specified
Muccioli et al. (2020) [33]	Case report	Encephalopathy	1	47 years olds	A woman with a positive nasopharyngeal swab for SARS-CoV-2, developed expressive aphasia and inattention, which later progresses to marked confusion and agitation. Brain MRI and cerebrospinal fluid studies were unremarkable, while EEG showed deceleration with frontal sharp waves. Neuropsychiatric symptoms resolved after treatment with Tocilizumab	No sequel
Farzi et al. (2020) [34]	Case report	Guillain-Barre syndrome	1	41 years olds	Man that 10 days after onset of pneumonia, experienced paresthesia in feet that progresses involving more proximal parts and mild weakness added. Seven days after the onset of these symptoms, he presented flaccid paralysis, absence of reflexes, and diminished reflexes in the upper extremities. There was Symmetrical limb weakness and symmetric and severe hyperesthesia in all 4 limbs. The findings were consistent with demyelinating pattern polyneuropathy, he received treatment with intravenous immunoglobulins, finding a satisfactory response.	Weakness in lower extremities

Table 1 (*continued*)

Author	Study type	Complication	Study population	Age	Description	Outcome
Khalifa et al. (2020) [35]	Case report	Guillain-Barre syndrome	1	11 years olds	A man presents acute onset of unsteady gait and weakness in lower limbs with tingling sensation. He had symmetrical weakness that affected lower limb muscle groups with reduced motor power, hypotonia, lost ankle and knee reflexes, and impaired sensitivity to pain and light touch on both feet. In upper extremities, reflexes were elicited with reinforcement. MRI of the brain and spinal cord was performed, which revealed an enhancement of the cauda equina nerve roots on postcontrast findings, supporting the diagnosis of GBS.	Weakness in lower extremities
Coen et al. (2020) [36]	Case report	Guillain-Barre syndrome	1	70 years olds	A man presented paraparesis, distal allodynia, difficulty urinating and constipation. Ten days before, he developed myalgia, fatigue and a dry cough. COVID-19 was diagnosed. The physical examination revealed bilateral lower limb flaccid paresis, absence of deep tendon reflexes of the upper and lower limbs and idiomuscular response to percussion of the tibialis anterior muscle, indifferent plantar reflexes. This is consistent with acute inflammatory demyelinating polyneuropathy.	Weakness in lower extremities
Frank et al. (2020) [37]	Case report	Guillain-Barre syndrome	1	15 years olds	A man presented frontal headache with retroorbital pain, fever and intense sweating. Examination revealed progressive symmetrical limb weakness, absence of deep tendon reflexes, normal plantar response and no sensory loss. Electroneurography revealed normal sensory nerve action potential, although severe reduction of the nerve compound muscle action potential amplitude in all motor nerves studied, with relatively preserved conduction velocities. The F waves were absent in the nerves studied. These findings are compatible with the acute motor axonal neuropathy variant of GBS.	Weakness in upper and lower extremities
Lyons et al. (2020) [38]	Case report	Status epilepticus	1	20 years olds	A man reported three days of myalgia, fever and lethargy, later a tonic-clonic seizure. COVID-19 diagnosis was confirmed.	No sequel
Carroll et al. (2020) [39]	Case report	Status epilepticus	1	69 years olds	A woman with a history of Type II Diabetes Mellitus, kidney transplant, medicated with prednisolone, tacrolimus and mycophenolate. The patient presented refractory status epilepticus 6 weeks after initial infection by COVID-19, elevation of inflammatory markers and hippocampal atrophy were demonstrated.	Discharged in stable condition
Monti et al. (2020) [40]	Case report	Status epilepticus	1	50 years olds	A man with fever and delirium, developed focal motor seizures with altered state of consciousness and orofacial dyskinesia. Brain MRI revealed no abnormalities. He was taken to critical care unit and treated with anesthetics for refractory status epilepticus, with anti-NMDA antibodies found in cerebrospinal fluid.	Discharged in stable condition
Elgamasy et al. (2020) [41]	Case report	Status epilepticus	1	73 years olds	A woman who presented two episodes of painful muscle spasms in the left upper limb and lower limbs. Radiological images, electroencephalography, lumbar puncture, and autoimmune profile were normal. Days after her admission to the hospital epileptic episodes were observed.	Discharged in stable condition
Panda et al. (2020) [19]	Systematic review	Status epilepticus	12	≤18 years olds	70% of the patients had severe COVID-19. All patients who presented status also developed generalized weakness. Electroencephalography showed delta wave activity.	No sequel

neuropathy associated with SARS-Cov-2 infection has been attributed to the strong immune response that triggers during the infectious process, with followup activation of pro-inflammatory cytokine cascades [15]. The clinical presentation ranges from mild symptoms such as decreased muscle strength in the extremities, paresthesia or facial paralysis, to respiratory muscles involvement [16,17]. Most of the patients with this disease, recover with long lasting sequelae after the resolution of COVID-19, and due to the short observation window, the final results cannot be determined at 6 months or a year. Considering that for the final diagnosis and management of this pathology, specialized examinations such as electromyography and histopathological evaluation must be carried out, the approach in lower-level health centers can be complex. Due to this, it is necessary to be attentive to clinical signs and activate the protocol to refer the patient to a neurological or more complex care center [16]. Furthermore, in the event that the neurological condition is resolved, but not the respiratory or multisystemic involvement, it will be very difficult to start the rehabilitation process to recover the functional capacity of the patient, which will be long and slow.

The rehabilitation should be established according to the degree of affection and the affected regions. It is pertinent to perform exercises that stimulate motor skills in order to recover muscle tone, training for the recuperation of facial mobility in case of paralysis, or in the case of greater severity, breathing exercises and external stimulation with robotic tools [18].

5. Status epilepticus

Panda et al. [19] carried out a systematic review and *meta*-analysis, where they reported cases of status epilepticus secondary to COVID-19 [19]. Of 3707 patients (all under 18 years old), 42 patients (1%) had neurological complications, 12 of these patients had seizures (0.3%), leaving neurological sequelae of diverse degrees of severity [19]. The global incidence of seizures in a patient with COVID-19 is increasing, being an evident manifestation of viral invasion of central nervous system. However, seizures are also a sign of acute brain injury caused by hypoxemia that results from severe pneumonia. In this group of patients, the presentation of metabolic alterations and septic encephalopathy is also common. Those with a history of status epilepticus have a less favorable prognosis since the intensity and frequency of seizures may increase due to a lower threshold [20]. The proposed mechanism for epiletogenesis to explain de novo status epilepticus is based on the fact that viral infections that affect the central nervous system activate a neuro-inflammatory cascade that increases and propagates neuronal depolarization. This leads to cellular and

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molecular metabolic derangements inducing status [21]. In patients with severe COVID-19, electrolyte and metabolic imbalances, hypoxia, and inflammatory processes contribute to the development of seizures or abnormal EEG background [4].

Analyzing the repercussion of certain systemic alterations on the severity of seizures, and their possible recurrence, it is crucial to control such disorders by monitoring the metabolic state and controlling electrolytes alterations, in addition to improving organ functionality through physiotherapeutic rehabilitation [21]. It is important to keep the respiratory system in optimal condition to avoid hypoxia, to perform respiratory exercises successfully, and to improve ventilatory function compromised by COVID-19. Also, performing aerobic exercises progressively in intensity and in time this may be beneficial for these patients [19].

6. Encephalopathy

In the same study by Panda et al. [19], 0.7% (25) patients developed encephalopathy. This study suggests that in general, these patients have worse prognosis and a lower survival rate [19]. This association may be mediated by ACE2 / SARS-Cov-2 interaction, which occurs on capillary endothelium and neurons. Thus, neurotropism directly affects the entire brain territory [22]. Neuronal damage results in damaged tissue, immune-mediated by significantly elevated interleukin activity [23]. More than a third of patients with severe COVID-19 experience impaired consciousness and / or delirium during the acute / subacute course of the disease, in the context of encephalopathy. Such neurological condition can trigger a comatose state, compromising the entire functional capacity of the individual [24]. Aforesaid scenario implies an early and precise identification and treatment of the main cause of the neurological complication. This helps avoid progression to multisystem failure or severe irreversible target organ damage [23].

Taking into account the level in which encephalopathy can affect the neurological functions, patients can benefit from exercises that stimulate neuroplasticity, such as music therapy, physical therapy, cognitive-behavioral therapy, gait training, telerehabilitation, among others. This can be achieved with the help of a multidisciplinary team that includes neurophysiology, biomechanics, biomedical engineering, physiotherapy, and clinical medicine [12,18,22].

7. Conclusion

Neurological complications caused by COVID-19 are frequent and represent a risk that compromises the functional capacity and the life of patients. The suspicion of these conditions, the strict control of metabolic alterations and cardiovascular risk factors, the effective and safe treatment of these entities, are a current challenge throughout the pandemic. The rehabilitation process in these patients is a challenge. This is due to the limitations generated by multi-organ damage, as well as risk of brain death. The prognosis of recovery from post-COVID neurological syndrome must be evaluated in a personalized way, depending on target organ damage, especially lungs and heart, which intervene in the process of physical activity and maintenance of daily life activities. It is necessary to design a specific protocol, as well as to establish directed spaces for the neurorehabilitation process, that include personnel, infrastructure and technological equipment that guarantee therapeutic success, especially in low and middle-income countries that do not have units of specialized rehabilitation. Currently there is no best quality evidence on this topic, so it is necessary to carry out multicenter prospective studies to evaluate the impact of specific interventions as well as the prognosis of these patients.

Declaration of Competing Interest

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

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