Chapter

Post-COVID-19 Condition and Its Presence in Mexico

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Abstract

In this chapter, we discuss general information about the post-COVID-19 condition, also known as long COVID. Since it is still under research, many questions remain unanswered. Nevertheless, post-acute complications due to infections have been previously reported for other viruses. Among those complications that remain are anosmia, fatigue, cardiovascular, and pulmonary. The evidence so far suggests that these complications decrease with time. The most worrying persistent symptoms due to COVID-19 are related to neurological damage. Most post-COVID-19 complications can be treated in a standard way, but their impact on life quality is unknown. Finally, we present a rough landscape of long COVID-19 in Mexico and Latin America. More studies are needed to study this condition and its impact on public health.

Keywords: long COVID-19, post-acute COVID-19, persistent symptoms, fatigue, brain fog

1. Introduction

In December 2019, an outbreak of pneumonia of unknown origin occurred in the City of Wuhan, China [1]. On January 9th, 2020, the virus behind the infections was identified as a new strain of β-coronavirus [2]. Subsequently, on February 11th, it was named by the World Health Organization (WHO) as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the associated disease was coronavirus disease 2019 (COVID-19) [2].

According to an interim WHO guidance for the management of patients with suspected COVID-19 [3], early reports from the China Center Disease Control (CCDC) suggested that most people who developed a confirmed case of COVID-19 infection manifested mild symptoms, 14% developed a severe disease that required hospitalization, of which 5% required admission to the intensive care unit; with a higher risk of death those with advanced age and presence of comorbidities [3].

Severe disease and death have been observed in patients older than 75 years. The comorbidities associated with a higher risk of death are hypertension, cardiovascular diseases, diabetes, chronic respiratory diseases, and cancer [4].

The COVID-19 symptoms related to neurological disease reported so far are anosmia, dysgeusia, muscle pain, and headache during the early stage of the infection [5]. These symptoms suggest many hypotheses about how the virus reaches the nervous system. Some of them are its potential entry via the olfactory groove or bloodstream [6–9].

In Mexico, the first official case was reported on February 28th, 2020 [10], and by March 11th, 2020, the WHO declared COVID-19 a global pandemic [11]. Up to May 5th, 2020, 3,525,116 confirmed cases were reported globally, having a case fatality rate of 3.4% [2].

In Mexico, up to January 26th, 2022, the national cumulative incidence rate was 36.00 cases per 1000 inhabitants. Meanwhile, the number of cases was 13,682,501. The mortality rate per 1000 inhabitants in age groups older than 60 was 12.04 [12].

According to Wang et al. [13], the estimated excess mortality in 2020–2021 was 18.2 million people. Mexico has not been the exception since, according to the same study, it is among the countries with the highest excess mortality induced by COVID-19, accounting for 798,000. According to Halabe-Cherem et al. [14], the impact of COVID-19 on health extends beyond disease and mortality rates, affecting the management of chronic conditions, preventive care, and vaccination programs. Moreover, many patients experience physical and mental sequelae that persist for months after recovery from the virus. This persistence of symptoms is known as "prolonged COVID" or "post-COVID syndrome" [14].

2. Sequels due to COVID-19, post-COVID-19 condition, or long COVID-19

Most patients with COVID-19 recover after acute infection with SARS-CoV-2, but some report persistent complications. Michelin et al. [15] conclude that the studies up to 2021 were quite heterogeneous and mostly from Western European countries, with little representation from low to mid-developed countries.

The definition of this disease has changed throughout the pandemic, emerging with various names, including long-term COVID or post-COVID-19 condition [15].

Syndromes due to post-acute infection have previously been reported [16]. According to the review by Choutka et al. [16], the possible causes of these syndromes are remnants or reservoirs of the pathogen that caused the primary infection, autoimmune response, dysbiosis or reactivation, and tissue damage.

In the case of COVID-19, the active SARS-CoV-2 virus has been found even 3 to 6 months after infection [17]. For their part, Wallukat et al. [18] explore the relationship between prolonged COVID and the autoimmune response, finding autoantibodies in most patients who developed long COVID-19. Regarding the last two possible causes of long COVID, gastrointestinal affectations have been reported, in addition to the damage to lung tissues [3].

Prolonged COVID-19 can generate limitations in the daily activities of patients. The situations where a person with long COVID-19 is affected in their daily activities are diverse, for example:

Those with lung damage will have shortness of breath, fatigue, and these effects are mainly related to a limitation in respiratory function [19]. Those presenting with symptoms such as intestinal pain and nausea that have persisted for months are associated with limited gastrointestinal function [19].

People who experience memory problems or "brain fog" suffer from issues related to concentration or thinking [19].

The long-term sequelae generated by COVID-19 are unknown. However, repercussions have been reported worldwide at various systemic levels. These include pulmonary, cardiovascular, neurological, and even mental health. Although these conditions are not lethal, they damage the quality of life. In the case of the Mexican population, these sequelae are associated with the comorbidities that occur most frequently in this population. Long-term complications secondary to COVID-19 could be expected later [20].

The following sections report the most common complications reported in the literature.

2.1 Pulmonary complications

Torres-Cuevas et al. [20] report studies suggesting that approximately 40% of the population infected by SARS-CoV-2 and Middle East Respiratory Syndrome (MERS) presented radiological changes and data suggestive of pulmonary fibrosis, which were associated with respiratory alteration, even 15 years after the infection. The same authors mention the following risk factors:

- Age
- Disease severity
- Stay in intensive care
- Mechanic ventilation
- Smoking and alcoholism
- These factors are expected to play a likewise role in the long COVID-19.

Torres-Cuevas et al. [20] reported that as many as one-third of COVID-19 patients exhibit signs of pulmonary fibrosis and lung function abnormalities 3 months after COVID-19. Pulmonary fibrosis is relevant because it is associated with higher morbidity and mortality. It may also be considered the most significant health sequel of the pandemic since it requires the implementation of pulmonary rehabilitation techniques [20].

Similarly, it has been identified that respiratory symptoms due to COVID-19 can persist even 110 days after the acute picture, the most frequent being chest pain, anosmia, cough, and dyspnea [20].

2.2 Cardiovascular complications

Viruses can cause pericarditis due to systemic inflammation generated in severe cases [21] due to cytotoxic mechanisms. In addition, SARS-CoV-2 infection induces an excessive inflammatory response. This inflammation is responsible for pericardial effusions or cardiac tamponade [20, 22].

Elevated Angiotensin-Converting Enzyme 2 (ACE-2) presence in the cardiovascular system allows direct viral invasion. Then, the immune response and cytokines

cause inflammation of the heart muscle, interfering with the conduction system and heart pumping capacity, leading to arrhythmias and cardiac arrest [23].

Infectious processes of viral origin are associated with cardiovascular complications, one of the chief causes of mortality. The effect can persist for up to 10 years after the acute infectious process [20].

Months after the acute phase of SARS-CoV-2 infection, regardless of severity, up to 60% of cases present myocarditis and 71% high-sensitivity troponin T elevation. It is due to a significant decrease in left ventricular ejection fraction [20].

Thrombotic events are considered one of the leading causes of death in patients with COVID-19. Various mechanisms generate a procoagulant state due to an unregulated release of proinflammatory cytokines, resulting in endothelial damage and dysfunction, as an increase in promoters of platelet aggregation and fibrin formation [20].

Different factors favor the presentation of these complications in patients after COVID-19, so an increase in the incidence of this group of diseases in the Mexican population can be expected [20].

2.3 Neurological symptoms and complications

Among the most frequent symptoms are anosmia, headache, myalgias, and mental fog [20].

Neurological alterations are of great relevance since they may significantly affect the quality of life of those who survived COVID-19 [20].

Different viral infections, including coronavirus infections, can manifest with neurosensory alterations, demyelinating diseases, or cerebral vascular events in surviving patients after recovering. After SARS-CoV-2 infection, neuropsychiatric alterations that persisted up to 4 years after recovery were identified [24].

Since the discovery of SARS-CoV-2, various hypotheses have emerged about the mechanism of development of this complication, including its neuroinvasive potential through the olfactory groove or invasion of the nervous system through the bloodstream [24].

Flores-Silva et al. [1] mention that up to 52% of patients may persist with fatigue 10 weeks after the onset of the disease, independent of the severity. This symptom is considered the most frequent in the long term [24].

After the acute phase, about 5–10% of patients persist with anosmia at 4 weeks, with the probability of developing parosmia. In 20–30% of patients, headache is present for 6 weeks, and in 10–20% for up to 9 months. Myalgias are observed during the acute phase, and some patients may present occasional osteoarticular and muscular pain [20].

Other complications from COVID-19 are cerebral vascular events, especially of the ischemic type, which, compared to patients without COVID-19, are usually more severe and have a worse prognosis. The sequelae can hinder the rehabilitation process and even permanently disable the survivors, making it difficult to reintegrate into working and social life. After the acute symptoms of COVID-19, 30% of patients present memory loss, difficulty concentrating, or insomnia. Other reported symptoms are vertigo, headache, and brain fog—discovered as a cognitive alteration, which combines a state of confusion and disorientation [20].

The factors associated with the development of new in-hospital neurological events seem to be related to the severity of the disease, both in respiratory parameters (PaO 2/FiO 2 ratio, Acute Respiratory Distress Syndrome (ARDS) severity, and chest CT findings) and inflammatory markers (C-reactive protein, D-dimer, and neutrophil/lymphocyte ratio) [24].

Flores-Silva et al. [1], by including non-specific neurological manifestations—such as headache, anosmia, dysgeusia, and myalgia—found a frequency of 69.3%, slightly higher than the reported overall frequency of 56.4% [24].

Neurological manifestations, as previously mentioned, have a variable spectrum of presentation, from headache and alterations in taste and smell to ischemic and hemorrhagic cerebrovascular disease [25].

In Mexico, a study carried out at the Specialty Hospital of the Siglo XXI National Medical Center in hospitalized patients with severe COVID-19 identified neurological manifestations in 78 patients (36.4%) out of 214. The most frequent were from the central nervous system: headache, encephalopathy, and cerebrovascular disease (24.8%). The second most were from the peripheral nervous system: anosmia, dysgeusia, and myopathies (8.9%) [25].

Albarran-Sánchez et al. [6] report an incidence of alterations in the sense of smell ranging from 4.9 to 85.6%. The incidence of taste disturbances has been highly variable, ranging from 0.3 to 88.8%, referred to as dysgeusia and ageusia. Finally, headache incidence was from 0.6 to 70.3% [25].

The acute cerebrovascular disease has been associated with COVID-19 with a worse prognosis due to increased mortality. It was also the most frequent neurological manifestation in the study conducted by Albarran-Sanchez et al. [25].

2.4 Anosmia

Anosmia is considered a sequel to COVID-19, caused by damage to the respiratory neuroepithelium. Some studies mention that the damage is driven by the viral invasion of ACE 2 and TMPRSS2 cell receptors—found in the nasal and olfactory epithelium [14].

In the olfactory epithelium, infiltrating leukocytes secrete various proinflammatory cytokines that affect olfactory receptor neurons and the stem cell niche, altering their odorant responses and ability to regenerate [14].

Halabe-Cherem et al. [3] mention that 1 out of 2 patients with COVID-19 will develop anosmia, which affects the quality of life. It influences the ability of people to enjoy smells or detect danger through them [14].

Gutierrez-Bautista et al. [23] observed that 27 of 30 people improved the odor detection threshold 2 months after the onset of the symptoms. Nevertheless, it was not significant in identifying them [23].

2.5 Mental health

In patients with previous SARS-CoV-2 infection, some mental health symptoms prevail up to 2 years later. Identified risk factors are [20]:

- Previous psychiatric illness
- Alcohol
- Unemployment

Regarding COVID-19, an increase in these disorders is expected in the Mexican population since 30.2% of the population over 12 years of age report feelings of depression, 35.5% meet the criteria for excessive alcohol consumption, and a

considerable increase in job losses after the pandemic. Within the mental health sequelae secondary to COVID-19, different neuropsychiatric disorders have been identified that can emerge after the acute phase of the disease, as well as an increase in mood-related symptoms, especially in patients with a pre-existing psychiatric illness [20].

A study by Granados-Villalpando et al. [15] which included 203 patients, 96 having prior COVID-19 infection, reported that the most common symptoms of persistent COVID-19 were tiredness, headache, deprivation, and an inconsistent sleep pattern in patients who did not present any previous mental pathology. Meanwhile, in patients who already had some mental pathology before the COVID-19 infection, the symptoms were sleep deprivation, an inconsistent sleep pattern, fatigue, headache, memory problems, brain fog, depression, anxiety, and stress. It shows that the presence of COVID-19 and mental health conditions increases the probability of developing depression, anxiety, or stress [26].

There is a clear relationship between prolonged COVID syndrome and mental disorders [26].

2.6 Obstetric complications

SARS-CoV-2 infection affects pregnant women and fetuses, causing preterm birth, fetal distress, premature rupture of membranes, and cesarean delivery [27].

ACE-2 in the ovary-which plays several functions-could be a potential target of SARS-CoV-2 [27].

Since the architecture of the tissue changes with each renewal of the menstrual cycle, the consequences of SARS-CoV-2 infection, such as menstrual disorders and fertility problems, could be restarted from one to another [23].

2.7 Male reproductive system

Patell et al. [15] analyzed the semen of nine hospitalized patients diagnosed with COVID-19 concluding that 39.1% met the criteria for oligospermia [15].

Expression of ACE-2 and TMPRSS2 in spermatogonia, Leydig cells, and Sertoli cells makes it possible for the virus to invade the testes [23].

The problem leads to cell deterioration, interfering with testosterone release and luteinizing hormone surge, altering sperm production [23].

The released proinflammatory cytokines induce a local inflammatory response that can cause orchitis and systemic inflammation, leading to a persistent fever that ultimately affects sperm morphology, motility, and DNA [28, 29].

Batiha et al. [16] reported normal testosterone levels and decreased testosterone/luteinizing hormone and follicle stimulating hormone/luteinizing hormone ratio without proving causality [28].

3. Treatments

This section presents recommendations for treating post-COVID-19 conditions or complications [30]. In **Table 1**, we summarize the content of this section.

Condition	Treatment	Observed benefit
Fatigue	Rest, supervised exercise, and supplements.	Increase in activity levels.
Neurologic and neurocognitive symptoms.	Neurocognitive rehabilitation.	Improved condition to prior states.
Psychological and emotional problems.	Serotonin reuptake inhibitors or medication according to preexisting conditions.	Improvement of mood and emotions.
Dyspnea and cough.	Breathing exercises and respiratory physiotherapy.	Recovery of normal breathing.
Olfactory-gustatory symptoms.	Supplements and therapy.	Recovery of olfactory-gustatory capacity.

Source: Elaborated by authors from [31, 32].

Table 1.
Conditions and its treatment.

3.1 Fatigue

Fatigue is the appearance of unexplained physical and mental asthenia, which can be persistent or recurrent, leading to a reduction in the patient's activity level [31].

Nowadays, there is no specific treatment, but patients can benefit from the following recommendations and symptom management:

- Rest: it is recommended to have good sleep hygiene (having a regular bedtime and waking hours, avoiding heavy, sugary, stimulant foods, and using computer or mobile screens before sleep). If necessary, consider treatment for sleep problems (melatonin).

- Exercise: it must be controlled and supervised by physiotherapists. It is crucial to carry out personalized and gradual rehabilitation and resume exercising to ease the symptoms associated with post-exercise fatigue or myalgic encephalitis.

- Supplementation: there is a hypothesis that the patient may benefit from the supplementation of coenzyme Q-10, L-carnitine, PQQ, L-Glutamine, or D-Ribose [31].

3.2 Neurologic and neurocognitive symptoms

Cognitive symptoms such as difficulty concentrating, attention problems, and memory failure have been described frequently. These symptoms tend to improve in the long term after performing neurocognitive rehabilitation [31].

Symptomatic treatment should be offered to people with headaches, with the one usually employed for the primary headache they present, depending on the tension or migraine type [31].

There is no pharmacological treatment to speed up smell recovery or to attenuate parosmia. In the case of myalgias, the treatment is symptomatic, where Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are commonly administered [31].

3.3 Psychological and emotional problems

For those presenting with mild to moderate anxiety and depression, Selective Serotonin Reuptake Inhibitors (SSRIs) should be initiated progressively to maintenance doses with a reassessment every 3–4 weeks [31].

In the case of neuropathic pain or a history of diabetes mellitus, duloxetine would be the antidepressant of choice. If the existing clinical picture includes diarrhea or digestive disorders, the chosen treatment would be paroxetine [31].

3.4 Dyspnea and cough

For mild symptoms of dyspnea that do not require oxygen and do not have a cardiac etiology, they may benefit from breathing exercises and respiratory physiotherapy.

The following is recommended for cough: antitussives such as dextromethorphan or guaifenesin, bronchodilators such as inhaled therapies, bronchodilators, or inhaled glucocorticoids [31].

3.5 Olfactory-gustatory symptoms

If symptoms do not resolve after 2 months, evaluation by an otolaryngologist may be necessary [31].

Treatment consists of olfactory rehabilitation. The use of oral or topical corticosteroid therapy for 15 days, vitamin D, sodium citrate, or theophylline is evaluated, recommending the performance of olfactometry [31].

They could benefit from the stimulation or rehabilitation of smell through occupational therapy or speech therapy [32].

4. Long COVID-19 studies in Mexico and Latin America

In Mexico, a case–control study carried out in the state of Zacatecas with 219 patients found a relative risk of 2 to 33 times higher for developing persistent symptoms such as dyspnea, nausea, and anosmia [20].

An ongoing longitudinal study of neurological syndromes associated with COVID-19 in Mexico City found a high frequency of neurological manifestations during hospitalization in patients with COVID-19, suggesting a higher number of short- and long-term sequelae for these patients [24].

In a follow-up study of patients discharged from a temporary hospital dedicated to COVID-19 in Mexico, the groups of symptoms that presented in more than 30% of the participants 90 days after discharge were neurological, dermatological, and mood disorders. In this study, women presented persistent symptoms more frequently than men, consistent with studies in Wuhan, showing a relationship between the female sex and the symptoms of prolonged COVID-19 [25].

Alvarez-Moreno et al. [33] reported that the most persistent symptoms in Bogotá, Colombia, were headache, fatigue, and insomnia. Likewise, they emphasize that their results are like those reported in other studies. Also, they suggest that there may be an underreporting effect in Latin America that could accentuate social inequalities.

In the study by González-Hermosillo et al. [34], patients who have persistent fatigue for 3 to 6 months were associated with ages between 40 and 50 years.

Patients with fatigue have a high prevalence of other symptoms such as bradypnea, cognitive decline, sleep problems, autonomic dysregulation, and psychological stress. In Mexican studies, the depression and anxiety prevalence among previous COVID-19 patients are up to 15.7% and 22.6%, respectively [34].

The prevalence of symptoms has a progressive decrease with time. A 6-month follow-up study in patients who recovered from the COVID-19 infection showed a reduction in fatigue prevalence—from 53 to 46.9%.

Gonzalez-Hermosillo et al. [34] found that 40.4% of the patients presented persistent symptoms. Of them, 9.1% had a progressive reduction after 4 weeks [34].

5. Conclusions

COVID-19 has a pronounced impact on society, mainly due to its repercussions on global health. Despite the various studies worldwide on pathophysiology, signs and symptoms, complications, and the best therapeutic option, the research is ongoing.

A persistence of symptoms for months has been observed in patients who had previously recovered from the disease. It was called prolonged COVID. The most frequent symptoms that persist are dyspnea, headache, dysgeusia, problems in the pattern of sleep, psychological problems—such as brain fog, anxiety, and depression. There are still vast unknowns, like how long residual post-COVID symptoms last and if they permanently affect the quality of life. Some authors comment that these symptoms decrease with time, a symptomatic treatment, and sometimes with the need for rehabilitation. In the reviewed literature, we did not find any other perspective to address the complications of COVID-19, in Mexico, besides the application of available treatments.

Since COVID is a disease that mainly affects the respiratory tract, its main complications are found in the lungs, taking into account the importance of comorbidities, which are considered the chief risk factor for the development of these, including patients with diabetes, hypertensive, or some cardiac pathology.

Conflict of interest

The authors declare no conflict of interest.

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