

Post-Covid-19 Syndrome in the orofacial region with emphasis in the Andes: Systematic Literature Revision

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Abstract

Post COVID-19 syndrome, according to the WHO, is a disease that occurs in individuals with a history of SARS-CoV-2 infection, usually within three months from its onset. It is characterized by persistent clinical manifestations related to the sensory organs. The objective of this review is to determine the Post COVID-19 symptoms in the orofacial region in Latin America with emphasis on the Andean region. A literature review was conducted based on publications from 2020 to 2022, using several digital databases, including PubMed, Latindex, and Google Scholar. After applying an inclusion and exclusion criteria, 24 articles were selected for the analysis of Post COVID-19 symptoms in the Andean region. The most common manifestations reported were fatigue, myalgia, and headaches. In regards to the orofacial region, the main symptoms included dysgeusia, anosmia, and to a lesser extent, tinnitus, and xerostomia. The symptoms with the highest prevalence within the Post COVID-19 syndrome were dysgeusia, hypogeusia, and ageusia as well as anosmia, which were among the most frequent in the orofacial region. Visual disturbances such as red eye and vision loss were also reported, as well as minor alterations of the oral mucosa. These conditions are important and have persistent symptoms, requiring further studies on the subject. A thorough medical history is recommended to identify specific symptoms and signs in Post COVID-19 patients.

Keywords: Post COVID-19 Syndrome; Long COVID; Sequelae; Orofacial; Craniofacial; Oral; Ageusia; Anosmia

1. Introduction

In December 2019, an infectious disease primarily affecting the respiratory system emerged. The WHO named it COVID-19, abbreviated from Coronavirus Disease 2019. It was later identified as SARS-CoV-2 (severe acute respiratory syndrome coronavirus2), and in March 2020, a global pandemic was declared by the WHO [1,2]. Those infected with this disease present fever, respiratory tract symptoms, and, in some patients, extrapulmonary manifestations, although it has also been reported that most infected individuals are asymptomatic [3].

According to a report from the Pan American Health Organization (PAHO), the average initial mortality rate due to SARS-CoV-2 was 291 per thousand inhabitants between 2019 and 2020. The number of deaths between January 1st 2020 and December 31st, 2021 was approximately 14.9 million [4,5].

This article focuses on the Andean region located in South America, which is made up of 7 countries: Argentina, Bolivia, Chile, Colombia, Ecuador, Peru, and Venezuela. The region is traversed by the Andes mountains. According to the guide "Sociodemographic Impacts of the COVID-19 Pandemic in Latin America and the Caribbean," it is mentioned that Andean countries like Peru have the highest mortality rate due to SARS-CoV-2. Therefore, it can be assumed that there is a very high rate of orofacial sequelae of COVID-19 in relation to other countries [6,7].

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In general, patients with SARS-CoV-2 recover within a few weeks, and in some cases, even before three weeks. However, some patients continue to experience long-term symptoms [8]. This condition is known as “Post-COVID Syndrome.” In October 2021, the World Health Organization (WHO) published a definition for this syndrome, stating that it is an illness that occurs in individuals who have a history of probable or confirmed SARS-CoV-2 infection, typically within three months from the onset of SARS-CoV-2. The symptoms and effects of this syndrome persist for at least two months [3].

According to several researchers, the Post-COVID-19 syndrome, also known as Long COVID or Post-Acute Sequelae of SARS-CoV-2 (PASC), is now referred to as PASC, which stands for Post-Acute Sequelae of SARS-CoV-2 [9]. It encompasses symptoms of SARS-CoV-2 that persist after an infection lasting more than four weeks and extends beyond twelve weeks [8,10]. The main clinical manifestations of patients with Post-COVID Syndrome include loss of taste or ageusia, hypogesia, and dysgeusia [2], as well as anosmia hyposmia, red eyes, blurred vision, hearing loss, and tinnitus [10]. Other symptoms may include salivary gland ectasia, dry mouth [11], headache [12], and a condition referred to as “brain fog”, characterized by concentration problems, disorientation, fatigue, and difficulty finding the right words [13].

One of the limitations of these reviews regarding PASC is the lack of knowledge about the prevalence of anosmia, hyposmia, ageusia, and hypogesia [10], as well as the manifestations and post-COVID sequelae in the oral region.

The objective of this review is to determine the post COVID-19 symptoms in the orofacial region in Latin America, with a focus on the Andean region. Through a systematic review of the literature based on publications in Latindex and PubMed from the period between 2020 and 2022.

1.1. Generalities

SARS-CoV-2 goes through several stages, including the acute stage, the subacute stage, and the chronic stage. The acute stage is considered the initial stage of SARS-CoV-2 and lasts approximately up to four weeks. During this stage, patients may experience symptoms such as fever, sore throat, cough, difficulty breathing, and chest pain. This presentation is usually mild to moderate, and hospitalization is not required for most patients. However, not all patients have been able to recover within this timeframe, and their symptoms may persist [1, 10].

The subacute stage is where symptoms persist for up to 4 to 12 weeks, and during this stage, several organs and systems are affected, requiring a multidisciplinary clinical intervention. The main manifestation in the maxillofacial region during this stage is ageusia [2-10].

In the chronic stage, symptoms persist beyond 12 weeks, and the clinical management also requires a multidisciplinary approach due to the involvement of multiple organs and systems. It has been demonstrated that various systemic sequelae are directly related to oral health, as they reduce the quality of life of patients. Therefore, leading to decreased oral care, less frequent dental check-ups, and potential exacerbation of chronic oral conditions. Additionally, post-SARS-CoV-2 depression and anxiety, cognitive impairment, and poor or inadequate control of diabetes mellitus can be observed [1-2].

1.2. Clinical Manifestation of Post-Covid Syndrome

SARS-CoV-2 can trigger autoimmune indicators, including the development of various antibodies, leading some to believe that specific antibodies are generated that result in autonomic nervous system dysfunction, which could explain many of the manifestations of PASC [3].

The most common symptom of PASC is fatigue, with an occurrence of 72%, 57% muscle pain/ myalgias, and 53% headaches. Within these symptoms there is migraines which occurs because of the peripheral activation of the trigeminal-vascular system through inflammatory cytokines [13]; this is a continuous cephalitis, holocranial and is not usually accompanied by nausea, vomiting, nor photophobia [14].

The infectious agent of SARS-CoV-2 has a high affinity for the angiotensin converting enzyme 2 receptor. This receptor is also expressed in neurons and glial cells, which could explain neurological manifestations such as olfactory neuropathy, that is, anosmia [15]. On the other hand, ageusia is the affection of the mucosa of the oral cavity, particularly the epithelial cells of the tongue, which causes the loss of modulation of taste perception. Anosmia and ageusia are the persistent mild symptoms most frequently observed in patients with Post-Acute Sequelae of SARS-CoV-2 infection (PASC) [16].

Certain studies have reported long-term auditory disorders in adults, such as ear pain, tinnitus, or ringing in the ears, which are sounds perceived in the absence of an auditory stimulus. Tinnitus is the result of an imbalance in physical, psychological, and social homeostasis [17].

Oral symptoms can include a decrease in salivary flow or xerostomia, which is the subjective sensation of a dry mouth. This occurs when there is dysfunction in the salivary glands, leading to a reduction in saliva production. Xerostomia contributes to a poor quality of life, causing discomfort for the patient related to oral health, as the lack of saliva increases the risk of dental cavities, periodontal diseases, mucosal ulcers, and oral candidiasis [18].

Mucormycosis is not a symptom of Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), but is worth mentioning as it is a fungal infection associated with SARS-CoV-2. It mainly affects immunocompromised patients and is characterized by direct tissue invasion and necrosis. It rapidly spreads from the paranasal sinuses to the orbit, cavernous sinus, and skull. Clinically, it can present with nasal congestion, facial pain, and edema [19].

2. Materials and Methods

This is a systematic review of the literature with a qualitative methodological approach, which consists of interpreting various scientific articles related to Post-COVID-19 Syndrome in the orofacial region, with an emphasis on the Andean region. The compilation of bibliographic references was conducted in several digital databases, including PubMed, Google Scholar, Scielo, BVS Lilacs, and Science Direct. The search for information was conducted in both Spanish and English, using the following keywords: Post-Covid Syndrome, long Covid, orofacial, craniofacial, oral, sequelae. The inclusion criteria used for this review were: full-text articles in Spanish and English, with no restriction on the type of study, addressing Post-COVID-19 symptoms in the orofacial region in adult patients, with an emphasis on the Andean Region.

In the initial search, a total of 3754 articles were obtained, out of which 61 articles were selected after a brief analysis of titles and abstracts. Finally, 20 articles that met the inclusion criteria were chosen, while 6 articles were excluded for not providing relevant information. This resulted in a total of 14 articles selected for this review. The selection process is illustrated in the PRISMA flowchart, as shown in Figure 1.

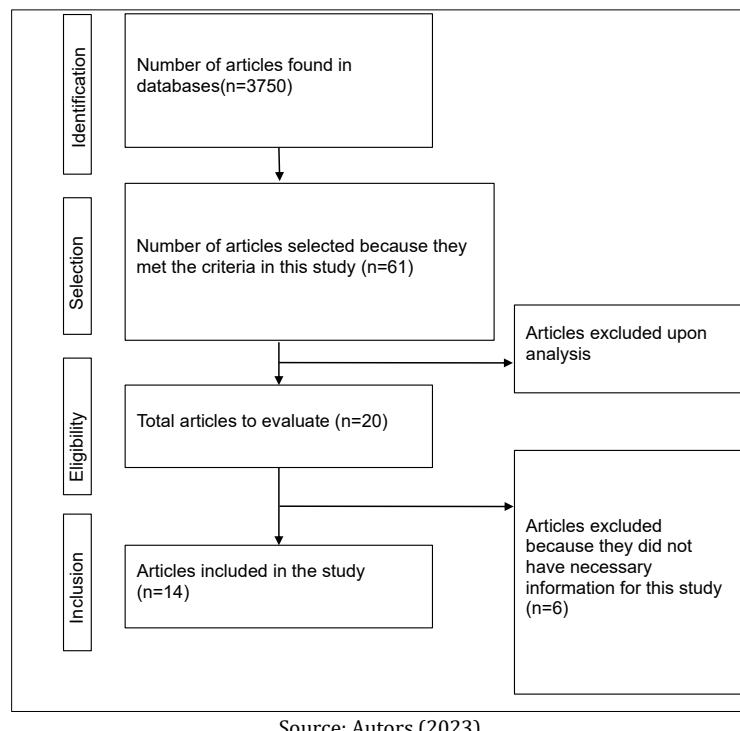


Figure 1 PRISMA flowchart for article selection

3. Results

Once the analysis of the diverse literature was finished, it became evident that Post-COVID syndrome refers to the persistent symptoms of SARS-CoV-2 that extend for more than four weeks. According to various studies, the most common symptoms are fatigue, myalgia, and headaches. As for the orofacial region, the main symptoms are dysgeusia, ageusia, anosmia, and to a lesser extent: tinnitus, xerostomia, and candidiasis.

Table 1 Characteristics of the articles included

	TITLE	AUTHOR/S	METHODOLOGICAL DESIGN	COUNTRY	PUBLICATION YEAR	JOURNAL	OBJECTIVE	PRODUCTION
1	Clinical epidemiological characterization of COVID-19 sequelae in adults recovered from a hospital in Huancayo	Mauricio PB, Gutierrez DN.	Cross-sectional study	Peru	2022	Peruvian J of Health Sciences	Describe the clinical and epidemiological characteristics of the persistence of post-COVID-19 symptoms in the population treated at a hospital in the city of Huancayo.	The patients experience persistent symptoms after recovering from COVID, including fatigue, and to a lesser extent, tinnitus.
2	Secondary oral findings due to infection from covid 19 evidences at the start of the pandemic systematic review	Caamaño AE et al.	Systematic review	Colombia	2021	Latin American repository network	The main objective is to synthesize the scientific information regarding oral manifestations secondary to COVID-19 available in health-related databases.	The most frequent symptoms were: hypogeusia (reduced sense of taste), dysgeusia (distorted sense of taste), ageusia (loss of taste), geographic tongue, herpetiform lesions, and candidiasis.
3	Post Covid syndrome. A cases series and comprehensive review	Anaya JM et al.	Case series and comprehensive review	Colombia	2021	Autoimmunity Reviews	The objective was to provide a case series of patients with Post-COVID Syndrome (PCS) attending a post-COVID unit and offer a comprehensive review on the topic.	The most frequent symptoms were fatigue in 34% of cases, xerostomia (dry mouth) in 26% of cases, tinnitus in 23% of cases, and ageusia (loss of taste) in 15% of cases.
4	Clinical and functional recovery and return to work 3 months after discharge in patients hospitalized for SARS-CoV-2 pneumonia. Relationship with the therapy received	Gutiérrez M et al.	Prospective cohort study	Chile	2022	Chilean Journal of Respiratory Diseases	The objective of this study is to describe aspects of occupational, clinical, and functional respiratory recovery, as well as their associated factors, in a cohort of hospitalized patients.	The symptoms of fatigue and cough persist.

5	Long-term (6 months) neurological and psychiatric consequences in mild COVID community patients	Allegri RF et al.	Retrospective cohort study	Argentina	2022	Journal of Applied cognitive Neuroscience	The objective of this study was to evaluate the occupational, clinical, and respiratory functional recovery at 3 months after discharge in patients hospitalized for COVID-19.	The frequent post-COVID symptoms included fatigue (20-30%), headache, vision loss (10-20%), tinnitus, and ageusia (10%).
6	The consequences of the SARS-CoV-2 pandemic on people's oral health: a challenge for dentistry	Ortuño D et al.	Narrative review	Chile	2022	International journal of interdisciplinary Dentistry	The objective of this narrative review is to describe possible consequences of the SARS-CoV-2 pandemic on oral health in individuals.	The symptoms of salivary gland ectasia and xerostomia persist.
7	Impact of covid-19 on the functional respiratory capacity and quality of life of post - hospital discharge patients	Pineda DK et al.	Retrospective quantitative study	Ecuador	2021	Social Science Journal	The objective of this article is to determine the impact of COVID-19 on respiratory functional capacity and quality of life in post-hospital discharge patients.	The persistent symptoms after COVID were fatigue (100%) and anosmia and/ or ageusia (43%).
8	Long-term effect of SARS-CoV-2 infection: Post-Covid-19 neurological syndrome	Caballero J et al.	Review	Peru	2021	Almanzor Aguinaga Asenjo National Hospital Medical Corps Journal, Chiclayo, Peru.	The present review aims to conduct a literature exploration in order to delve into the late neurological manifestations post COVID-19	The most frequent symptom is fatigue, followed by headaches, and less frequently, anosmia, and ageusia.
9	Prolonged disease or post-COVID-19 sequela?	Tarazona A et al.	Descriptive cross-sectional study	Peru	2020	Act Medical Peruvian	The report emphasizes the need to organize a multidisciplinary healthcare response and to recognize the severity and prognosis of patients through systematic assessments.	Among the most frequent symptoms are fatigue and headache, along with other symptoms such as rhinitis, red eye, and dysgeusia (distorted sense of taste).

10	Post-COVID-19 conditions in Ecuadorian patients: an observational study	González F.	Observational study	Ecuador	2021	Elsevier The Lancet Regional Health Americas	The objective of this study is to compare post-COVID symptoms in three groups of Ecuadorian outpatients with mild, moderate, and severe infections.	The main symptoms are as follows: Fatigue: 67.12% Headache: 45.27% Loss of smell: 28.28% Sore throat: 19.18% Loss of taste: 18.45%
11	Post-acute COVID-19 syndrome: A new pandemic?	Lara AP et al.	Descriptive cross-sectional study	Chile	2021	Venezuelan Archives of Pharmacology and Therapeutics	The objective of this review is to evaluate the epidemiological and pathophysiological aspects related to COVID-19 in order to facilitate its identification in clinical practice.	The most frequent symptoms are fatigue, anosmia (loss of smell), and ageusia (loss of taste).
12	COVID-19 and its impact on dentistry	Curay YT et al.	Systematic review	Peru	2021	J Stomatologic al Herediana	The objective of this literature review is to present the information collected during the health crisis and the update of protocols adopted by dentists and healthcare personnel to provide appropriate care during the pandemic. Additionally, it aims to recognize the clinical picture, transmission, diagnosis, treatment, and impact of the pandemic within the current scenario of the COVID-19 health crisis.	It appears that there are no post-COVID symptomatology.
13	A literature review about post-COVID-19	Perilla EJ et al.	Systematic review	Colombia	2022	Cuban Journal of Higher Medical Education	The objective of this research was to present relevant scientific	The most persistent symptoms are fatigue, headache, anosmia (loss

							information about the post-COVID syndrome. of smell), and ageusia (loss of taste).
14	Mucormycosis associated with COVID-19 patients: a first report in Venezuela	Barazate D et al.	Clinical case	Venezuela	2022	Lat Am J Oral Maxillofacial Surg	<p>The research was conducted on a patient in the post-COVID period with a diagnosis of mucormycotic.</p> <p>Mucormycosis has been explained as a consequence of the increased number of patients with some form of immunosuppression and the use of therapies in the management of COVID-19.</p>

Source: Autors (2023)

4. Discussion

During the 2020-2022 period, certain symptoms have been identified and categorized within the Post-COVID Syndrome (PASC), with fatigue and headache being among the main neurological symptoms, as reported by Pineda DK, et.al., [20] in a quantitative retrospective study where fatigue was present in 100% of the affected patients. This is consistent with the findings of an observational study by Gonzales F. [8], which mentions that the main neurological symptoms of PASC are fatigue (67%) and headache (45%). We have compared these results with studies conducted in Indonesia by Mutiawati E. et.al. [21], where they also found that headache and fatigue are the main symptoms of PASC, with percentages of 47% and 38% respectively. This demonstrates the consistency between our study and international studies. However, in this review, we specifically highlight the manifestations in the orofacial region.

According to the analysis of the information used for this article on PASC manifestations in the orofacial region, it was determined that ageusia is the most frequent symptom in patients affected by this syndrome, as suggested by Caamaño AE et.al [2] in their systematic review conducted in Colombia, mentioning that hypogeusia, dysgeusia, and ageusia are the most persistent symptoms. This is also supported by the descriptive cross-sectional study by Lara, AP et.al. [22] and Perilla EJ et al [23], conducted in Chile and Colombia respectively, which includes various clinical manifestations such as ageusia and anosmia. The latter is classified in our analysis as the second most common symptom of PASC. This is in line with the findings of Caballero J. et.al. [24], who emphasize anosmia as another frequent symptom within the Republic of Peru. Similarly, Algahtani, SN et.al. [25] expressed in their retrospective cross-sectional study conducted in Saudi Arabia that the most frequent and long-lasting symptoms experienced by patients, even those who were not hospitalized and were evaluated at 4 and 7 months after infection, are anosmia and ageusia, which are considered chemosensitive in nature, as mentioned by Agustín M et.al. [26] in their study conducted in Germany.

Supporting the cross-sectional study by Mauricio PB et.al. [27], the study by Anaya JM et. Al. [28] titled “Post Covid Syndrome. A case series and comprehensive review,” and a retrospective study by Allegri RF. et.al. [29], tinnitus is mentioned as an important symptom with a prevalence of 23%, while the prevalence of tinnitus is reported as 10%. These symptoms are considered the third most frequent manifestation in our study. As mentioned in the cohort study by Dos Santos RJ. et. al. [30], tinnitus is classified as one of the most common auditory symptoms in PASC, which is a multifactorial condition that affects various aspects of the patient's life. Similarly, Degen CV. et.al [31] emphasize that 30% of the participants in their study experienced tinnitus during and after SARS-CoV-2 infection. The study also mentions the presence of acufenos (ringing in the ears) as part of the auditory symptoms, although they do not pose a significant health risk to the patients to seek treatment for the issue.

Within the oral manifestations associated with PASC, xerostomia (dry mouth) and salivary gland ectasia are described as fewer common symptoms. However, they are considered persistent symptoms according to the studies conducted by Anaya JM et.al. [28] and Ortuño D. et.al. [11] in Colombia and Chile, respectively. Rocha RC. et.al. [18] reported cases of patients experiencing dry mouth due to reduced saliva production after the infection. They also reported a case in Fernandopolis, Brazil, where a patient presented these symptoms, but they were already receiving treatment with antidepressants. Thus, suggesting that the condition worsened after infection. This study concludes that xerostomia can occur individually or be related to medication use of pre-existing systemic diseases.

Regarding alterations associated with the sensory organs, vision is also affected, as described by Allegri RF et.al. [29] in their study conducted in Argentina, where vision loss was mentioned as one of the most frequent symptoms of PASC at 6 months. Similar results were found by Tarazona A et.al. [32] in their study conducted in Peru, where persistent symptoms at 2.5 months included red eyes and rhinitis. Abdul SE et.al [33] claim in their study that ocular manifestations range from conjunctivitis and surface eye alterations to conditions affecting the uvea, retina, and optic nerve. Szkodny D et.al. [34], in a cross-sectional study conducted a study on adult patients in Poland who had experienced systemic SARS-CoV-2 infection within a range of 1 to 6 months, found the following most common ocular symptoms: subjective decrease in vision, conjunctivitis, and eye pain, which are similar to the results described in our studies regarding visual alterations.

Gutierrez M et.al. [35] reported the persistence of cough as a PASC sequelae in 20% according to their prospective cohort study. Thus, based on the percentage of cough, we can correlate it with the persistence of sore throat, which was reported at 19% in the observational study conducted by Gonzalez F. [8]. It is known that sore throat can be related to the initial symptoms of SARS-CoV-2, but it can also be present as a manifestation of PASC in post-extubation patients who have experienced dysphagia and odynophagia after discharge and are prone to coughing [36].

Oral mucosal alterations in PASC, such as geographic tongue, herpetiform lesions, and candidiasis, were not significant as they represented the least frequent symptom in our review, with only one author, Caamaño AE et.al. [2], reporting them in a systematic review conduction in Colombia.

Rhino-orbital-cerebral mucormycosis is an opportunistic and potentially life-threatening fungal infection that affects immunocompromised patients. While the highest number of cases is found in India, there is insufficient data on this condition in the Andean region. However, our study includes a case report from Venezuela that explains mucormycosis as a consequence of some form of immunosuppression and the use of therapies in the management of SARS-CoV-2, complicating the patient's prognosis, leading to the term CAM [37].

5. Conclusion

Before the pandemic, orofacial alterations such as dysgeusia, hypogeusia, anosmia, hearing loss, tinnitus, visual impairment, and xerostomia were rare and compared to the post-pandemic period. Currently, we observe symptoms and signs associated with SARS-CoV-2 infection and its sequelae that are very different from what was seen previously.

There is a lack of data on this topic in the Andean region, but considering the high incidence of post-COVID-19 sequelae, we assume that further research is needed. High rates of post-COVID-19 orofacial sequelae have been reported in Asia, Europe, North America, and Central America. This calls for greater attention to be paid to patients' medical history to identify specific symptoms and signs in individuals who have experienced single or repeated SARS-CoV-2 infections. In-depth studies involving speech therapists, neurologists, dentists, otolaryngologists, and other specialists are necessary to establish appropriate tests and diagnoses.

It would be interesting to delve deeper into these issues and conduct specific studies to assess the impact on patients. Currently, there are no health policies in place to address post-COVID sequelae adequately. We recommend the development of health policies to address the needs of patients with post-COVID sequelae. It is crucial to pay attention to the initial evaluation and consider the medical history of individuals who have had SARS-CoV-2, with particular focus on those who have experienced more than two clinical episodes. This is because we anticipate a gradual increase in orofacial diseases in the post-pandemic period.

Compliance with ethical standards

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Disclosure of conflict of interest

We declare that we have no conflict of interest regarding this research. We have not reviewed any funding and have not been influenced by any organization or entity that may have a personal or financial interest in the results of this study. Our only motivation is to contribute to scientific knowledge and promote appropriate care for patients affected by post-COVID syndrome.

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