

ORAL LESIONS AFTER INFECTION BY SARS COV 2: TWO CASE REPORTS

Lesiones bucales posteriores a infección por SARS CoV 2 presentación de dos casos

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ABSTRACT

Introduction: The SARS CoV 2 infection has resulted in several health, economic, and social crises in all areas. The disease shows a substantial biological diversity in humans causing a series of sequels in the trans- or post-infection period in the entire organism.

Case Report: The manifestations that occur in the oral cavity and pharynx have not been evaluated. In this study, two clinical cases are reported. The first patient, a 67-year-old male, presents erosive lesions on the dorsal surface of his tongue after SARS CoV 2 infection.

Results: Therapy consisting of reinforcing oral cleaning, use of antifungal solutions, mouthwashes containing superoxidation solution and B complex was given to the patient. The reported lesions improved satisfactorily. The second case, a 47-year-old male patient, presented vesiculobullous lesions on the lingual and labial mucosa accompanied by severe painful symptoms after SARS CoV 2 infection. An incisional biopsy was performed. The histopathological result was compatible with pemphigus vulgaris, and the treatment protocol was started with 0.1% topical mometasone and 2g miconazole gel, observing adequate involution of the lesions after 20 days.

Conclusions: The aim of this study is to report on the lesions affecting the oral cavity and pharynx in post-COVID patients with the aim of carrying out a thorough intraoral examination, establishing a clinical or histopathological diagnosis to implement a specific treatment plan in each case to improve the health and quality of life of the patients.

Keywords: SARS-CoV-2; Oral manifestations; Oral ulcer; Pemphigus; Mouth; Mucous membrane.

RESUMEN

Introducción: La infección por virus de SARS CoV 2 ha dejado a su paso una estela de crisis en materia de salud, económica, social y en todos los ámbitos a la fecha seguimos realizando la observación del comportamiento de la enfermedad en los seres humanos con una diversidad biológica importante y que ha traído como consecuencia una serie de secuelas que se presentan en el periodo trans o posterior a la infección en toda la economía corporal

Reporte de Caso: Se ha evaluado poco las manifestaciones que se presentan en la cavidad bucal y faringe; se presentan dos casos clínicos el primero paciente masculino de 67 años de edad posterior a la infección por SARS CoV 2 presenta diluciones de continuidad en bordes laterales de la lengua se indica terapia y refuerza limpieza bucal, antimicótico, colutorios con solución de superoxidación y complejo B, las úlceras involucran de manera satisfactoria

Resultados: El segundo caso masculino de 47 años posterior a la infección por SARS CoV 2 debuta con lesiones vesículo-ampollosas en mucosa lingual, labial con sintomatología dolorosa severa, se realiza biopsia incisional donde el resultado histopatológico es compatible con pénfigo vulgar, se inicia protocolo de tratamiento con mometasona tópica al 0.1% y miconazol gel 2g observándose una adecuada involución de las lesiones a los 20 días

Conclusiones: El objetivo de este trabajo es poner en contexto de la comunidad médica y científica las lesiones concernientes a la cavidad bucal y faringe que están presentando los pacientes postcovid con el objetivo de realizar una exhaustiva exploración intraoral, establecer un diagnóstico clínico o histopatológico y con base en esto instaurar un plan de tratamiento específico en cada caso en particular con el fin fundamental de mejorar la salud y calidad de vida del paciente.

Palabras Clave: SARS-CoV-2; Manifestaciones bucales; Úlceras bucales; Pénfigo; Boca; Membrana mucosa.

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CITE AS: Villanueva-Sánchez F & Escalante-Macías L. Oral lesions after infection by SARS CoV 2: two case reports. J Oral Res. 2023; 12(1): 75-85. doi:10.17126/joralres. 2023.007

Received: January 16, 2023
Accepted: May 19, 2023
Published online: July 19, 2023

ISSN Print 0719-2460
ISSN Online 0719-2479.

INTRODUCTION

The SARS CoV 2 infection identified in the city of Wuhan, China, at the end of 2019, and later declared a pandemic by the World Health Organization in March 2020, has brought about a major health emergency. Additionally, the pandemic has evidenced the vulnerability of healthcare services and the lack of an effective strategy to deal with a crisis of such magnitude. Consequently, it has significantly affected the economic, social, and environmental areas, among many others.¹

This disease, initially described as an acute respiratory syndrome that resulted in fatal pneumonia, has shown that it is not exclusively a respiratory condition. It affects most of the organs and systems, causing a life-threatening, multiple organ failure in its most serious manifestations.²

At this point in the evolution of the disease, it is well known that the inoculation model through its spike protein has affinity for the angiotensin-converting enzyme receptors in the membranes of most host cells. Once the virus enters the cell, it uses the endoplasmic reticulum, ribosomes, and Golgi apparatus to produce the necessary proteins for its replication and the formation of new virions that later leave the cell through exocytosis to continue infecting more cells or individuals.^{1,2}

In the oral cavity, the squamous cells of the lingual mucosa and the glandular reservoirs are the ones with the highest amounts of angiotensin-converting enzyme receptors. Once the virus has undergone exponential replication and begins to affect the upper and lower air tract, rhinorrhea, cough,

fever, pharyngitis, nasal congestion, myalgia, arthralgia, and affectation of the general health status of the patient, are the main clinical manifestations of the disease. Severe SARS CoV 2 infection may cause fulminant pneumonia, involving septic shock and multiple respiratory and organ failure, which eventually lead to the death of the patient.^{2,3,4}

A significant number of publications have reported the oral manifestations of SARS CoV 2 infection. The most frequent include erosive lesions or ulcerative states, vesiculobullous lesions, geographic tongue, fungal infections, and parotid sialadenitis.^{1,5} The etiology of oral lesions, even in this stage of the infection, is uncertain. It is believed that they can be classified as multifactorial, for example, correlating the direct action of the virus on the cells of the oral mucosa and the glandular parenchyma, the hypersensitivity of both systemic and topical drugs involved in the treatment protocol for the infection, the bronchodilator aerosols containing steroids used by the patients and, ultimately, the general condition of the patients as well as their prolonged periods of hospitalization.^{6,7} We believe that there is a direct correlation between SARS CoV 2 infection and the presence of oral manifestations.

Unfortunately, hospital triage does not include a thorough evaluation of the oral cavity, because priority is given to evaluating pulmonary and systemic involvement. The main objective of this report is to present cases of patients who had oral lesions after SARS CoV 2 infection and to emphasize the importance of a complete evaluation of the soft and adjacent tissues of the oral cavity and oropharynx to provide more

solid evidence in the study of these types of lesions.

CASE REPORT

A 67-year-old male patient treated at the Oral and Maxillofacial Pathology & Oral Medicine clinic of the Postgraduate Division of the National School of Higher Studies, campus León, at the National Autonomous University of Mexico. The patient sought help due to erosive lesions in both dorsal surfaces of his tongue with 1 month of evolution after being diagnosed with SARS CoV 2 infection by PCR in October 2020 at the health establishment that he attended. At the clinical evaluation the patient had an oxygen saturation of 89%, respiratory rate of 14, heart rate of 95, and 140/95 mmHg of blood pressure.

The patient was treated with azithromycin 500 mg every 24 h for 3 days, paracetamol 500 mg every 8 h for 5 days, Salmeterol/ Fluticasone 25 micrograms/250micrograms one dose per day for 15 days, and nasal prongs with oxygen concentrator 2 liters per minute for one month. Intraoral exploration showed two erosive lesions on the lateral edges of his tongue of approximately 1.5x0.5x0.2cm showing characteristics of a granular erythematous base in the central part, whitish edges, and an erythematous halo, accompanied by painful symptoms that prevented him from having an adequate intake of food (Figure 1). General oral cleaning measures were indicated, application of miconazole gel 2 g every 12 h for 10 days, mouth rinses with superoxidation solution and active ions 3 times a day after oral hygiene, and intramuscular application of complex B (hydroxocobalamin, vitamin B1, B6) 4 vials

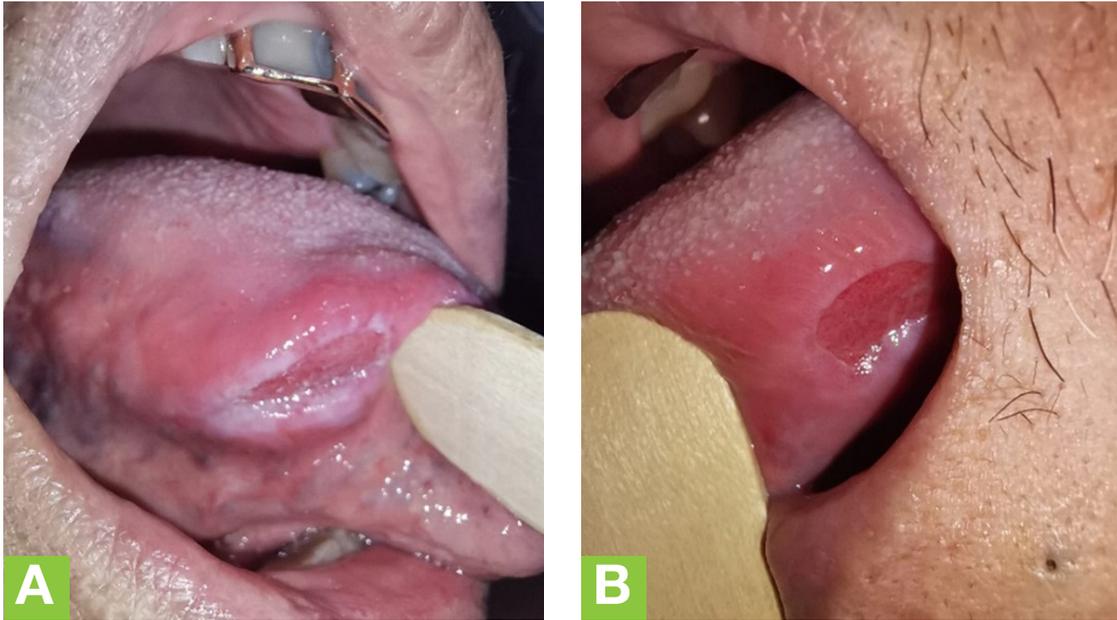
every third day. The patient was evaluated after a week, 15 days, and a month, showing a clear improvement in the process of tissue repair and re-epithelialization of ulcers on the lateral edges of the tongue with a decrease in symptoms, satisfactorily improving food and liquids intake, as well as an improvement in his general condition (Figure 2).

RESULTS

A 47-year-old male patient treated at the Oral and Maxillofacial Pathology & Oral Medicine clinic of the Postgraduate Division of the National School of Higher Studies, campus León, at the National Autonomous University of Mexico, in November 2021. The patient presented multiple vesiculobullous lesions distributed on the lower and upper labial mucosa, the anterior third of the tongue, and the buccal mucosa with severe painful symptoms on examination that made it impossible to take adequate photographic records. Additionally, as a precaution, little manipulation as possible was performed because the mucosa was friable and removable. Upon direct questioning, the patient reported having been diagnosed with SARS CoV 2 infection by means of a PCR test in a private laboratory. He reported visiting a physician who prescribed symptomatic treatment consisting of paracetamol 750 mg every 8 h for 10 days, benzonatate pearls 100 mg every 8 h for 10 days, azithromycin 500mg 1 every 24 h for 3 days.

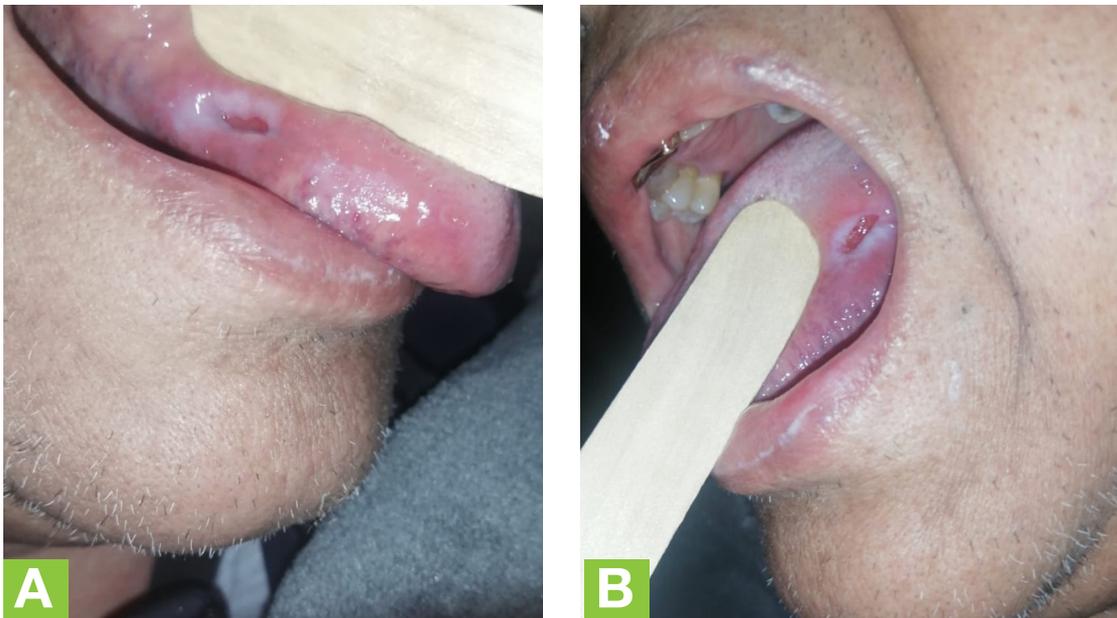
At the time of his SARS CoV 2 diagnosis, the patient had cough, pharyngitis, and tonsillar exudates. Intraoral exploration revealed frank lesions of erosive nature, irregular and erythematous bullae with a whitish background in

Figure 1: Erosive lesion on the right and left lateral border.



- A:** The right lateral edge presents an erosive lesion with an erythematous background and whitish borders.
- B:** Erosive lesion on the left lateral edge with erythematous background and smooth borders similar to the adjacent mucosa.

Figure 2 : Right and left lateral border in the process of re-epithelialization.

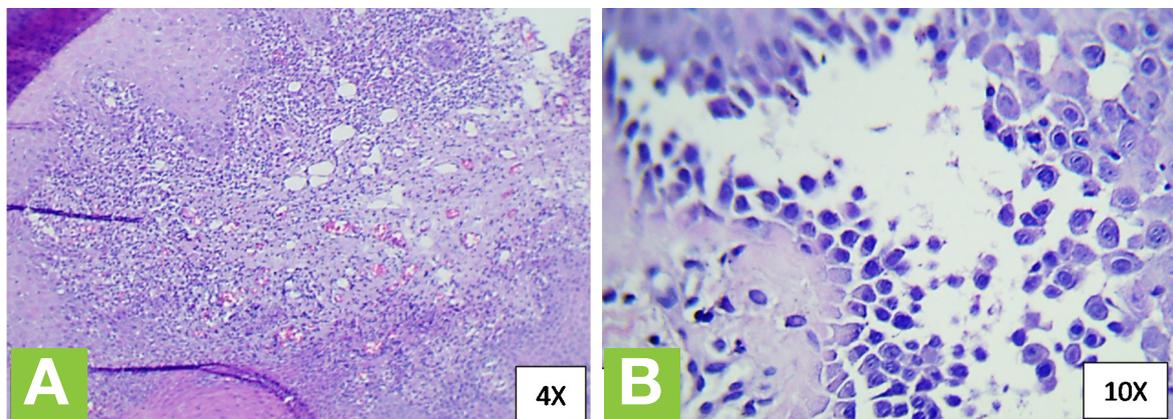


- A:** The right lateral edge in the process of tissue repair showing adequate involution of the initial ulcer.
- B:** Left lateral edge with a favorable re-epithelialization process, whitish borders, and reduced erosive lesion with a clean background.

Figure 3: Anterior lingual mucosa with bullous and erosive lesions, lower and upper labial mucosa with bullous lesions with a whitish background and erythematous halo.



Figure 4: Sección histológica.



A: The right lateral edge presents an erosive lesion with an erythematous background and whitish borders.
B: Erosive lesion on the left lateral edge with erythematous background and smooth borders similar to the adjacent mucosa.

Figure 4: Healthy tongue and labial mucosa without the presence of bullous lesions, slight inflammation, erythematous areas in the process of tissue repair and remission of the inflammatory process.



the buccal mucosa of the anterior lingual and labial third, both upper and lower (Figure 3). Complete blood count and blood chemistry tests were taken. Results revealed that the patient had leukocytosis.

After signing the informed consent, the patient underwent an incisional biopsy to determine his histopathological diagnosis and make a clinical correlation. After asepsis and antisepsis with povidone-iodine, a local anesthetic blockade was performed with articaine and epinephrine (a cartridge), surgical spindle was performed in the lower left labial region, treatment of the base and, finally, isolated sutures with 4-0 Vicryl. Therapy consisted mainly of 250 mg lysine clonixinate every 12 h for 5 days, mouthwashes with super oxidation solution and active ions after each mouthwash until the end of the treatment. The sample was placed in 10% formalin for its subsequent histopathological process. Once in the laboratory, a fragment of soft tissue measuring 0.5x0.5x0.2 cm was received, irregular brown in color with a firm consistency and recent signs of hemorrhage.

Microscopic evaluation revealed an epithelial lesion characterized by a para-keratinized stratified squamous epithelium that presented an intraepithelial bulla with abundant inflammatory infiltrate, predominantly lymphoplasmacytic, isolated eosinophil acantholysis, spongiosis and hydropic degeneration. The underlying connective tissue was loosely arranged, discreet and disorganized. A diagnosis of possible pemphigus vulgaris was established (Figure 4).

It is worth mentioning that the patient had not presented similar lesions in his life before

the SARS CoV 2 infection.

Consequently, once the diagnosis was established and after having carried out the post-surgical evaluation 8 days after taking the incisional biopsy, adequate tissue repair was observed, sutures were removed and the treatment protocol for pemphigus vulgaris was started consisting of the application of 0.1% mometasone gel on the affected areas three times a day, alternating with 2 g miconazole gel twice a day for 20 days. After this period, the patient came for an assessment. He had better general conditions with involution of most of the lesions of the buccal and lingual mucosa. Currently, the patient is still being monitored and receiving treatment for pemphigus, which is now under control (Figure 5).

DISCUSSION

Scientific evidence shows that the most affected organs are those that have a greater number of angiotensin-converting enzyme 2 (ACE2) receptors. They are areas with a greater susceptibility for the viral RNA sequence to enter the host cell.³ In the oral cavity and in accordance with this anatomical distribution, it has been shown that these receptors are found in greater number and dissemination in the lingual mucosa, as well as in the glandular elements as viral reservoirs. Likewise, an individual evaluation was carried out by cells, where it was possible to observe a higher expression in epithelial cells, followed by T cells, fibroblasts, B cells, macrophages, endothelial cells, and mast cells.⁴ On the

other hand, the pharmacological prescription for the treatment of SARS CoV 2 infection is certainly different in each healthcare center and between each physician. For example, infectologists use different medications ranging from antivirals, antibiotics, steroids, NSAIDs, bronchodilators, anticoagulants, among others. These drugs, in many cases, have the adverse effects of decreasing salivary flow, causing dysgeusia, inflammatory states such as gingivitis, erosive lesions, local pharmacological hypersensitivity, which contribute significantly to reducing the immunological status of the mucous membranes in the oral cavity and pharynx, which favors the development of opportunistic infections by bacteria, viruses, fungi, and other microorganisms because of the dysbiosis produced in the microenvironment of the oral cavity.^{1,5,7}

All these factors, along with the manifestations of the disease, such as the state of stress, inflammation, vasculitis, and poor oral hygiene associated with the biology of each individual, significantly increase the presence of lesions associated with SARS CoV 2 infection.¹ In relation to the presentation of the erosive lesions of the first case and once the anatomical areas with the highest number of ACE2 receptors have been explained, it is logical to think that the most frequent lesions will be located in the mucosa of the tongue, especially in the anterior and middle thirds.^{3,4,9} Zarch *et al.*,⁸ describe in their review that there is evidence of more than 170 SARS CoV 2 positive patients who presented oral manifestations such as dysesthesia, burning, and tongue ulcers, which is very similar to the case of the 67-year-old male patient

presented in this report. Hanna *et al.*,¹⁰ recommend the use of biophotomodulation, which is well documented not only in these cases but also in pharmacological mucositis due to oncological chemotherapeutics.¹⁵ In this case, we opted to use a topical as well as intramuscularly treatment involving the B complex, obtaining a satisfactory evolution of tissue repair a month after the start of the treatment.

Regarding case number 2, the 47-year-old male patient reported never having been affected by bullous-type lesions in his oral cavity before the SARS CoV2 infection. However, after his diagnosis, it is difficult to assert a cause-effect correlation as a triggering factor of a local state of autoimmunity in the oral cavity. But if we consider that the virus per se can be a triggering factor of an uncontrolled immune reaction, as happens with the cytokine storm, it is possible, from a pathophysiological approach, that it may be the case.

The virus enters the epithelium of the oral cavity in the anterior and middle region of the lingual mucosa. Once included as an intrachromosomal RNA sequence in the host cell, it will seek the basal layer where cell division is carried out and it is possible that the lymphocytes identify these cells with greater responsiveness than the rest of the cells of the superficial layers and that these are the targets that these cells infiltrate, which causes collateral aggression to adhesion proteins, such as desmogleins, integrins, cadherins, desmosomes, etc.¹¹⁻¹³ Despite the fact that this is a reasonable assumption, a more solid explanation

is required as well as another type of intervention, such as an histological and immunofluorescence analysis to assert that the virus is the trigger for a probable pemphigus vulgaris.

However, as all the scientific evidence up to now in relation to this infection is still being collected, considering the spectrum of the disease, we are still integrating these possible lesions in the oral cavity and the pharynx of infected individuals into a pattern connected to this condition. It is noteworthy that the patient had never suffered from isolated mouth ulcers or ulcerative states, such as recurrent aphthous stomatitis, and the fact that, after this infection, these conditions have developed in such an exacerbated manner.^{11,14}

Other authors such as Dos Santos have mentioned other oral manifestations such as recurrent herpes simplex, candidiasis, and migratory glossitis.¹⁶ All this evidence highlights the need to comprehensively approach patients with SARS CoV 2 infection. And although it is true that there are systems such as the pulmonary and cardiac that require special care, the oral cavity cannot be separated and underestimated regarding the evaluation and treatment of the lesions that have been found in many reports worldwide.

Likewise, and due to the isolation that the infected patients require, different ways of referring patients to specialists in oral health, such as oral and maxillofacial pathologists, have been proposed. A practical suggestion is to use technology, such as telemedicine. On its part, stomatological therapy can also be carried out by using oral photographs taken

during the acute process of the infection. Through these images and the basic data of the pharmacological treatment, in addition to the clinical history of the patient, the treating specialist can decide on the most effective topical or systemic treatment for treating the oral conditions of the patient with SARS CoV 2.^{14,16}

CONCLUSION

In relation to the cases presented, it is concluded that the lesions of the patients may be associated with post-infection by SARS CoV 2, especially considering their clinical history, in reference to the fact that they had not presented such conditions before and that they appeared suddenly after the infection.

Regarding the first case, the erosive lesions could be related to inadequate nutrition and hydration due to the poor health conditions of the patient, respiratory compromise, and asthenia, as well as the adynamia that led the patient to a polydeficiency state. So once the therapy focused on restitution of complex B, adequate hydration, and local general measures were given to the patient, his lesions regressed satisfactorily. In the second case, it is possible that the autoimmune deregulation that the patient presented due to the SARS CoV 2 infection, and the alteration in the cytokine storm and the systemic inflammatory state, triggered a loss of immunological tolerance in the oral cavity, resulting in the histomorphological characteristics of intraepithelial bullae with a lymphoplasmacytic component and acantholytic cells, characteristic of

pem-phigus vulgaris. It is necessary to carry out correlation studies of these atypical presentations of oral mucosal lesions.

They will allow researchers to identify more clearly if they occur due to the biological response of each individual to SARS CoV 2 infection, or if there is any genetic or epigenetic predisposition or variability between the patients who present it and those who do not, even in the manifestation of the same infection.

Due to the above, oral and maxillofacial health professionals must take on the commitment and document cases of oral lesions that appear after SARS CoV 2 infection and refer the patients to Oral Pathology centers, so they can be properly managed and receive a suitable treatment. Besides, it would also allow for documentation and dissemination of the characteristics of such cases.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

ETHICS APPROVAL

Informed consent was obtained from the patients.

FUNDING

None.

AUTHORS' CONTRIBUTIONS

Villanueva-Sánchez F: Conceptualization; investigation; methodology; writing – original draft; writing – review and editing.

Escalante-Macías L: Supervision; validation; visualization

ACKNOWLEDGEMENTS

None.

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PUBLISHER'S NOTE

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This manuscript was evaluated by the editors of the journal and reviewed by at least two peers in a double-blind process.

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ISSN Print 0719-2460 - ISSN Online 0719-2479.

<https://www.joralres.com/index.php/JOralRes/issue/archive>

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