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## REVIEW ARTICLE

### Oral manifestations of COVID- 19 infections- A review

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#### ABSTRACT

Corona Virus Disease 2019 is an RNA virus, with a typical crown-like appearance under an electron microscope due to the presence of glycoprotein spikes on its envelope. The present review article mentioned oral manifestations of patients with COVID- 19 infection.

**Key words:** COVID- 19, Pandemic, oral lesions.

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#### INTRODUCTION

In January 2020, deep sequencing analysis from lower respiratory tract samples identified a novel virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as causative agent for that observed pneumonia cluster.<sup>1,2</sup> On February 11th, 2020, the World Health Organization (WHO) named the disease caused by the SARS-CoV-2 as "COVID-19", and by March 11th, 2020 when the number of countries involved was 114, with more than 118,000 cases and over 4000 deaths, the WHO declared the pandemic status. Corona Virus Disease 2019 (COVID-19) is an RNA virus, with a typical crown-like appearance under an electron microscope due to the presence of glycoprotein spikes on its envelope.<sup>3</sup> It is not the first time that a coronavirus causing an epidemic has been a significant global health threat: in November 2019, an outbreak of

coronaviruses (CoVs) with severe acute respiratory syndrome (SARS)- CoV started in the Chinese province of Guangdong and again, in September 2012 the Middle East respiratory syndrome (MERS)-Co V appeared. There are four genera of CoVs: (I)  $\alpha$ -coronavirus (alpha CoV), (II)  $\beta$ -coronavirus (beta CoV) probably present in bats and rodents, while (III)  $\delta$ -coronavirus (delta CoV), and (IV)  $\gamma$ -coronavirus (gamma CoV) probably represent avian species.<sup>4</sup>

The pathogenic mechanism that produces pneumonia seems to be particularly complex. The data so far available seem to indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a reaction takes place, which as a whole is labelled a "cytokine storm". The effect is extensive tissue damage. The protagonist of this storm is interleukin 6 (IL-6). IL-6 is produced by activated

leukocytes and acts on a large number of cells and tissues.<sup>5</sup>

It is able to promote the differentiation of B lymphocytes, promotes the growth of some categories of cells, and inhibits the growth of others. It also stimulates the production of acute phase proteins and plays an important role in thermoregulation, in bone maintenance and in the functionality of the central nervous system. Although the main role played by IL-6 is pro-inflammatory, it can also have anti-inflammatory effects. In turn, IL-6 increases during inflammatory diseases, infections, autoimmune disorders, cardiovascular diseases and some types of cancer. It is also implicated into the pathogenesis of the cytokine release syndrome (CRS) that is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunction.<sup>6</sup>

Oral mucosa could be the first area infected with SARS-CoV-2, it could be hypothesized that oral mucosa lesions could be the first COVID-19 signs to arise, if they were to be considered COVID-19 signs. If studies will confirm this hypothesis, the dental practitioners would be the first to identify suspect SARS-CoV-2 positive patients and could send them to get tested and treated appropriately. The SARS-CoV-2 positive patient had pain in her tongue, which may be due to the higher expression of angiotensin-converting enzyme 2 - the receptor for SARS-CoV-2 - in the epithelial cells of the tongue, in comparison with the buccal or gingival tissues. Taking into account that anosmia and ageusia (olfactory and gustatory dysfunctions) are confirmed to be inflammation-induced COVID-19 symptoms we suggest COVID-19 might include oral signs and symptoms, which need to be particularly investigated.<sup>7</sup>

Oral mucosa lesions could be the result of plenty other factors, such as stress due to social-life restrictions during COVID-19 pandemic lockdown, lack of oral hygiene, work pressure, or herpes simplex virus. Topical antiseptic oral applications recommended to reduce the oral viral load such as hydrogen peroxide-based mouth rinse solutions could also induce oral ulcers. The thorough anamnesis should identify the cause of the oral lesion.<sup>8</sup>

Martín Carreras-Presas et al<sup>9</sup> described three patients who developed oral ulcerative lesions during the COVID-19 lock-down period: a 56-year-old healthy man, a 58-year-old-man with diabetes and hypertension, and a 65-year-old woman with hypertension. These comorbidities are strongly associated with a poor prognosis in patients with SARS-CoV-2; thus, it is more likely that fear and emotional stress were the underlying cause that triggered herpetic lesions on the palate of two of these patients. Furthermore, it is unlikely that the third patient's lesions (desquamative gingivitis and lip blisters) can be considered to be oral

manifestations of COVID-19, simply because they appeared approximately one month after the patient was diagnosed with COVID-19 and after more than one week after she had been discharged from the hospital. In agreement with the authors, further studies are needed to investigate the oral manifestations of COVID-19, although the literature from other countries and the anecdotal evidence collected from COVID-19 patients sharing their experience do not fit the narrative that COVID-19 is associated with oral vesiculo-bullous lesions.

Governments have been exhausting all possible measures to detect, test, treat, isolate, and trace all possible patients to combat the COVID-19 pandemic; thus, it is very unlikely that public health officials in all the pandemic epicenters, frontline first responders, and healthcare workers have not identified such oral manifestations of COVID-19. Had there been any association between oral ulcers and infection with SARS-CoV-2, it would have been reported by the thousands of symptomatic patients who have been affected by the disease because oral ulcers are very painful and interfere with chewing, swallowing, and speaking. The current literature supports the evidence that dysgeusia is the only oral symptom of COVID-19.<sup>10</sup>

Giacomelli et al<sup>11</sup> verbally interviewed 59 hospitalized patients with COVID-19, and their primary objective was to evaluate the prevalence of olfactory and taste disturbances, in particular the presence or absence and the characteristics of these disturbances at or before the patients were hospitalized, none of the interviewed patients reported oral ulcerations or vesiculobullous lesions. Ulcerations and blisters of the oral cavity are more likely to be reported, noted, and documented by any researcher interested in evaluating dysgeusia. Furthermore, undocumented and documented numbers of nurses, physicians, and other healthcare workers who fell ill with COVID-19 would have reported similar oral manifestations to increase awareness and to allow for early detection of infection with SARS-CoV-2.

Soares et al<sup>12</sup> reported the clinical and microscopical characteristics of oral reddish lesions and ulceration that occurred in a 42-year-old male patient positive for SARS-Cov-2 confirmed by polymerase chain reaction (PCR). The patient also had a history of diabetes and hypertension, and when admitted to the hospital presented fever (temperature of up to 39.3°C), cough and shortness of breath. On the skin it was observed some petechia-like and small vesicobullous lesions of unknown aetiology. A treatment with dexamethasone and dipyron was established for 1 week. The patient also complained of a painful ulceration in the buccal mucosa that was biopsied. Oral examination showed besides the ulcerated lesion, multiple reddish macules of different sizes scattered along the hard palate,

tongue, and lips. After 3 weeks of follow up the lesions presented complete remission.

## CONCLUSION

Authors suggested that occurrence of oral lesions especially oral ulcers may be indicative of COVID- 19 infections.

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