

ORAL SIGNS AND SYMPTOMS IN COVID-19

Mihajlo Petrovski

Faculty of medical sciences, Goce Delcev University, Stip, Republic of North Macedonia
mihajlo.petrovski@ugd.edu.mk

Kiro Papakoca

Faculty of medical sciences, Goce Delcev University, Stip, Republic of North Macedonia
kiro.papakoca@ugd.edu.mk

Abstract: The clinical symptoms of COVID-19 infection are not fully described, and most of them are still documented and collecting. The disease is characterized with a numerous clinical signs and symptoms predominant of the respiratory system, including dry cough, which is usually accompanied by fever, difficulties in breathing, and adynamia, but also other less typical symptoms of infectious disease have been described. The cause of this disease is present in both the oral cavity and saliva, which means that the environment in which we work is an excellent reservoir of viral microorganisms. As mentioned, in patients with COVID-19 the most common symptoms are occurrence of fever (more than 38 ° C), cough, shortness of breath, myalgia, rhinorrhea, sore throat, anosmia and aggeusia (the last two symptoms are most often associated with this infection). Given the fact that patients with COVID-19 may have oral signs and symptoms, there is a need for research that will note the most common oral signs and symptoms in these individuals. Hence, the main goal of the research was to make aadequate literary review of the most common oral signs and symptoms in people with COVID-19. For the realization of the main goal, a literary review was made using the following keywords "COVID-19", "SARS-CoV-2", "coronavirus-19", "oral health", "oral changes" and "oral lessions". Scientific data published exclusively in English, in professional and scientific journals from the last three years (2019, 2020 and 2021) were used. Although at the beginning of the COVID-19 pandemic, it was believed that this infection would have no effect on oral health, nowadays it is known that have an impact on oral structures. Inadequate oral hygiene, the occurrence of opportunistic infections, stress, the presence of additional systemic diseases (diabetes mellitus, immunosuppression, etc.), trauma (as a consequence of intubation), vascular influences and hyperinflammatory reaction that occurs secondary, are the most important predisposing factors for the development of oral lesions in positive COVID - 19 patients. Based on the literature data, it can be noted that in patients with COVID-19 can be noted numerous orofacial signs which may help clinicians to identify suspicious cases. These changes are most commonly manifested- oral ulcers, erithematous macules, vesicular-bullous lesions and acute inflammation of the parotid gland. However, the fact presented in the modern literature that oral manifestations are rarely reported, due to the lack of dental examinations of patients with COVID-19 (insufficient attention paid to not so serious oral signs and symptoms compared to typical clinical manifestations). We believe that further studies are needed using large groups of COVID-19 patients to document all orofacial manifestations associated with COVID-19. Dentists should play a key role in the fight against KOVID-19 by recognizing oral manifestations, and before the appearance of the first systemic signs and symptoms of the disease. Therefore, dentists should be familiar with all potential orofacial manifestations of COVID-19.

Keyword: COVID-19, oral signs, oral symptoms, SARS-CoV-2.

1. INTRODUCTION

Although oral health of COVID-19 positive patients can be affected by the infection, one of the biggest dilemma is whether these manifestations could be a typical pattern resulting from the direct viral infection. Oral lesions can be also result from some systemic deterioration, considering the possibility of opportunistic infections and also adverse reactions of treatments. Some authors such as Dos Santos et al (2020) assume that oral lesions are secondary resulting from the deterioration of systemic health or due to treatments for COVID-19. In additionally, COVID-19 acute infection and its therapeutic measures, could potentially cause to negative outcomes concerning oral health, like opportunistic fungal infections, recurrent oral herpes simplex virus infections caused by HSV-1, unspecific oral ulcerations, erythema fixum, dysgeusia, xerostomia linked to decreased salivary flow, ulcerations and gingivitis as a result of the impaired immune system and susceptible oral mucosa. (Dziedzic & Wojtyczka, 2020)

Relatively early stages of research in this field, there are few researches providing dental professionals with useful information regarding possible oral signs of COVID-19. Given the fact that patients with COVID-19 may have oral signs and symptoms, there is a need for research that will note the most common oral signs and symptoms in these individuals. Hence, the main goal of the research was to make a literary review of the most common oral signs and symptoms in people with COVID-19. For the realization of the main goal, a literary review was made using the following keywords "COVID-19", "SARS-CoV-2", "coronavirus-19", "oral health", "oral changes" and "oral

lessions" . Scientific data published exclusively in English, in professional and scientific journals from the last three years (2019, 2020 and 2021) were used.

2. ORAL SIGNS AND SYMPTOMS OF COVID-19

Oral cavity is frequently involved and deserves specific examination under the appropriate circumstances to avoid contagion risk among patients with COVID-19. The clinical symptoms of COVID - 19 infection are not fully detected, so most of them are still being documented and collecting.

The most common clinical symptoms of the patients suffering from COVID-19 are fever, cough, shortness of breath, myalgia, tiredness, and abnormal chest radiological findings and CT. Less common and usual symptoms are headache, production of sputum, hemoptysis, stomach pain, dizziness, nausea, diarrhea, and vomiting.

According to Mehat et al (2020) SARS-CoV-2 can not be effectively defeated by human first-line protective mechanisms, biomolecular and cellular, so cause number of death cases in middle aged healthy persons, regardless their immune status. (Mehta et al., 2020). Due to indirect complex effect of the virus and intensified therapeutic methods, multi-drug treatment, it is assumed that some pathological oral conditions could be deteriorated by SARS-CoV-2, particularly among patients with compromised immune response or defense mechanisms. These conditions can be linked to long-term pharmacotherapy. Therefore, strategies to boost immune responses (for example with vaccination) at this stage of pandemic are essential. (Dziedzic & Wojtyczka, 2020)

Like blood, saliva is rich in multiple biomarkers such as DNA, RNA, proteins, and also microorganisms. Hence, there is a high probability of antibodies and viruses of the human body being present in saliva. It has been reported that some viruses of large-scale infectious diseases, particularly the respiratory diseases such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), can be detected in saliva. (Wang et al, 2004; To et al, 2019). As a result, it is imperative to determine whether SARS-CoV-2 can be detected in saliva. In one study from Chen et al (2020) is noted that the positive saliva detection rate is very high as 75% (3/4) in critically ill patients on ventilator support. According to the authors, there might be two possible explanations for this. First, viral replication in critically ill patients is unchecked by a weakened immune response, so there is a very large amount of virus in the blood and other tissue fluids, such as saliva. Hence, the salivary glands are attacked due to the high viral load. Secondary, in critically ill patients, there is usually a weakened immune system, electrolyte disorders and multiple organ dysfunctions, particularly at the late stage of the disease which could destroy the salivary glands and lead to virus invasion of the salivary glands. The results indicated that as SARS-CoV-2 infection progressed, the chances of viral particles appearing in the saliva increase. The emergence of the virus in saliva may be an indication that the disease condition of the patient has deteriorated and that the disease has entered the terminal stage. Also healthcare workers (HCWs) should pay more attention to increased risks of transmission of COVID-19 virus through saliva, and that patients with positive saliva detection may indicate a poor prognostic outcome.

Most of studies have found that taste and smell chemosensory dysfunctions are the initial and only signs of this disease in a most of the patients. Additionally, numerous recent studies have reported clinical orofacial manifestations in COVID-19-positive patients, including oral ulcerative lesions, vesicubullous lesions, and acute sialoadenitis. It has been reported that these oral manifestations, in general, appear concomitant with the loss of smell and/or taste a few days later (up to 14 days) and progress more rapidly and severely among older patients. Interestingly, resolution of the oral lesions occurs in parallel with the resolution of COVID-19 indicating an association between virus infection, oral clinical manifestation and their recession. (Rodriguez et al, 2020)

Previously published data have shown that most oral lesions can generally be categorized into two types. The first type refers to lesions similar to aphthous-like ulcers that occur in younger patients with mild Covid-19 symptoms. The second type resembles herpetic ulcers that are spreading throughout the oral cavity and are commonly reported in older patients with some degree of immunosuppression. (Brandini et al, 2021).

As a result of life-saving therapies, including external ventilation and aggravated blood oxygenation, among severely ill hospitalized patients, oral health can be seriously deteriorate, especially in cases in patients staying in intensive care units. A deficiency of oral care as treatment priority is given to advanced medical care; intubation, tracheostomy, external ventilation, as well as mouth breathing, hyposalivation can lead to rapid oral health deterioration and subsequent complications, affecting also the lower respiratory track, similar to aspiration pneumonia (Wu et al., 2020).

Once more, it should be noted that orofacial manifestations among COVID-19 patients are numerous. In contemporary scientific literature most common noted oral signs among these patients are ulcerative lesions, vesiculo-bullous lesions, macular erythematous lesions and acute parotitis. The most commonly affected intraoral site was the hard palate, followed by the dorsum of the tongue and labial mucosa. The diagnosis of oral mucosal lesions are mainly based on clinical features in most of the included studies and only few studies included performing biopsies to confirm the diagnosis.

Ulcerative oral lesions were the most commonly reported orofacial manifestations of COVID-19. Most of the patients have single ulcers, (Ansari et al, 2020; López-Sánchez et al, 2020) while in some cases, the patients presented with several small painful ulcers. (Capaccio et al, 2020; Kahraman, 2020) In only one study, the patient had severe erosions, ulcerations, and blood crusts on the labial mucosa along with gingival and palatal petechia. (Ciccarese et al, 2020) The localization of ulcers varied among the studies, but the dorsum of the tongue was the most frequently affected site, followed by the hard palate and the buccal mucosa. Interestingly, in one study published by Chaux-Bodard et al (2020) oral ulcers were the first sign of the disease.

Some studies reported presence of oral vesiculobullous and macular oral lesions in patients with COVID-19. The clinical presentations varied greatly, ranging from blisters, big erythematous lesions, petechial and erythema multiform-like lesions. Of these, erythema multiform-like lesions are the most common presentation and are accompanied by skin target-like lesions. Most of the cases with vesiculobullous/macular manifestations are associated with cutaneous lesions. (Jimenez-Cauhe et al,2020; Labé et al, 2020).

Capaccio et al in 2020 first reported acute parotitis in the context of COVID-19. The study is showing a 26-year-old patient with COVID-19 with painful swelling of the left parotid gland, with no purulent discharge upon parotid massage. According to authors, acute parotitis was the first clinical sign of COVID-19, followed by other typical symptoms such as fever, myalgia, hyposmia and ageusia. Serological tests showed negative results for cytomegalovirus and paramyxovirus antibodies. In another study, Lechien et al. (2020) noted three COVID-19 patients with acute parotitis and parotitis was the initial sign of COVID-19 in two of these patients. In the last year, Fisher et al. (2021) presented COVID-19- associated parotitis in a 21-year-old female with unilateral left-sided facial and neck swelling.

Most common localization of the oral lesions among patients with COVID-19 described in the literature are: tongue, palate, lip mucosa and gingiva. (Brandini et al, 2021).

Other clinical manifestations in the oral cavity, related to COVID-19 are- tongue depapillation, Candida- associated lesions, xerostomia, aphthous like-lesions, recurrent herpesvirus infection, non-typical ulcers, necrotising gingivitis, erythema multiforme-like lesions and salivary gland infections. (Rodriguez et al, 2020)

At the end it must be noted that among patients with COVID-19 some periodontal manifestations can be diagnosed. Periodontal diseases (PDs) as inflammatory conditions affecting the supportive tissues around the tooth are most commonly associated with long-term biofilm accumulation. But in COVID-19 patients, except a wide variety of oral manifestations, also it can be found acute periodontal lesions. The prevalence of patients who present periodontal manifestations associated with Covid-19 remains uncertain because of limited case reports with small cohort size. Patel and Woolley (2020) published a case of necrotizing gingivitis.

3. CONCLUSION

In patients with COVID-19 can be noted numerous orofacial signs which may help clinicians to identify suspicious cases. These changes are most commonly manifested- oral ulcers, erithematous macules, vesicular-bullous lesions and acute inflammation of the parotid gland. However, most fact presented in the modern literature is that oral manifestations are rarely reported, due to the lack of dental examinations of patients with COVID-19 (insufficient attention paid to not so serious oral signs and symptoms compared to typical clinical manifestations). We believe that further studies are needed done on large groups of COVID-19 patients to document all orofacial manifestations associated with COVID-19. Dentists should play a key role in the fight against COVID-19 by recognizing oral manifestations, and before the appearance of the first systemic signs and symptoms of the disease. Therefore, dentists should be familiar with all potential orofacial manifestations of COVID-19. It should be expected increasing of cases with oropharyngeal symptoms or conditions, and it is certain that more reliable scientific data will appear in the nearest future, including information relevant to oral medicine/oral pathology in the light of COVID-19 infection, allowing us to understand SARS-CoV-2 pathogenesis and its impact on head and neck pathologies.

REFERENCES

- Ansari, R., Gheitani, M., & Heidari, F. (2020). Oral cavity lesions as a manifestation of the novel virus (COVID-19): a letter-to-editor. *Oral Diseases*.
- Brandini, D. A., Takamiya, A. S., Thakkar, P., Schaller, S., Rahat, R., & Naqvi, A. R. (2021). Covid-19 and oral diseases: Crosstalk, synergy or association?. *Reviews in Medical Virology*.
- Capaccio, P., Pignataro, L., Corbellino, M., Popescu-Dutruit, S., & Torretta, S. (2020). Acute parotitis: a possible precocious clinical manifestation of SARS-CoV-2 infection?. *Otolaryngology–Head and Neck Surgery*, 163(1), 182-183.
- Chaux-Bodard, A. G., Deneuve, S., & Desoutter, A. (2020). Oral manifestation of Covid-19 as an inaugural symptom?. *Journal of Oral Medicine and Oral Surgery*, 26(2), 18.

- Chen, L., Zhao, J., Peng, J., Li, X., Deng, X., Geng, Z., ... & Wang, S. (2020). Detection of SARS-CoV-2 in saliva and characterization of oral symptoms in COVID-19 patients. *Cell proliferation*, 53(12), e12923.
- Ciccarese, G., Drago, F., Boatti, M., Porro, A., Muzic, S. I., & Parodi, A. (2020). Oral erosions and petechiae during SARS-CoV-2 infection. *Journal of medical virology*.
- Dos Santos, J. A., Normando, A. G. C., da Silva, R. L. C., De Paula, R. M., Cembranel, A. C., Santos-Silva, A. R., & Guerra, E. N. S. (2020). Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations?. *International Journal of Infectious Diseases*, 97, 326-328.
- Dziedzic, A., & Wojtyczka, R. (2021). The impact of coronavirus infectious disease 19 (COVID-19) on oral health. *Oral diseases*, 27, 703-706.
- Fini, M. B. (2020). What dentists need to know about COVID-19. *Oral oncology*, 105, 104741.
- Fisher, J., Monette, D. L., Patel, K. R., Kelley, B. P., & Kennedy, M. (2021). COVID-19 associated parotitis. *The American Journal of Emergency Medicine*, 39, 254-e1.
- Halboub, E., Al-Maweri, S. A., Alanazi, R. H., Qaid, N. M., & Abdulrab, S. (2020). Orofacial manifestations of COVID-19: a brief review of the published literature. *Brazilian Oral Research*, 34, e124-e124.
- Jimenez-Cauhe, J., Ortega-Quijano, D., Carretero-Barrio, I., Suarez-Valle, A., Saceda-Corrado, D., Del Real, C. M. G., & Fernandez-Nieto, D. (2020). Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings. *Clinical and experimental dermatology*.
- Kahraman, F. C., & Çaşkurlu, H. (2020). Mucosal involvement in a COVID-19-positive patient: a case report. *Dermatologic therapy*.
- Labé, P., Ly, A., Sin, C., Nasser, M., Chapelon-Fromont, E., Saïd, P. B., & Mahé, E. (2020). Erythema multiforme and Kawasaki disease associated with COVID-19 infection in children. *Journal of the European Academy of Dermatology and Venereology*.
- Lechien, J. R., Chetrit, A., Chekkoury-Idrissi, Y., Distinguin, L., Circiu, M., Saussez, S. & Carlier, R. (2020). Early Release-Parotitis-Like Symptoms Associated with COVID-19, France
- López-Sánchez, A. F., Jané-Salas, E., & ML, S. P. (2020). Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Diseases*.
- Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., & Manson, J. J.(2020). HLH Across Speciality Collaboration, UK COVID-19: Consider cytokine storm syndromes and immunosuppression [published online ahead of print, 2020 Mar 16]. *The Lancet*, 395, 1033–1034.
- Patel, J., & Woolley, J. (2021), Necrotizing periodontal disease: Oral manifestation of COVID-19. *Oral Dis*, 27: 768-769.
- Ramírez-Amador, V., Zambrano, J. G., Anaya-Saavedra, G., Zentella-Dehesa, A., Irigoyen-Camacho, E., Meráz-Cruz, N., & Ponce de León-Rosales, S. (2017). TNF as marker of oral candidiasis, HSV infection, and mucositis onset during chemotherapy in leukemia patients. *Oral diseases*, 23(7), 941-948.
- Rodríguez, M. D., Romera, A. J., & Villarreal, M. (2020). Oral manifestations associated with COVID-19. *Oral diseases*.
- To, K. K. W., Chan, K. H., Ho, J., Pang, P. K. P., Ho, D. T. Y., Chang, A. C. H. & Yuen, K. Y. (2019). Respiratory virus infection among hospitalized adult patients with or without clinically apparent respiratory infection: a prospective cohort study. *Clinical Microbiology and Infection*, 25(12), 1539-1545.
- Wang, W. K., Chen, S. Y., Liu, I. J., Chen, Y. C., Chen, H. L., Yang, C. F. & Chang, S. C. (2004). Detection of SARS-associated coronavirus in throat wash and saliva in early diagnosis. *Emerging infectious diseases*, 10(7), 1213.
- Wu, C., Chen, X., Cai, Y., Xia, J., Zhou, X., Xu, S., & Song, Y. (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Internal Medicine*, e200994.