COVID-19's Repercussions on Oral Health

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Oral manifestations related to COVID-19, including fungal infections, recurrent HSV, oral ulcerations, drug-related eruptions, dysgeusia, xerostomia or decreased salivary flow, and gingivitis, may be a result of the impaired immune system and/or susceptible oral mucosa.

Keywords: COVID-19 ; SARS-CoV-2 ; pandemic ; oral lesions ; oral manifestations ; periodontal disease ; temporomandibular disorders ; dental medicine

1. The Essentials about CoVs

CoVs are known to affect different animal species and cause mild to severe respiratory infections in humans. In 2002 and 2012, two highly pathogenic coronaviruses of zoonotic origin, causing the severe acute respiratory coronavirus syndrome (SARS-CoV-1) and the Middle East respiratory coronavirus syndrome (MERS-CoV), respectively, affected humans, resulting in fatal respiratory diseases [1][2], and turning coronaviruses into a 21st century public health problem. The virus has been identified in various non-human hosts [3][4][5][6]. Extremely pathogenic CoVs belong to the genus Beta-coronavirus, group 2, which causes severe disease [7].

In 2019, a new type of coronavirus, SARS-CoV-2, a Beta-coronavirus causing the COVID-19 disease, was first detected in Wuhan, China [8]. SARS-CoV-2 is composed of 16 non-structural proteins with specific roles in replication [9]. COVID-19 has spread rapidly around the world and, on 11 March 2020, the World Health Organization declared it a pandemic [10].

The SARS-CoV-2 genome sequence shares ~80 % sequence identity with SARS-CoV-1 and ~50% with MERS-CoV [11]. The structural spike protein (S), which mediates SARS-CoV's entry into host cells, is highly variable in the case of SARS-CoV-2. Its receptor-binding domain enables direct contact with the cell receptor angiotensin-converting enzyme II (ACE2) [4][12].

ACE2, and thus any cells that express ACE2, may be target cells and therefore susceptible to COVID-19 infection [11]. Zou et al. [13] explored the expression of the ACE2 receptor on different cells from human body tissues and classified the infectious risk potential. Lung, heart, esophagus, kidney, bladder, and ileum have been considered organs at risk [13]. A high ACE2 expression was found in the oral mucosa and the epithelial cells of the tongue [14]. After entering the cell, the virus delays the immune system response, allowing the infection to progress, and it becomes much harder to fight [15].

2. Oral Lesions Related to COVID-19

Reports of different oral manifestations related to COVID-19 cases were described in
the literature. Oral lesions reported in patients with COVID-19 were quite heterogeneous, varying in the kind of lesion and location. In most cases, the pathogenesis of these manifestations was not clearly defined, being categorized as a direct result of the viral infection, a consequence of immune misbalance, or an adverse reaction to treatment
[47–49]. Poor oral hygiene in hospitalized or quarantined COVID-19 patients should also be considered as an aggravating condition [50].
According to the reviewed data, the most frequent types of oral lesions found in
COVID-19 patients are: ulcers (42 cases, 25.92%), aphthous stomatitis/aphtae (29 cases, 17.90%), angular cheilitis/cheilitis (21 cases, 12.96%), glossitis/lingual papillitis (21 cases, 12.96%), petechiae (8 cases, 4.93%), macules (7 cases, 4.32%), erythematous and erosive lesions (6 cases, 3.70%), herpetic lesions (6 cases, 3.70%), candidiasis (4 cases, 2.46%), and
bulla (2 cases, 1.23%).

3. The Association between Periodontal Disease and COVID-19

Periodontal disease, a severe inflammatory gum disease, mainly affects the supporting structures of the teeth, gingiva, and alveolar bone, and it is frequently associated with poor oral hygiene and age. As the human organism normally responds to bacterial infection through inflammation, this process can result in a “cytokine storm”, where proteins are released and associated with an exuberant inflammatory response that destroy tissues in other parts of the body [16].

The inflammatory products can enter the bloodstream through periodontal pockets and reach other organs, causing tissue damage [17]. Pro-inflammatory cytokines and oxidative stress, involved in the development of periodontal disease and other metabolic diseases, are highly elevated among COVID-19 patients [18]. Bacteria in the gums spread the IL-6 inflammatory protein. High levels of IL-6 in the body are a predictor of respiratory failure, with a 22 times higher risk for respiratory complications being reported, thus highlighting the importance of reducing the amount of oral bacteria and subsequent systemic inflammation [19].

On the other hand, the high prevalence of periodontal disease among patients experiencing metabolic diseases, such as obesity and diabetes, and cardiovascular diseases is well-documented. These types of comorbidities, which affect systemic health, are also known to increase the risk for severe COVID-19 [20][21][22]. The association between periodontal disease and severe COVID-19 could help identify risk groups and establish pertinent recommendations [23].

A study on 568 patients, showed a clear association between periodontitis and increased levels of biomarkers associated with severe COVID-19 disease, as well as complications including death, ICU admission, and the need for assisted ventilation [24].

The investigations of a possible link between the microbial oral flora and COVID-19 also revealed that there is a risk that oral secretions may be aspirated into the lungs and cause infection [25]. Oral bacteria, such as the periodontal pathogens Porphyromonas gingivalis, Fusobacterium nucleatum, and Prevotella intermedia, may accelerate viral infectious diseases such as COVID-19 and aggravate lung damage [26]. Cytokines such as interleukin 1 (IL1) and tumor necrosis factor (TNF), which are present in the saliva as a consequence of their bacterial activity, can easily reach the lungs [24].

Poor oral hygiene, a frequent consequence of low income or psychological troubles, can lead to COVID-19 aggravation due to the aspiration of periodontopathic bacteria, which induces the expression of ACE-2, a known receptor for SARS-CoV-2, and the production of inflammatory cytokines in the lower respiratory tract. Long-term hospitalization of patients with COVID-19 leads to reduced professional oral care. Poor oral hygiene, and limited access to dental care in patients with COVID-19, may increase the inter-bacterial exchanges between the oral cavity and the lungs and thus the risk of a much more severe respiratory infection [27][28][29].

The degree of periodontal inflammation may help to determine the severity of COVID-19 infection. Routine dental and periodontal treatment may also help decrease the symptoms of COVID-19 [26][25].

4. Temporomandibular Disorders Associated with COVID-19 Pandemic

Among the most common symptoms of temporomandibular disorders (TMDs) are soreness in the jaw joint area and jaw muscles and clicking or crunching noises when opening or closing the mouth or when the patient chews, yawns, or even speaks. TMD may be linked with headaches, neck pain, and discomfort in the temple or teeth. TMD reflects the dysfunction of the masticatory system, one of its major causes being stress and psychosocial impairment [30].

Pandemics are stressful, like most public health emergencies. The literature presents aspects of psychological reactions related to epidemics and pandemics, which depend on individual vulnerability, intolerance to uncertainty, perceived vulnerability to disease, and anxiety [31]. The anxiety, depression, and stress people experience during the COVID-19 pandemic may lead to TMD [32].

Uncertainties about the origin and nature of the virus and about governments’ abilities to prevent its spread, lack of confidence in the medical system and its ability to cope with new cases, fear of infection, misinformation, and feelings of loneliness and anger in quarantined people due to lack of socialization play important roles in the development and maintenance of TMD [33].

These psychosocial factors, often associated with sympathetic activity and additional release of adrenocortical steroids, may lead to muscle vasoconstriction and increased peripheral vascular resistance. Autonomic insufficiency can increase

the sympathetic impulse and the feeling of hyper-excitement that creates and perpetuates sleep disorders, accompanied by sensations such as heat and cold, palpitations, tachycardia, nausea, abdominal pain, diarrhea, and constipation [34].

Reports have noted an increased number of people experiencing teeth grinding and oral pain during the COVID-19 pandemic as a consequence of increased stress due to health worries, the loss of work, and lockdown or separation from family members [35][36]. On the other hand, stress, anxiety, and depression due to COVID-19 lead to increased orofacial pain, TMD, and bruxism symptoms [37][38].

According to another recent study, people with chronic TMD are more susceptible to COVID-19 distress, resulting in deterioration of their psychological status, and increased chronic facial pain severity, supporting the hypothesis that stress acts as an amplifier of central sensitization, anxiety, depression, chronic pain, and pain-related disability in TMD cases [39].

Two concomitant studies aimed to evaluate the effect of lockdown on TMD and bruxism symptoms among 700 subjects from Israel and 1092 from Poland, respectively, by using online questionnaires. The results showed significant altered psychoemotional status, leading to aggravated bruxism and TMD symptoms, accompanied by increased orofacial pain [38].

Even after the lockdown period ended, patients with high risk for severe COVID-19 limited their dental appointments to emergencies only, which was not the case for TMD and bruxism. As they were neglected, these conditions got worse [40].

Medical staff, including dental practitioners, have also been reported to experience moderate to severe levels of anxiety because of possible COVID-19 repercussions [31][35][41].

A study carried out on 641 dental surgeons found TMD in 24.3% of the participants, sleep bruxism in 58%, and awake bruxism in 53.8% [42]. The incidence of TMD reported by a study carried out on 699 dental university students during the COVID-19 pandemic was of 77.5%, accompanied by impaired sleep quality, depression, anxiety, and stress [43]. Another study, based on 113 questionnaires filled out by dental students, also reported that the social isolation and stress due to the COVID-19 pandemic had led to increase symptoms of TMD, anxiety, and depression [44].

5. Conclusions and Future Perspectives

Oral manifestations related to COVID-19, including fungal infections, recurrent HSV, oral ulcerations, drug-related eruptions, dysgeusia, xerostomia or decreased salivary flow, and gingivitis, may be a result of the impaired immune system and/or susceptible oral mucosa [45].

Although, it is difficult to state which of the various oral lesions associated with COVID-19 are the most prevalent, it seems that a higher frequency can be found in older, hospitalized patients with severe infection [46].

A number of factors, such as immune impairment, co-morbidities, poor oral hygiene, adverse drug reactions, stress, secondary hyper-inflammatory responses, and iatrogenic trauma following intubation, may be involved [47].

The hypothesis that the oral manifestations are secondary lesions resulting from the deterioration of systemic health or treatments for COVID-19 is most probably correct. The pharmacological agents against COVID-19 are related to several adverse reactions, including oral lesions [48].

The authors of one study stated that “The oral mucosal examination has been neglected during the pandemic on reasonable grounds” [49]. A routine intraoral examination should always be performed on patients with suspected or confirmed SARS-CoV-2 infection, as it can represent a sign of potentially life-threatening conditions [50][51].

It has also been stated that “Whether the currently emerging new viral variants will have an impact on the oral manifestations is unknown” [46]. It is our belief that extensive knowledge about all possible manifestations in cases of COVID-19, including oral lesions, is of great importance in the present uncertain context. The fourth wave of COVID-19 and the alarming spreading of the Delta strain, which is highly contagious and potentially severe, keep the subject actual; skin manifestations are increasingly frequent. It can be assumed, based on the correlation between skin and oral manifestations, that new outcomes regarding this subject will emerge.

Dentists are not only implicated in providing specialty assistance in times of pandemics but also in fighting against them. A special note that seems worth mentioning is that, during the anti-COVID-19 vaccination campaign in Romania, marathon vaccinations were carried out during weekends in an effort to encourage attendance and limit the spread of the pandemic.

Dentists took part as volunteers, together with fellow doctors and students, and 6722 people were vaccinated in the authors' hometown during the first organization of this marathon series.

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