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The Impact of Coronavirus Disease 2019 on Oral Health: A Literature Review

Hadeel M. Alfayadh[1], Ashwag Y. Aloyouny[2]

[1] General dentist, Ministry of Health, Riyadh, Kingdom of Saudi Arabia.

[2] Basic Dental Science Department, College of Dentistry, Princess Nourah bint Abdulrahman University, Riyadh, Kingdom of Saudi Arabia.

Abstract: **The impact of Coronavirus Disease 2019 is related to the immune system and acts indirectly via various routes, which reflects the pathological nature of the virus's invasion of the respiratory tract via mucous membranes. Because of this intricate and indirect effect, and because of multi-drug treatments and intensive therapies, it is thought that Coronavirus Disease 2019 could aggravate some oral conditions, especially those with autoimmune aetiology, which have been linked to a long-term pharmacotherapy or a compromised immune system. Objective: This review aims to draw attention to the impacts of Coronavirus Disease 2019 on oral health and advance dental healthcare workers' knowledge. Method: The PubMed Medline database was used to explore original research articles published in English language in the timeframe 2019–2021. Result: It evaluates the effects of Coronavirus Disease 2019 on oral health. Conclusion: This review article illustrates that patients who have survived the adverse oral effects of Coronavirus Disease 2019 and its treatments may have lasting symptoms that require further care.**

Keywords: **Viral infection; Oral lesions; Oral manifestations, COVID-19, Pandemic, dental issues.**

I. INTRODUCTION

On December 31, 2019, the WHO Regional Office in China became aware of a type of respiratory infection of unknown origin in Wuhan City, China. In the beginning of 2020, the Chinese authorities made an announcement that they had found a new virus which was responsible for these cases [1]. According to the Saudi Ministry of Health (MOH), coronaviruses are defined as "a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV)". In 2002, SARS-CoV originally transferred from civettictis civetta cats to individuals in China, and in 2012 in Saudi Arabia MERS-CoV was transmitted from Arabian camels to people. Coronavirus Disease 2019 (COVID-19) is believed to have its origins in the animal and seafood markets of Wuhan, China. Two modes of SARS-CoV-2 transmission have been identified: indirect and direct transmission. Direct transmission involves coming into contact with an infected person's bodily fluids, salivary or respiratory droplets, and other fluids including tears, urine, faeces, and semen. [2] There are respiratory and extra-respiratory manifestations of COVID-19. Commonly reported respiratory symptoms are cough, fever, and dyspnea [3]. Other symptoms include headaches [4,5,6], associated myofascial pain [7,8,9], oral mucosal lesions such as ulcers [10,11,12], and neurological dysfunctions, such as burning sensation [13,14,15], vesicles [16,17], ageusia [17,18,19], anosmia [18,19, 21] and xerostomia [22,23, 24].

Over the previous year, COVID-19 has resulted in 37 million cases and over one million deaths globally (WHO, 2020). In Saudi Arabia, there have been 492,785 confirmed cases and 7,876 deaths (Saudi, MOH). Several studies have shown a link between oral health and systemic disease, including respiratory diseases, cardiovascular disease, systemic infections, and pregnancy outcomes [25,26].

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The oral cavity is a potential source for respiratory pathogens, containing over 700 bacterial species or phylotypes [27]. Yun Feng et al. found that severe cases of COVID-19 were significantly associated with secondary bacterial infections [28]. Furthermore, a number of trials have linked the severity of COVID-19 to a high viral load of SARS-CoV-2 in the mouth and nose [29,30].

Generally, COVID-19 has a multidirectional effect on oral health, both immune related and with an indirect effect. COVID-19 medications can also cause side effects in oral health; however, the advantages outweigh the disadvantages [31]. As an effect of the intense use of medication, some patients who have fully recovered from COVID-19 may experience oral problems [32]. COVID-19 patients in intensive care units undergo external ventilation, intubation, tracheostomy, mouth breathing, and hypo salivation, leading to subsequent complications to oral health [26].

In theory, there may be a connection between expression of the epithelium and ACE2 protein localization in the nasopharynx and oral and nasal mucosa. This is because the ACE2 protein is a known SARS-CoV-2 functional receptor [31]. SARS-CoV-2 has distinct mucotropic and neurotopic functions and may affect taste and smell, salivary gland function, oral mucosa integrity, and microbiota balance [33]. A severe infection of COVID-19 combined with therapeutic actions may have an adverse effect on oral health, leading to potential fungal infection, gingivitis, ulceration, and xerostomia due to weakened oral mucosa or body defense system. Patients who have recovered from COVID-19 should undergo close observation of their oral condition, distinctly when moving from emergency facilities to homes or other health services [34]. The aim of this literature review is to draw attention to the impact of Covid-19 on oral health built on accessible data to date.

II. METHODS

This research, "The Impact of Coronavirus Disease 2019 (COVID-19) on Oral Health", presents an extensive and pervasive search of the relevant literature. The PubMed Medline database was used explore original research articles published in English in the timeframe 2019–2021. Review articles were not included. Article selection and retrieval is presented in Figure 1, with the following subthemes: the role of COVID-19 in oral lesions, the role of COVID-19 in dental status, the role of COVID-19 in salivary glands, the role of COVID-19 in the periodontium, the role of COVID-19 medications in the mouth, and the monitoring of oral health during the pandemic. The themes discuss the occurrence and prevalence of COVID-19 in addition to its effects towards oral health.

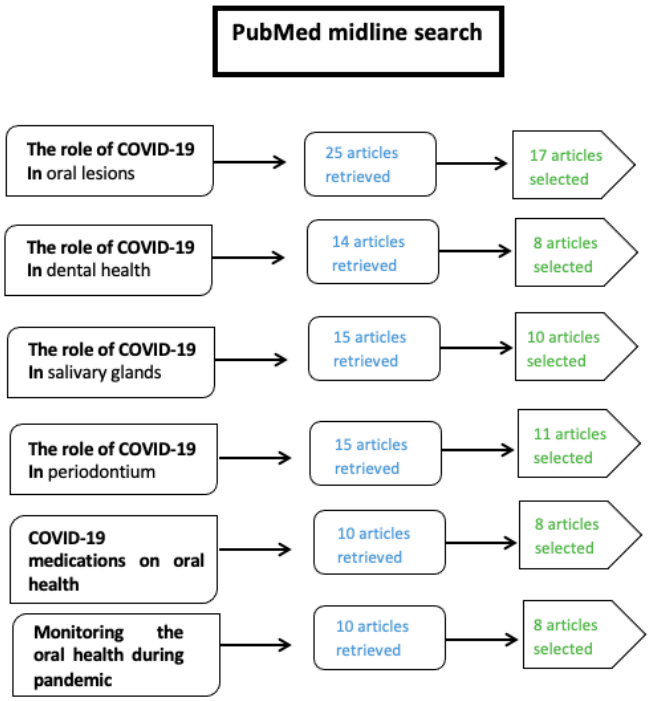

Figure 1: Flow chart identifying the themes of individual searches and the numbers of articles retrieved.

III. DISCUSSION

Oral manifestations of COVID-19

The American Dental Association (ADA) examined the link between COVID-19 infection and negative outcomes to oral health. The pathology of viral infection has been linked to the immune reaction of the host and the consequences of viral invasion, such as the destruction of cells or viral antigens. Viral infections disrupt epithelial cells of the oral mucosa and trigger abrupt onset local inflammatory reactions and solitary or multiple ulcerations or blisters [35]. In SARS-CoV-2, damage to the epithelium can result in other similar pathogenic effects to oral tissues. For example, oral ulceration, tongue fissures, the formation of vesicles, papules, macules, plaque, oral pigmentation, petechiae, swelling, erythema, atypical sweet syndrome, Melkerson-Rosenthal syndrome, and Kawasaki-like angular cheilitis [36,37,38]. Fidan [39] et al. found that the most frequently detected oral manifestation amongst COVID-19 patients is an ulcer (54.1%); followed by aphthous-like ulcer, erythema, lichen planus which revealed around 37 %, 26 %, and 16 %, respectively. Similarly, Favia [40] et al., found that the most detected lesions in COVID-19 patients were ulcers (52.8%). Different types of candidiasis were also diagnosed in a sample of 28 patients.

Haleapas [41] et al. discovered that, in children who have SARS-CoV-2 antibodies, common symptoms of multisystem inflammatory syndrome include strawberry tongue and fissured lips. 48.9% of pediatric patients with COVID-19 had swollen or red lips, with only 10.6% having strawberry tongue. Systemic rash was significantly associated with oropharyngeal or oral findings (P = .04). In terms of the sites involved, they are tongue, labial mucosa, palate, gingiva, buccal mucosa, oropharynx, and tonsils, which represent 38%, 26%, 22%, 8%, 5%, 4%, 1%, respectively [36]. Also reported have been oral ulcers, petechiae, and red macules on the palate [12,13,42, 43], as well as the tongue, lips, and buccal mucosa [40].

Oral lesions were evenly split across genders (51% male and 49% female), with an increase in age correlating with a higher severity of COVID-19 and severe oral lesions [37]. The histological findings show that there is chance that the oral cavity has a relationship with COVID-19 related vascular haematalogic damage. The pathogenesis of COVID-19 related oral mucosal lesions are related to lymphocytic infiltration and Langerhans cells in the subcutaneous junction vasculature; the virus can also induce keratinocyte destruction [44]. Research has found predisposing factors responsible for oral lesion onset in COVID-19 patients, such as oral hygiene being neglected, anxiety, stress, infection, vasculitis, immune suppressant conditions and medications, and inflammatory reaction secondary to COVID-19 [36,45].

Research has reported that COVID-19 has psychologically impacted the global community and led to oral ulcerations as a result of stress [46,47, 48]. Yet it is still unclear whether such lesions specifically result from COVID-19, the stress of the disease, or its treatments. Thus, additional research is required to obtain a better understanding of the pathogenesis of these lesions [36]. Tongue lesions associated with COIVD-19 could be the result of viral activity on the epithelial mucosa of the tongue and/or immune suppression which results in the accumulation of pathogens such as Candida albicans. The management of COVID-19-induced oral mucosal lesions includes mouthwashes, systemic antibiotics, systemic or topical corticosteroids, and antivirals [44,45].

Dental Health

After the first lockdowns there was more advanced gum disease and higher incidence of tooth decay. People began to skip twice-daily tooth brushing, eating between meals in the home and avoiding going to the dentist. President of FDI World Dental Federation [49], Dr Gerhard Konrad Seeberger, stated that “Restrictions have certainly played a part in oral health hesitancy, but they don’t tell the whole story”. Brondani et al. revealed that the frequency of cleaning teeth, using dental services, and the perception of needing dental treatment declined significantly during the pandemic. Dr Vanishree MK, stated that “Dental caries that could have been treated with a simple restoration have now gone to the stage of apical periodontitis and abscesses, which call for more sophisticated treatment,” and that “Patients should set aside their fear and not postpone essential, routine dental treatment” [49]. Depression may also affect oral health, including tooth loss and dental decay, leading to lower quality of life [50]. Furthermore, Zhang [51] et al., reported a significant higher prevalence between psychological emotions and oral health. The frequency of toothbrushing, use of dental services, and self-perceived need for dental treatment decreased significantly during the pandemic.

Alshammari et al. reported that over 30% of patients suffer from bone and joint diseases, and that patients suffering from hypertension and more than one chronic disease are neglecting their oral hygiene. In hypertensive patients, for example, poor oral hygiene may interfere with and worsen the regulation of blood pressure. Furthermore, 90% of the respondents suffering from thyroid and blood disorders, despite seeming to have decent brushing habits before the onset of the pandemic, reported that their oral-health habits had worsened during the pandemic [52, 53]. Moreover, Samuel [54] et al. found that during the COVID-19 pandemic preschool children had a high dental pain score as a result of decayed teeth; they also has dmft >5 which can be explained by greater parental distress and fear of COVID-19 among caregivers.

Salivary glands

The salivary glands are known to be a major source of the virus in saliva . Xerostomia is the cause of a primary undesirable effect of COVID-19 on oral condition, possibly as a direct result of SARS-CoV-2 on the salivary glands [23]. Research conducted on rhesus macaques discovered rapid infection of SARS-CoV-2 in the salivary glands, which indicates that they are early proliferation sites for coronaviruses[55], as reported in several studies [56,57,58,59,60,61,62].

Lechian et al. reported three patients in France who had parotitis resulting from COVID-19. Magnetic resonance imaging (MRI) was conducted which illustrated lymphadenitis in the parotid glands. The patients obtained 1 g of acetaminophen, three to four times per day for two weeks to reduce the symptoms of COVID-19 [57]. Intraparotid adenitis is different from primary diffuse parotitis, as found by Capaccio in a unique case of COVID-19. This case involved a healthy man, aged 26, who developed left parotid swelling, which was painful but did not have purulent discharge. Blood assays showed small increases in normal white blood cell count and reactive C-protein (8.9 mg/L).

The ultrasonography revealed that the structure of the hypoechoic parotid gland was diffuse and enlarged, with an increase in vascularisation - no stones or salivary duct enlargement were found [58]. Furthermore, Alexander et al. found a case of parotitis and submandibular gland sialadenitis, which is potentially an early sign of COVID-19 [63].

Periodontium

Studies have acknowledged a possible link between periodontitis and different systemic diseases. There is a need to review this link in the COVID-19 era. Periodontal disease is comprised of a group of inflammatory conditions of the teeth supportive tissues which are caused by the Carranza bacteria. Pro-inflammatory cytokines contribute to bacterial stimulation and tissue destruction. Furthermore, these cytokines determine the association between periodontitis and systemic illness.

Sahni et al reported a connection between COVID-19 and periodontal disease via cytokines storms. Therefore, patients with periodontitis have a high risk of exhibiting adverse outcomes to COVID-19 [64]. Cytokine release in gingival crevicular fluid mixes with saliva, and during aspiration can induce lung infection or inflammation [65]. Moreover, bacterial exchange between mouth and lungs likely increases respiratory infection risk [66].

Zheng [67] et al. reported that the incidence of microbial infections, particularly bacteria, could be prevalent in advance cases of COVID-19, and that this infection may lead to the replacing of the original viral infection. Zhou [68] et al. also revealed that secondary bacterial infection was the cause of mortality in fifty percent of patients with advance COVID-19.

Research has detailed the association between comorbidities such as chronic obstructive pulmonary disease, diabetes, hypertension, cardiovascular and cerebrovascular diseases, and oral biofilm dysbiosis in periodontal disease [69,70]. The link between periodontitis and COVID-19 are therefore a key to understand and acknowledge. Viruses thrive in the environment of a periodontal pocket [71]. Studies have also suggested that microbes of SARS-CoV-2 could be accumulates in the periodontal pockets as a source of infection [72,73].

Gupta [74] et al. studied 33 COVID-19 patients to determine if there was any evidence of gingival crevicular fluid (GCF). Therefore, surgical, and non-surgical periodontal therapy as well as emphasising oral hygiene could minimise the systemic spread of viral pathogens.

Medications of COVID-19 on Oral Health

COVID-19 medications can cause side effects, though the advantages outweigh the disadvantages. The effect of intense medication, even in patients who fully recovered from COVID-19, may lead to issues with saliva secretion, oral soft tissues, oral sensations. Based on WHO recommendations, COVID-19 treatments are currently going through clinical tests.

These medications may significantly affect the oral cavity [75] and involve remdesivir chloroquine/hydroxychloroquine, interferon-β, a combination of ritonavir and lopinavir, and azithromycin [76,77]. Chloroquine/hydroxychloroquine is established for treating malaria and is known to induce specific diseases of the autoimmune system which can lead to oral disease, especially allergic lichenoid reaction and xerostomia [78].

Combined ritonavir ad lopinavir may cause mouth ulcers, stomatitis, and dry mouth [79]. Interferons are well reported and can result in oral thrush [80]. Also, azithromycin which is a common antibiotic, recently under investigation for its therapeutic effect against COVID-19 and it has succeeded to show no oral effects [81].

Monitoring oral health

The oral cavity reflects overall body health. Hence, neglecting oral hygiene increases the transmission of microbes between the mouth and the respiratory system, therefore increasing post-viral bacterial complications and respiratory infections [82, 83].

Hany [84] et al. reported that the delayed recovery period of 6 weeks was significantly higher where there was a poor state of oral health (40.6%) ($p < 0.001$) and the recovery period of 2 weeks was significantly hastened in those who possessed good oral health (82.1%) ($p < 0.001$). These findings show that oral health impacts upon COVID-19 severity. This agrees with other research which implicates the role of oral health in secondary viral or bacterial respiratory infections [82, 84]. During the pandemic, Peloso [85] et al. performed an assessment of the degree of anxiety and concern in regard to dental appointments. Faris [86] et al. found that during the pandemic mothers were less likely to bring their child to a dental appointment (except for emergencies) as they had anxieties and concerns about contamination. For patients concerned about dental appointments, there is a need for them to be encouraged to return and for any misinformation to be dealt with. To prevent the progression of dental disease, control measures are required to continue with routine dental care.

IV. CONCLUSION

This review evaluated the effects of COVID-19 on oral health. An evaluation was performed of the cohort literature to assemble information regarding the impact the virus on oral health. The general consensus from the aggregated information indicates that COVID-19 has a no impact on general mouth condition. The direct effects of the COVID-19 crisis on affected patients, combined with exacerbation of existing oral health challenges, reinforces the need to address these concerns. Patients who have survived the adverse oral effects of COVID-19 and its treatments may have lasting symptoms that require further care. Moreover, postponed operative and preventive dental care should be resumed with attention and caution paid towards patient concerns about the safety of treatment during the current pandemic.

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