DERLEME / *Review*

Novel Coronavirus Disease (COVID-19) and Dental Public Health

Yeni Koronavirus Hastalığı (COVID-19) ve Toplum Ağız-Diş Sağlığı

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ABSTRACT

Dental public health prioritizes protection and it is important to handle infectious diseases in terms of oral health, which will be addressed specifically for the 2019 novel coronavirus in this review. In severe COVID-19 infection, damaged immune system might facilitate the transmission of virus from oral cavity, and could potentially aggravate existing autoimmune and inflammatory conditions within the oropharyngeal area. Besides, intense pharmacotherapy might be related with problems in soft tissues, saliva production, and neurological-based oral sensations, also. Moreover, delayed non-emergent dental service during pandemics would have a potential impact on the experience and rehabilitation of patients with oral diseases. Although there are many grey sides still existing in the relation of COVID-19 and oral health, close monitoring of the patients during the illness and recovery period is so important, in terms of dental public health for the possible short-mid-long-term effects, as well as primary prevention measures.

Keywords: *coronavirus; oral health; public health; infections; therapy*

ÖZ

Toplum ağız-diş sağlığı korunmaya öncelik verir, ağız sağlığı açısından bulaşıcı hastalıkların değerlendirilmesi önemlidir ve bu derlemede 2019 yeni koronavirüs özelinde ele alınacaktır. Şiddetli COVID-19 enfeksiyonunda, sitokin fırtınası nedeniyle zarar görmüş bağışıklık sistemi, virüsün ağız boşluğundan bulaşmasını kolaylaştırabilir ve orofaringeal alandaki mevcut otoimmün ve enflamatuar durumları ağırlaştırabilir Ayrıca, yoğun farmakoterapi yumuşak dokulardaki, tükürük üretimindeki ve nörolojik temelli oral duyumlardaki problemler ile de ilişkili olabilir. Bunun yanı sıra, pandemi sırasında acil olmayan dişhekimliği hizmetlerinin gecikmesinin, ağız hastalıkları olan hastaların deneyimi, bilişi ve rehabilitasyonu üzerinde de potansiyel bir etkisi olacaktır. COVID-19 ve ağız sağlığı ilişkisinde hala çok sayıda bilinmeyen yön olmasına rağmen, hastaların hastalık ve iyileşme döneminde yakından takip edilmesi, toplum ağız-diş sağlığı kapsamında birincil önleme tedbirlerinin yanı sıra kısa-orta-uzun dönem olası etkileri açısından çok önemlidir.

Anahtar Kelimeler: *koronavirus; ağız sağlığı; halk sağlığı; enfeksiyonlar; tedavi*

1. Introduction

One of the non-communicable chronic diseases (NCDs) is 'oral health problems', and it has common risk factors as free sugar consumption, tobacco use, harmful alcohol consumption and some social determinants of health like other NCDs. Although largely preventable, oral diseases are a global public health problem and persist with high prevalence, particularly in low/middle-income countries (1, 2).

Dental Public Health (DPH) is *the science and art of preventing and controlling dental diseases and promoting dental health through organized community efforts* (3). This is a branch of dentistry related to clinical epidemiology, risk assessment in patient care, social justice, dental care programming, public policy development and advocacy (4, 5). In this extent, DPH is one of the practice area of public health and in line with a whole of public health philosophy that *promotes and protects the health of people and the communities,* and *try to prevent people from getting sick or injured,* and *promote wellness by encouraging healthy behaviors* (6). DPH comprises preventive dentistry that corresponds primary health services.

Dental public health prioritizes protection and it is important to handle infectious diseases in terms of oral health, which will be addressed

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specifically for the novel coronavirus in this review. Various infectious diseases and/or agents cause oral lesions including candidiasis, *herpes simplex*, *varicella zoster*, syphilis, *HPV*, *HIV*, hepatitis and tuberculosis (7). The importance of these conditions comes from their potential transmissibility and the possible place of first manifestations of the diseases that is oral cavity (8). Encountering the possibility of the symptoms of some infectious diseases in the oral cavity like measles, mumps, tonsillitis, viral hepatitis, and AIDS requires the dentist to be careful for consulting medical treatment before dental operation and also for the use of appropriate personal protective equipment against the cross-infections, which makes the dental team under risk more than the other professions.

2. A brief explanation of novel coronavirus infection (COVID-19)

Infectious diseases are transmissible and may have potential for global outbreaks. In this point of view, emerging infectious diseases (EID) definition comes up. EID is a disease newly recognized in a population or have existed but recently and rapidly increased in incidence or geographic range (9, 10). In this frame as an EID, 2019 novel coronavirus (used as 2019-nCoV/ SARS-CoV-2/ COVID-19) had been first diagnosed in China and spread all over the world in a short period of time (11, 12). COVID-19 was declared a controllable pandemic disease by World Health Organization on March 11, 2020 (13). In Turkey, the first confirmed case was announced on 11th of March 2020 and until 23.11.2020, according to the Ministry of Health, there were a total of 453.535 confirmed patients (14).

Millions of individuals, especially elder people and patients with comorbidities have been affected by COVID-19. Hypertension, chronic respiratory system diseases, diabetes and cardiopathies were highlighted as potential risk factors to severe outcomes from COVID-19 (15). It has detected not only in medically compromised people but also in healthy young individuals (16).

The virus mainly spread from person-to-person who are in close contact with one another. The main transmission route is respiratory droplets produced when an infected person coughs, sneezes, and talks even not showing any symptoms. Another transmission possibility is contact transmission, which first touching a surface or an object contaminated by the virus and then touching own mouth, nose, or eyes. However, this has not considered as the main route of transmission according to Centers for Disease Control and Prevention (17). The possibility of fecal–oral transmission of COVID-19 had been also reported (18).

COVID-19 mainly effects the respiratory, gastrointestinal, and central nervous system of humans and mammals (19) and causes high rates of both morbidity and mortality (20). Patients infected with COVID-19 had a wide range of symptoms from mild to severe as fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea (21). Digestive symptoms, such as diarrhea, might be a presenting feature of COVID-19 that arise before respiratory symptoms, and on rare occasions the only presenting symptom (22).

3. COVID-19 infection and treatments & oral health in terms of DPH

3.1. COVID-19 infection and oral health

Angiotensin-converting-enzyme II (ACE2) expressing cells were reported as the target cells, which are the host cell receptors and plays a crucial role in the entry of virus into the cell lead to COVID-19 infection. Among children, COVID-19 was observed less than the older people and with light symptoms. It is thought that the immaturity of ACE2 receptors in children was the cause of this situation (23). Highly ACE2 expressing organs (lungs, colon, myocardial cells, kidney, etc.) were stated at high risk for COVID-19 (24, 25). There is a lack of data about the relationship between COVID-19 and oral diseases, yet. However, the results of a study from China demonstrated that the ACE2 expressed on the mucosa of oral cavity and highly enriched in epithelial cells of tongue (25) and

salivary glands (26), and the basic mechanism that the oral cavity is a potential high risk for COVID-19 infection susceptibility was explained by this way. Except that, COVID-19 has different routes to be presented in saliva: from the lower and upper respiratory tract with the liquid droplet, from blood through the gingival crevicular fluid and from salivary gland with release from salivary ducts (27). Besides, saliva may serve as a gatekeeper, and prevent pathogens from spreading to the gastrointestinal and respiratory tract (28). So, the importance of oral cavity specifically for the COVID-19 infection is obvious. Though, the overall impact of COVID-19 on oral health seems to be multi-directional.

On the other hand, it is thought that coronavirus may compromise the immune mechanisms in humans. "*Cytokine storm*" is a general term for large amounts of pro-inflammatory cytokines and chemokine release in response to infection (16, 29). In other words, "*hit and run*" virus alters the immune system, causes distinct changes in response reactions that can turn against the host leading to autoimmune damage, particularly of connective tissue of lungs. This immune response may make even a healthy person prone to extremely serious complications, primarily associated with lower respiratory tract (30). Besides, as well as lungs, the damaged immune system might facilitate the transmission of virus from oropharyngeal area, too. Severe COVID-19 acute infection could potentially contribute to negative outcomes with regard to oral health (such as ulcerations, gingivitis) by the cytokine storm as a result of impaired immune system and/or susceptible oral mucosa, and could aggravate existing autoimmune conditions within the oropharyngeal area (30).

COVID-19 may potentially affect the functioning of salivary glands, taste/smell sensations and oral mucosa integrity (27, 30). Due to possible salivary gland hypo-function and dry mouth, the risk of a lot of dental problems like dental caries, dental erosion, opportunistic fungal infections, oral burning sensation, taste disturbances, and halitosis increases (31). Moreover, patients with HIV, under head and neck anticancer therapy, etc. are known to be frequently related with some oral manifestations, having oral bacterial, fungal, viral infections, mucositis, dental cavities, periodontal diseases, that may show increase due to the COVID-19 (32, 33).

COVID-19 infection might have some specific effects on younger and elder population. The elder people have some characteristics different from the younger. Particularly they require high quality of oral care including daily oral hygiene related to their special needs, and they generally use frequent medicine, and oral problems may occur more severely. In this context, COVID-19 infection undergoes more severe among these people (15, 34). Youngers have some other special conditions. In dental formation period, it is known that an infectious disease with high fever could affect the mineralization of teeth and may cause molar-incisor-hypo-mineralization (MIH) -a dental anomaly that make the tooth tend to dental caries (35, 36, 37). In this point, having COVID-19 infection with high fever during the first four years of life, which the permanent first molars and incisors have continued formations, might result with MIH.

Among patients with COVID-19 infection, serum procalcitonin was reported normal, while C-reactive protein (CRP) was reported increased in laboratory findings (23, 38). Reportedly, higher serum C-reactive protein levels decrease with periodontal treatment among patients with atherosclerotic cardiovascular disease (39). Considering the possible long-term continued abnormalities related to COVID-19 (38), and existence of a bi-directional link between periodontal health and these pathologies (cardiovascular disease, diabetes) (40), careful follow-up for dental and periodontal health of recovered people is crucial, due to similar inflammatory patterns.

Cigarette smoking is detrimental to oral health. In smokers, oral mucosa become prone to various infections, as it increases the incidence and severity of oral cancer, periodontal diseases, and tooth loss. Besides, negative impact on patients' response to dental treatment increases (41).

Furthermore, smoking is harmful to immune system and its responsiveness to infections. This situation turns the smokers more vulnerable to infectious diseases, as well as COVID-19. Smokers had higher risk for contact, had more severe symptoms and noted to have higher mortality in the previous MERS-CoV outbreak as an example (42). The additional continuing effect of smoking on COVID-19 infection might increase the possibility of premalignant lesions on the oral mucosa during the illness or recovery period of the infection.

3.2. Treatment of COVID-19 and Oral Health

There are no specific antiviral drugs for COVID-19 treatment at present. All of the drug options come from previous experience treating SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) or some other new influenza viruses (43). "Solidarity", which is one of the largest international randomized trials for COVID-19 treatments that launched by the World Health Organization and partners in over 30 countries showed that all four treatments evaluated (remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon) had little or no effect on overall mortality, initiation of ventilation and duration of hospital stay in hospitalized patients (44).

Anti-viral drugs may be responsible for side effects affecting oral cavity among the other parts of gastrointestinal track, such as stomatitis, ulcers and dry mouth which can result in frequent cases of oral candidiasis (45, 46) (30). Due to the intensified therapeutic methods and/or multi-drug treatments against the virus, some pathological oral conditions could be aggravated, especially those with the etiology of compromised immune and/or defense mechanisms, or related to long-term pharmacotherapies (30). Additionally, some autoimmune and inflammatory conditions like pemphigus, lichen planus, pemphigoid, lupus erythematosus may potentially exacerbate in COVID-19-positive patients, since systemic and topical steroids are contraindicated in this infection (28, 31). Exacerbation of these diseases could also exacerbate mouth lesions that occur with them.

As a consequence of intense pharmacotherapy, some of the patients may suffer from dental/oral problem associated with soft tissues, salivary gland function, saliva production, dry mouth, and neurological-based oral sensations. During COVID-19 symptomatic period and especially during recovery phase, it is likely that will need an adjunct antifungal and/or antimicrobial treatment for post-acute care to recuperate from primary and concomitant infection, supported by cytoprotective topical measures (30). Close monitoring of their oral health is need to be observed alongside, the dental treatment if necessary, that was postponed due to emergency measures introduced (27).

Oral health had been found to deteriorate, especially in case of those staying in intensive care units, as a direct result of life-saving therapies in severely ill hospitalized patients. Since treatment priority is given to advanced medical care in hospitalized COVID-19 patients, mouth care usually neglected, that might cause complications, affecting also the lower respiratory track similar to aspiration pneumonia. In terms of intubation, tracheostomy, and external ventilation mouth breathing and hyposalivation may occur and lead to rapid oral health problems (30, 47). During the period of intense hospitalization and after discharge, the side/adverse effects of experimental drugs used for treatment on oral health should be evaluated as well as the complex pharmacotherapy.

4. COVID-19 and dental settings under the DPH

During the pandemic, dental and health organizations have issued recommendations to postpone all elective dental treatments and non-essential procedures and limit services only to urgent and emergency visits. Delay of non-emergent dental service will have a potential impact on the experience, cognition, treatment and rehabilitation of patients with oral diseases (48). Negative impact on dental treatment of patients, such as prolonged orthodontic treatment time (49); possible negative effects of postponed permanent restorations, root canal fillings or

denture prosthesis for dental health alongside the life quality of patient may occur. Besides the anxiety related with postponed possible negative effects of elective dental treatments, fear from the possibility of COVID-19 transmission during the dental treatment among patients might be a great problem, also. These both, could overlap and might have a negative effect on the psychological status of patient. Correspondingly, psychological status of patients (e.g. fear of infection) would affect the progression of some oral mucosa diseases such as recurrent aphthous ulcer, oral lichen planus, and burning mouth syndrome (50). According to Qu and Zhou, in various studies, the oral psychosomatic diseases like oral mucosal disease, temporomandibular joint disease and bruxism were found closely related to the patients' psychological status. Patients with these disorders might be more susceptible to the impact of stress events, and need to be paid more attention by dental specialists (48). Dentist usually plays not only the role of expert for professional guidance in dentistry, but also giving psychological counseling for patients. Therefore, telecommunication or tele-dentistry (that is keeping direct contact with the patient by phone or text messages (51) recommended to be used prior the dental treatment to evaluate the needs of the patient and to minimize the risk of infection during this period (52). When possible, dentist should offer advice, prescribe medication for analgesia and/or antimicrobial and postpone the visit of the patient to the office (51). Dental services via a web-based and/or mobile based network, and free online professional consultations are used for determining whether a condition was necessary for emergency treatment, and providing home dental and oral care guidance (49). The online consultation, being a subset of tele-dentistry, would provide education and preventive care to dental patients and has the potential to identify high-risk populations during pandemic conditions (53).

Beyond all above-mentioned, oral mucosa is highly susceptible to COVID-19 infection since saliva can host several viruses including COVID-19, and it is a source of infected aerosol spread through saliva, is unavoidable in a dental office (54). Exposure to viral or bacterial infections in dental settings could be transmitted through different routes: direct contact with blood, oral fluids, or other infected materials; contact of conjunctival, nasal, or oral mucosa with droplets containing microorganisms from an infected person scattered by coughing, sneezing, or talking or inhalation of airborne microorganisms which could remain suspended in the air for long periods (55); or possible aerosol transmissions (11). There is another way of transmission as indirect contact with contaminated equipment, and environmental surfaces (55). Transmission directly or indirectly through saliva and aerosols when aerosol-generating medical procedures (AGMPs) are performed, was also reported (17, 19, 56). A great risk in dental practice is obvious due to the main routes for COVID-19 are close proximity to a patient's respiratory tract or contaminated surfaces with droplets (17, 56). Patients have potential to transmit as well as acquire the disease and a cross-contamination concern between the patient, dentist and dental staff has been exhibited (55). As it should always be, during the pandemic period, keeping healthcare providers safe, healthy, and available to work is critical in the purpose and scope of DPH. The protective approach is reciprocal and crucial for both the caregiver (dentist/other dental staff) and the caretaker (patient).

5. Conclusion

Under the light of all information mentioned above, in order to keep and protect individuals oral and general health, the following suggestions have been recommended related to oral health and COVID-19 from DPH perspective:

It is very important to continue the routine oral health care during pandemic period for healthy people. It should be remembered that daily tooth brushing twice, dental floss use and use of mouth-rinse are crucial. According to WHO, besides, protection from COVID-19 infection necessitates obeying the social-distance rules, hand hygiene, wearing a mask, avoiding crowds, keeping rooms well ventilated, coughing into a bent elbow or

tissue. Mask type was recommended depending on how much virus circulating around, where the person goes and who the person is. Wearing fabric mask if not in a particular risk group, while a medical/surgical mask if being over 60, having underlying medical conditions, feeling unwell and/or looking after an ill family member was recommended (57).

Being infected with COVID-19 should not change the routine daily oral care to avoid any additional inflammation and/or infection sourced from the mouth. If possible, patient should continue oral health measures by him/herself, if not by the nurse or the caregiver in the hospitalization period.

Dentists should also maintain the social distance, hand cleaning routinely. Moreover, they should clean and disinfect frequently touched surfaces, and use appropriate PPE when (17) providing any care for a suspected or confirmed COVID-19 patient (56, 58). However, in order to protect both sides (patient and dentist), all patients should be considered as infected. Dentists should remember that a substantial number of COVID-19 infected individuals (including children) do not show any signs and symptoms, and could transmit the virus. In addition, a pathology in the oral mucosa should bring in mind a possible COVID-19 related lesion and dentist should carefully examine. On the other hand, a dentist is responsible in reminding to the patient of the relation of infectious diseases with mouth and oral health.

Although there are highly not known sides of COVID-19 related with dental oral health, close monitoring of the patients during the illness and recovery period is so important in terms of dental public health for the possible short-mid-long-term effects.

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REFERENCES

1. Peres M A, Macpherson L M D, Weyant R J, Daly B, Venturelli R, Mathur M R, et al. Oral diseases: a global public health challenge. Lancet 2019; 394(10194): 249-60.

2. Kassebaum N J, Smith A G C, Bernabe E, Fleming T D, Reynolds A E, Vos T, et al. Global, Regional, and National Prevalence, Incidence, and Disability-Adjusted Life Years for Oral Conditions for 195 Countries, 1990-2015: A Systematic Analysis for the Global Burden of Diseases, Injuries, and Risk Factors. J Dent Res 2017; 96(4): 380-7.

3. Amini H, Shenkin J D, Chi D L. Dental Public Health Issues in Pediatric Dentistry. In: Nowak AJ, Christensen JR, Mabry TR, Townsend JA, Wells MH, editors. Pediatric Dentistry Infancy Through Adolescence. 6 ed. Philadelphia: Elsevier; 2019. p. 159-68.e2.

4. McLaren L, Figueiredo R. Special section on dental public health: A collaboration between the Canadian Journal of Public Health and the Canadian Association of Public Health Dentistry. Can J Public Health 2017; 108(3): e219-e20.

5. Brondani M A, Pattanaporn K, Aleksejuniene J. How can dental public health competencies be addressed at the undergraduate level? J Public Health Dent 2015; 75(1): 49-57.

6. APHA. American Public Health Association. What is public helath? 2020 [accessed 23 November 2020].

7. Cowan G M, Lockey R F. Oral manifestations of allergic, infectious, and immune-mediated disease. J Allergy Clin Immunol Pract 2014; 2(6): 686-96.

8. Anders P L, Drinnan A J, Thines T J. Infectious diseases and the dental office. N Y State Dent J 1998; 64(4): 29-34.

9. McArthur D B. Emerging Infectious Diseases. Nurs Clin North Am 2019; 54(2): 297-311.

10. Petersen E, Petrosillo N, Koopmans M. Emerging infections-an increasingly important topic: review by the Emerging Infections Task Force. Clin Microbiol Infect 2018; 24(4): 369-75.

11. Ge Z Y, Yang L M, Xia J J, Fu X H, Zhang Y Z. Possible aerosol transmission of COVID-19 and special precautions in dentistry. J Zhejiang Univ Sci B 2020; 21(5): 361-8.

12. Gralinski L E, Menachery V D. Return of the Coronavirus: 2019-nCoV. Viruses 2020; 12(2).

13. WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 2020 [accessed 23 November 2020].

14. TC Saglik Bakanligi. Türkiye□deki Güncel Durum 2020 [accessed 23 November 2020].

15. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al.

Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis 2020; 94: 91-5.

16. Mehta P, McAuley D F, Brown M, Sanchez E, Tattersall R S, Manson J J, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020; 395(10229): 1033-4.

17. CDC. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID 19) How it Spreads 2020 [accessed 23 November 2020].

18. Yeo C, Kaushal S, Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? Lancet Gastroenterol Hepatol 2020; 5(4): 335-7.

19. Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int J Oral Sci 2020; 12(1): 9.

20. Lipsitch M, Swerdlow D L, Finelli L. Defining the Epidemiology of Covid-19 - Studies Needed. N Engl J Med 2020; 382(13): 1194-6.

21. CDC. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID 19) Symptoms 2020 [accessed 23 November 2020].

22. Lee I C, Huo T I, Huang Y H. Gastrointestinal and liver manifestations in patients with COVID-19. J Chin Med Assoc 2020; 83(6): 521-3.

23. Jin Y-H, Cai L, Cheng Z-S, Cheng H, Deng T, Fan Y-P, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Military Medical Research 2020; 7(1): 4.

24. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020; 14(2): 185-92.

25. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020; 12(1): 8.

26. Xu J, Li Y, Gan Fw, Du Y, Yao Y. Salivary Glands: Potential Reservoirs for COVID-19 Asymptomatic Infection. J Dent Res 2020: 22034520918518.

27. Sabino-Silva R, Jardim A C G, Siqueira W L. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. Clin Oral Investig 2020; 24(4): 1619-21.

28. Li Y, Ren B, Peng X, Hu T, Li J, Gong T, et al. Saliva is a non-negligible factor in the spread of COVID-19. Mol Oral Microbiol 2020.

29. Coperchini F, Chiovato L, Croce L, Magri F, Rotondi M. The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor Rev 2020; 53: 25-32.

30. Dziedzic A, Wojtyczka R. The impact of coronavirus infectious disease 19 (COVID-19) on oral health. Oral Dis 2020; 00: 1-4.

31. Pedersen A M L, Sorensen C E, Proctor G B, Carpenter G H, Ekstrom J. Salivary secretion in health and disease. J Oral Rehabil 2018; 45(9): 730-46.

32. Sroussi H Y, Epstein J B, Bensadoun R J, Saunders D P, Lalla R V, Migliorati C A, et al. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. Cancer Med 2017; 6(12): 2918-31.

33. Heron S E, Elahi S. HIV Infection and Compromised Mucosal Immunity: Oral Manifestations and Systemic Inflammation. Front Immunol 2017; 8: 241.

34. Astvaldsdottir A, Bostrom A M, Davidson T, Gabre P, Gahnberg L, Sandborgh Englund G, et al. Oral health and dental care of older persons-A systematic map of systematic reviews. Gerodontology 2018; 35(4): 290-304.

35. Ghanim A, Manton D, Bailey D, Marino R, Morgan M. Risk factors in the occurrence of molar-incisor hypomineralization amongst a group of Iraqi children. Int J Paediatr Dent 2013; 23(3): 197-206.

36. Whatling R, Fearne J M. Molar incisor hypomineralization: a study of aetiological factors in a group of UK children. Int J Paediatr Dent 2008; 18(3): 155-62.

37. Tourino L F, Correa-Faria P, Ferreira R C, Bendo C B, Zarzar P M, Vale M P. Association between Molar Incisor Hypomineralization in Schoolchildren and Both Prenatal and Postnatal Factors: A Population-Based Study. PLoS One 2016; 11(6): e0156332.

38. Bansal M. Cardiovascular disease and COVID-19. Diabetes Metab Syndr 2020; 14(3): 247-50.

39. Roca-Millan E, Gonzalez-Navarro B, Sabater-Recolons M M, Mari-Roig A, Jane-Salas E, Lopez-Lopez J. Periodontal treatment on patients with cardiovascular disease: Systematic review and meta-analysis. Med Oral Patol Oral Cir Bucal 2018; 23(6): e681-e90.

40. Liccardo D, Cannavo A, Spagnuolo G, Ferrara N, Cittadini A, Rengo C, et al. Periodontal Disease: A Risk Factor for Diabetes and Cardiovascular Disease. Int J Mol Sci 2019; 20(6).

41. Lee J, Taneja V, Vassallo R. Cigarette smoking and inflammation: cellular and molecular mechanisms. J Dent Res 2012; 91(2): 142-9.

42. Park J E, Jung S, Kim A, Park J E. MERS transmission and risk factors: a systematic review. BMC Public Health 2018; 18(1): 574.

43. Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). Biosci Trends 2020; 14(1): 69-71.

44. WHO. "Solidarity" clinical trial for COVID-19 treatments. 2020. [accessed 23 November 2020].

45. Mahase E. Covid-19: what treatments are being investigated? BMJ 2020; 368: m1252.

46. PubChem Database. Ritonavir 2020 [accessed 23 November 2020]. .

47. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020.

48. Qu X, Zhou X D. [Psychological intervention for patients with oral disease during the pandemic period of COVID-19]. Zhonghua Kou Qiang Yi Xue Za Zhi 2020; 55(4): 235-40.

49. Yang Y, Zhou Y, Liu X, Tan J. Health services provision of 48 public tertiary dental hospitals during the COVID-19 epidemic in China. Clin Oral Investig 2020; 24(5): 1861-4.

50. Lin L, Duan N, Wang X, Song Y, Wang W. Study on the correlation between common diseases of oral mucosa and psychological factors. J Prev Treat Stomatol Dis 2019; 27: 236-40.

51. Hurley S, Neligan M. Preparedness letter for primary dental care.: NHS England and NHS Improvement; 2020. Contract No.: 08.06.2020.

52. Pereira L J, Pereira C V, Murata R M, Pardi V, Pereira-Dourado S M. Biological and social aspects of Coronavirus Disease 2019 (COVID-19) related to oral health. Braz Oral Res 2020; 34: e041.

53. Estai M, Kanagasingam Y, Tennant M, Bunt S. A systematic review of the research evidence for the benefits of teledentistry. J Telemed Telecare 2018; 24(3): 147-56.

54. Baghizadeh Fini M. Oral saliva and COVID-19. Oral Oncol 2020; 108: 104821.

55. Upendran A, Geiger Z. Dental Infection Control. StatPearls. Treasure Island (FL)2020.

56. Lockhart S L, Duggan L V, Wax R S, Saad S, Grocott H P. Personal protective equipment (PPE) for both anesthesiologists and other airway managers: principles and practice during the COVID-19 pandemic. Can J Anaesth 2020; 67: 1005-15.

57. WHO. Coronavirus disease (COVID-19) advice for the public: When and how to use masks. 2020 [accessed 23 November 2020]..

58. Gralton J, Tovey E, McLaws M L, Rawlinson W D. The role of particle size in aerosolised pathogen transmission: a review. J Infect 2011; 62(1): 1-13.