

SARS AND ORAL CAVITY: A CORRELATION AND LIVING SYSTEMATIC REVIEW

Zeba Khalid¹, Aruna Das², Santosh Kumar³, Prabhakar Kumar⁴, Mohammad Zakiuddin⁵

1. Post graduate student, Department of Oral Medicine and Radiology, Azamgarh Dental College, Azamgarh, U.P, India

2. Professor & Head, Department of Oral Medicine and Radiology, Azamgarh Dental College, Azamgarh, U.P, India

3. Reader, Department of Oral Medicine and Radiology, Azamgarh Dental College, Azamgarh, U.P, India

4. Reader, Department of Oral Medicine and Radiology, Azamgarh Dental College, Azamgarh, U.P, India

5. Professor & Head, Department of Physiology, Madhubani Medical College, Madhubani, Bihar, India

ABSTRACT

Background: COVID-19 is an infectious disease caused by the SARS-CoV-2 coronavirus transmitted from person to person via droplets in the air or by contact with contaminated surfaces.

Aims And Objective: To investigate the potential link between SARS-CoV-2 and bacterial load in the mouth and the connection between COVID-19 and oral health.

Methods And Materials: This study systematically reviewed the published literature and the guidelines of international health care institutions on dentistry and COVID-19. We searched PubMed, Web of Science, and SCOPUS electronic databases using MESH terms. The recommendations identified were tested with a convenience sample of experienced practitioners, and a practical step-by-step protocol is presented in this paper.

Result: To the date this paper was drafted, 18 articles were found, of which 9 satisfied our inclusion criteria. As all the nine studies were proposed in a general consensus, any elective non-emergency dental care for patients with suspected or known COVID-19 should be postponed for at least 2 weeks during the COVID-19 pandemic. Only urgent treatment of dental diseases can be performed during the COVID-19 outbreak taking into consideration.

Conclusion: The currently available evidence has not demonstrated a clear and direct relationship between dental treatment or surgery and the possibility of the transmission of COVID-19, there is clearly the potential for transmission. Therefore, following the protective protocols in the COVID-19 crisis is of utmost importance in a dental setting.

Key Words: SARS-CoV-2, pandemic, corona virus, dentistry, transmission, prevention.

INTRODUCTION:

Current point of view:

The present outbreak of the 2019 coronavirus strain (COVID-19) constitutes a public health emergency of global concern. International centres for disease control and prevention are monitoring this infectious disease outbreak.

Epidemiology COVID-19

The etiological agent of the emerging COVID -19 infections referred to as

‘SARS-CoV-2’ has been identified and analysed phylogenetically ¹. Coronavirus SARS-CoV-2 is part of the order Nidovirales, family Coronaviridae, genus - β -CoV, having an RNA genome. Nucleotide sequences of SARS-CoV-2 are similar to other coronaviruses of the same genus responsible for previous emerging human epidemics, having approximately 80% similarity with SARS-CoV and 50% with MERS-CoV ². Phylogenetic analysis indicates the zoonotic origin of SARS-CoV-2 from the bat, via an intermediate

host, most likely pangolin³. Different concentrations of biocidal substances are tested for inactivation of coronaviruses, including ethanol (78-95%), 2-propanol (70-100%), 2-propanol 45% and I-propanol 30%, glutaraldehyde (0.5-2.5%), formaldehyde (0.7-1%), and povidine-iodine (0.23-7.5%). The best results were obtained with ethanol at concentrations of 62-71%, exposed for one minute⁴. The new coronavirus SARS-CoV-2 was first detected in late 2019 and has quickly developed into a global pandemic⁵. On 30th January 2020, World Health Organization identified COVID-19, caused by the virus SARS-CoV-2, to be a global emergency. The risk factors already identified for developing complications from a COVID-19 infection are age, gender and comorbidities such as diabetes, hypertension, obesity and cardiovascular disease. These risk factors however, do not account for the other 52% of deaths arising from COVID-19 is often seemingly healthy individuals. Age is one of the highest risk factors for developing severe symptoms of COVID-19, the disease caused by infection with SARS-CoV-2⁶. Thus, individual over the age of 65 and those living in long term care facilities are especially vulnerable to morbidity and mortality due to infection with SARS-CoV-2. However, persons with chronic lung disease, moderate to severe asthma, severe obesity, diabetes, chronic kidney disease and liver disease are also at high risk for severe COVID-19 symptoms. A recent study lists hypertension, obesity, diabetes as the three major underlying conditions with the most unfavourable outcomes in COVID-19 patients requiring hospitalization⁷. While COVID-19 can affect multiple organs in the body, including the kidneys and liver^{8, 9}, the

main cause of mortality is due to the ability of SARS-CoV-2 to infect the respiratory tract, leading to severe pneumonia. Patients with COVID-19 display symptoms of fever, cough, dyspnoea and other complications associated with acute respiratory distress syndrome (ARDS)¹⁰⁻¹². A salient feature of COVID-19 is its ability to trigger an excessive immune reaction in the host, termed a 'cytokines storm', which causes excessive tissue damage, particularly in the connective tissue of the lungs¹³. The lung pathology of patients who die from COVID-19 pneumonia includes oedema, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration and multinucleated giant cells¹⁴.

The Oral mucosa

The oral mucosa is a mirror of the state of health, representing a natural barrier to infection, an entry gate for a large number of pathogens, a site for microbial multiplication and for initiating disease-specific pathological processes, expressed by lesions, signs and characteristic symptoms for diagnosis. The implication of the current COVID-19 epidemic in oral pathology are still little known, the research in this field being limited by the novelty of the etiological agent and the insufficient observation time since the outbreak of this phenomenon.

Oral health and non-oral systemic diseases

Over the past few years, it has been clear that oral health has a large impact on general health. Several studies suggest that cytokines or microbial products released systemically in response to oral infection

causes inflammation in distant organs, which enhances development of systemic diseases such as Alzheimer's disease, diabetes, atherosclerotic heart disease and cerebrovascular disease¹⁵⁻¹⁸. Conversely, obesity predisposes individuals to oral diseases, especially, gingivitis and periodontitis¹⁹. Furthermore, the oral cavity is a significant reservoir for respiratory pathogens, including chlamydia pneumoniae and patients with periodontal disease are more likely to develop hospital-acquired pneumonia as a complication²⁰⁻²². Several mechanism may explain the ability of oral pathogens to exacerbate lung infection, including aspiration of oral pathogens in to the lower respiratory tract, especially in high risk individuals, modification of mucosal surfaces along the respiratory tract by salivary enzymes, which thereby facilitate colonization, by pathogens, and secretion of pro-inflammatory cytokines during periodontitis which can promote adhesion to lung epithelium and lung colonization by respiratory pathogens^{23, 24}. Improving oral hygiene may thus reduce oropharyngeal colonization and the risk of respiratory complications. It has also been shown that improved oral hygiene and frequent professional oral health care reduces the progression or occurrence of respiratory diseases, particularly in the elderly population and those in intensive care units²⁵. This population is at risk for developing serious complication related to COVID-19^{26, 27}.

Saliva as protective shield against SARS-CoV-2

Hyposalivation as a potential risk factor for a SARS-CoV-2 infection was discussed in an article **published in oral**

diseases. Human saliva is a very complex fluid and plays a crucial role in the prevention of viral infections and protection against them, since it contains a large number of proteins and peptides with antiviral effects. In addition, such proteins have been reported to inhibit the replication of other coronaviruses.

Improved oral hygiene may reduce risk of complications

A study published in the **British Dental Journal** highlighted the importance of improved oral hygiene during a SARS-CoV-2 infection in order to reduce the bacterial load in the mouth and the risk of bacterial superinfection. Those patients who were reported to have a severe form of COVID-19 (20%) had associated higher levels of inflammatory markers and bacteria. Therefore, the author of the study recommended that poor oral hygiene be considered as a risk factor for COVID-19 complications.

AIMS AND OBJECTIVE:

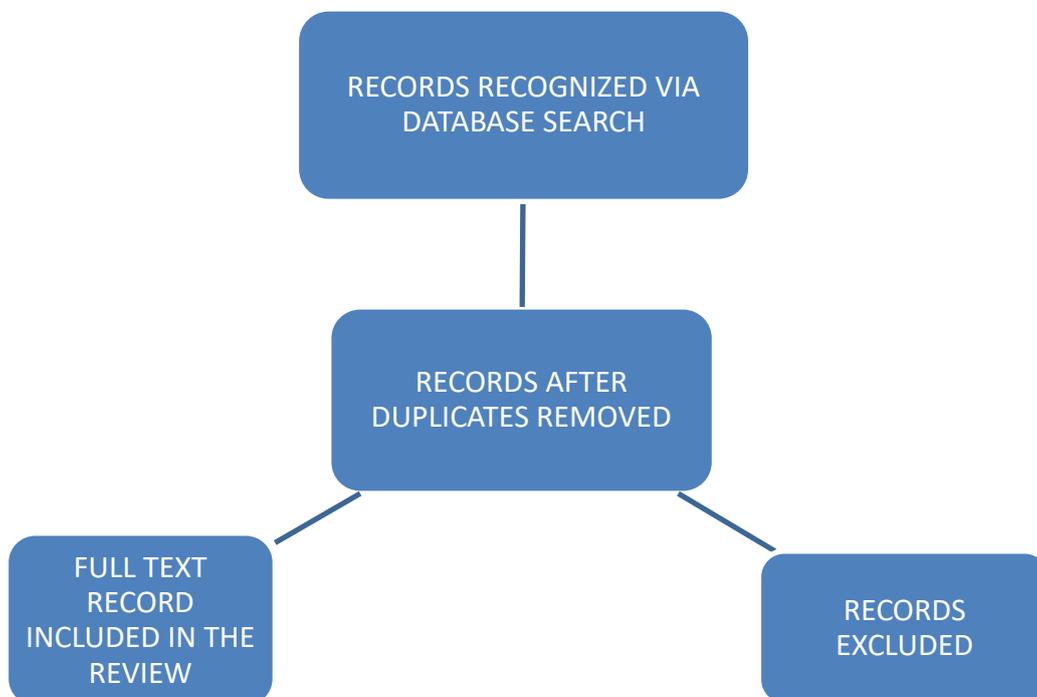
1. To investigate the potential link between SARS-CoV-2 and bacterial load in the mouth.
2. The connection between COVID-19 and oral health and periodontal disease as comorbidities are at highest risk.

MATERIAL AND METHODS:

In this systematic review of the literature, we searched PubMed, ISI, and SCOPUS electronic databases using MESH terms and the following keywords: ("Covid-19" OR "Covid19" OR "Corona" OR "Coronavirus" OR "SARS-CoV-2") AND

("Dentistry" OR "Dental"). **All articles from the 10.01.2021 until 10.06.2021 that satisfied our selection criteria** of being recommendations or guidelines for dental practice during the COVID-19 pandemic were retrieved. Articles were excluded if they were not found to be relevant, produced before the COVID-19 pandemic, or opinion-based without any supporting evidence. Some clinical organizations for example; The World Health Organization (WHO), The Centres for Disease Control and Prevention (CDC), The National Health Service (NHS), The American Dental Association (ADA) and, American Dental Hygienists' Association (AHDA) had also published recommendations and guidelines through their websites. Therefore, we also undertook a Google search for these sources and used the English, German, and Farsi languages. We outlined the

competency criteria using a PICO model as follows: Population: All articles and/or guidelines for dental practice during the COVID-19 pandemic. Intervention: Knowing and applying the special precautions and therapeutic considerations in dentistry. Comparison: Despite the fact that due to the novelty of COVID-19, it is difficult to compare the effectiveness and applicability of the proposed precautions and interventions, but the comparisons have been made based on country, and organization of the article and guidelines. Outcome: the application and effectiveness of the intervention for reducing risks of transmission. Figure 1 shows a flow chart of the literature screening method used. Articles were critically appraised and data extracted to compile a summary clinical protocol for dental practice during the COVID-19 pandemic.



RESULT:

To the date this paper was drafted, 18 articles were found, of which 9 satisfied our inclusion criteria. We noted that some researchers preferred to publish their work rapidly and in alternative ways of using peer-reviewed journals. As all the nine studies were proposed in a general consensus, any elective non-emergency dental care for patients with suspected or known COVID-19 should be postponed for at least 2 weeks during the COVID-19 pandemic. Only urgent treatment of dental diseases can be performed during the COVID-19 outbreak taking into consideration pharmacological management as the first line and contagion-reduced minimally invasive emergency treatment as the secondary and final management. Furthermore, some of the guidelines provided by specific clinical organizations were reviewed. Since these protocols were very long, they were summarized, and the key elements were extracted from these published guidelines.

According to the recommended guidelines during COVID-19, the protective measures that should be undertaken in a **dental setting can be categorized into three phases: 1)** prior to dental treatment, **2)** during the dental procedure, and **3)** after dental treatment.

Pre-dental treatment

Before entering a dental office Patient triage, identification of possible suspects, delay of non-urgent dental care, management of dental appointments, and active screening of dental staff are among the protective protocols that should be considered prior to the patient entering the dental office.

At the dental office/reception

Active screening of patients, management of social distancing in the dental office, offering sanitation measures to the patients, use of facemasks by everyone entering the dental office, patient education, use of PPE by the dental team, and management of dental operatory room are among the procedures required to be carried out in dental offices.

During dental treatment

Maintaining hand hygiene, offering a preoperative antimicrobial mouth rinse to patients, using rubber dams, high-volume saliva ejectors, and extra oral dental radiographs, using 4-handed dentistry, avoiding aerosol generating procedures, one-visit treatment, and environmental cleaning and disinfection procedures should be implemented during dental procedures.

Post dental treatment

Cleaning and disinfecting reusable facial protective equipment, as well as management of laundry and medical waste following routine procedures should be considered after dental treatment.

Possible risk of transmission of COVID-19 in dentistry

While it may be difficult to identify the particular mechanism of infection for individual patients, we are aware of the common routes of transmission. Droplet transmission and transmission through fomites (objects or materials which are likely to carry infection) are the main modes of transmission by the respiratory system in intrapersonal contact and especially during sneezing, dry coughing,

or even talking ²⁸. We also know that COVID-19 is present in saliva, but transmission through this route has not been conclusively confirmed ²⁹. Considering the main path of transmission of the COVID-19 disease, dental procedures that lead to the spray of saliva particles into the air (which means almost all dental procedures) could heighten the possibility of contamination ³⁰. Much effort has been made in the literature to define droplets and aerosols and to distinguish between their ability to carry the COVID-19 virus, knowing which dental procedures produce aerosols that could carry the virus is important to help define the level of risk. Given the fact that the majority of dental instruments are made from metal and polymers, the COVID-19 could adhere and persist on these surfaces for several days. Consequently, they could present a risk of virus transmission if they are not adequately decontaminated ^{31, 32}. Fundamentally, COVID-19 in dentistry may be transmitted through air, droplets, and contact ^{33,34}.

Special precautions in dental procedure

Due to the fact that dentists have close contact with the patients and their hands are exposed to the mouth fluids and aerosols, using an antiseptic solution before treatment of each patient is of the utmost importance. Although broad types of antiseptic solutions are available, the ethanol solutions (above 70% concentration) are suitable for this process because of the non-toxic entity, while ethanol solutions are useful in hand hygiene; using soap and water is also effective ³⁸. Using masks with pores of less than 50 μm is necessary for dental

professionals. On the other hand, these particles could be transmitted through the eyes; therefore, using appropriate goggles or face shields could decrease the risk of the infections. As the aerosols spread from the mouth, suggesting to patients, they use an antiseptic oxidative mouth rinse would be protective prior to and after treatment. Currently, ADA and CDC only recommend peroxide to eradicate the virus. Moreover, public health authorities have advised 0.2% chlorhexidine mouthwash (CHX), 1% povidine-iodine (P.I.), 1.5% hydrogen peroxide (H₂O₂), or 0.05% hypochlorous acid (HOCl). CHX is weak in terms of virucidal, and the other three (P.I., H₂O₂, HOCl) all have excellent virucidal properties but are weak in substantively, because saliva flow can potentially replace the virus.

DISCUSSION:

The results of our study showed that the CoV-19 pandemic led to a decrease in the emergency dental treatment, this is because the patients were reluctant to have dental treatment because of the potential risk of infection by going outside. Oral hygiene and preventive practices have always been very important, but now, in the current condition, they are more critical than ever. Higher levels of oral hygiene could decrease the need for a person to attend a dental clinic for urgent matters; and at the same time, could significantly help the person to remove the virus from the body in the early contamination phase in day to day life and also to reduce the bacterial load in the mouth and the risk of bacterial superinfection especially in patients who are prone to altered biofilms due to diabetes, high blood pressure or cardiovascular

disease³⁵. The COVID-19 pandemic has led to the closure of dental offices around the world. Some countries are currently re-opening or planning to re-open dental services. There are many protocols that need to be considered and integrated into a comprehensive and concise protocol. Smart appointment systems and generally avoiding crowding in dental clinics are vital³⁶. Adequate time should be given between appointments so that appropriate decontamination procedures can be carried out³⁶.

Oral and maxillofacial radiology

For diagnosis purposes, using extra oral radiographic such as Dental Panoramic Radiographs (DPRs) or Cone-Beam Computed Tomography (CBCT) are endorsed over the intraoral radiographs. As reducing face-to-face appointments is necessary to reduce the risk of infection, the Tele dentistry provides an opportunity for many patients to access uninterrupted clinical and supportive care and the chance to triage increasingly critical conditions needing face-to face clinic visits. Furthermore, Tele dentistry allows for the continuing clinical training of dental practitioners. The COVID-19 pandemic may cause a permanent transformation in dentistry with the advancement of Tele dentistry. In fact, the visual nature of dental procedures makes telemedicine practical in the dentistry field³⁷.

Specific therapeutic considerations in dentistry

Suggestions have been made to preserve a high level of oral hygiene in patients in order to diminish the risk of any emergencies; including washing teeth at least twice a day, daily flossing, and using a 1% povidine-iodine mouth-wash 3 to 4 times a day³⁸.

CONCLUSION:

Older adults and people of any age who have serious medical condition such as chronic lung disease, diabetes, heart conditions or chronic kidney disease are at high at risk for developing severe illness due to SARA CoV-2 infection. At the same time, poor health increases the risk of developing the same medical conditions. Therefore, improving oral health in people of any age, by reducing their risk of developing non-oral systemic diseases, may reduce the morbidity of COVID-19 (**FIGURE -1**). Although the association between oral health and severity of COVID-19 symptoms appears logical, more research is needed to demonstrate the association empirically. In the process of infection with SARS-CoV-2, the oral cavity has the role of an entrance gate and a natural barrier, which is overcome by the virulence of this agent, under the conditions of an immune response of the dysfunctional host, incompletely elucidated. The consequences of COVID-19 on the practice of oral medicine are difficult to estimate, but it is obvious that we must learn to protect ourselves and coexists with this virus.

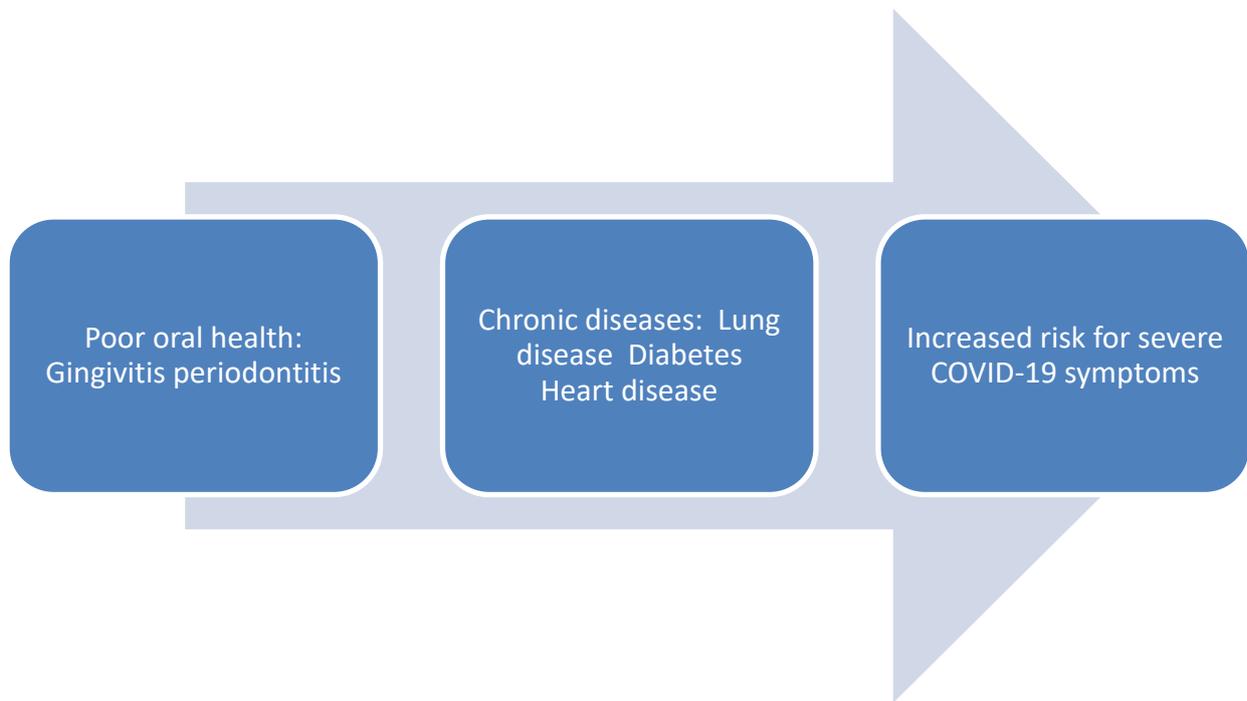


Fig: 1- Association between oral health and severity

REFERENCES:

1. Gorbalenya AE, Baker SC, Baric RS. et al. severe acute respiratory syndrome-related coronavirus species: classifying 2019-nCoV and naming it. SARS-CoV2. Nat. Microbiol.5,2020,536-544; Available on line: URL - <http://doi.org/10.1038/s41564-020-0695>.
2. Wu F, Zhao S, Yu B. A new coronavirus associated with human respiratory disease in China. Nature 579, 2020,265-269; Available on line: URL- <http://doi.org/10.1038/s41586-020-2008-3>.
3. Wahbal L, Jain N, Z fire AZ, Shoura MS, Karen L, Artiles Kl, et al. Identification of a pangolin niche for a 2019 nCoV-like coronavirus through an extensive meta-metagenomic research. <https://www.boirxiv.org/content/10.1101/2020.02.0939660v2>.
4. Kampf G, Todt D, Pfaender S, Steinmann E, Persistence of coronavirus in animate surfaces and their inactivation with biocidal agents. J Hosp. Infect, 104(3), 2020, 246-251.
5. Liu YC, Kuo RL, Shih SR. COVID-19: the first documented corona virus pandemic in history. Biomed J 2020; 43:328-33.
6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395:1054-62.
7. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. presenting characteristics, comorbidities and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020; 323:2052-9.

8. Li MY, Li L, Zhang Y, Wang XS. Expressions of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty* 2020; 9:45.
9. Kisslings S, Pruijm M. COVID-19 from the nephrologist's point of view. *Rev. Med. Suisse* 2020; 16:842-4.
10. Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, Xu T, et al. Identification of a novel coronavirus causing severe pneumonia in humans: a descriptive study. *Chin Med J* 2020; 133:1015-24.
11. Chen J. Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses. *Microb Infect* 2020; 22:69-71.
12. Li JY, You Z, Wang Q, Zhou ZJ, Qiu Y, Luo R, et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious disease in the future. *Microb Infect* 2020; 22:80-5.
13. Pederson SF, Ho YC. SARS-CoV-2: a storm is raging. *J Clin Invest* 2020; 130:2202-5.
14. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao SY. Pulmonary pathology of early phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. *J Thorac Oncol* 2020; 15:700-4.
15. Bui FQ, Almeida-da-silva CLC, Huynh B, Trinh A, Liu J, Woodward J, et al. Association between periodontal pathogens and systemic disease. *Biomed J* 2019; 42:27-35.
16. Wu Z, Nakanishi H, connection between periodontitis and Alzheimer's disease: possible role of microglia and leptomeningeal cells. *J Pharmacol sci* 2014; 126:8-13.
17. Jepsen S, stadlinger B, Terheyden H, Sanz M. Science transfer: oral health and general health-the links between periodontitis, atherosclerosis and diabetes. *J Clin Periodontol* 2015; 42:1071-3.
18. Khumaedi AI, Purnamasari D, Wijaya IP, Soeroso Y. The relationship of diabetes, periodontitis and cardiovascular diseases. *Diabetes Metab Syndr* 2019; 13:1675-8.
19. Godson JM, Disease reciprocity between gingivitis and obesity. *J Periodontol* 2020; 01:1-9.
20. Scannapieco FA, Role of oral bacteria in respiratory infection. *J Periodontol* 1999; 70:793-802.
21. Scannapieco FA, pneumonia in nonambulatory patients. The role of oral bacteria and oral hygiene. *J Am Dent Assoc* 2006; 137(Suppl):21S-5S.
22. Almeida-da-silva CLC, Alpagot T, Zhu Y, Lee SS, Robert BP, Hung SC, et al. Chlamydia pneumoniae is present in the dental plaque of periodontitis patients and stimulates an inflammatory response in gingival epithelial cells. *Microb cells* 2019; 6:197-208.
23. Gomes –Filho IS, Passos JS, Seixas da Cruz S. Respiratory disease and the role of oral bacteria. *J Oral Microbiol* 2010; 21:2.
24. Varanat M, Haase EM, Kay JG, Scannapieco FA, Activation of the TREM-1 pathway in human monocytes by periodontal pathogens and oral commensal bacteria. *Molecular oral microbiology* 2017;32:275-87.
25. Azarpazhooh A, Leake JL, Systematic review of the association between respiratory diseases and oral health. *J periodontol* 2006; 77:1465-82.
26. Boccardi V, Ruggiero C, Mecocci P. COVID-19: a geriatric emergency. *Geriatrics* 2020; 5:24.
27. Swiss Academy Of Medical S. COVID-19 pandemic: triage for intensive-care treatment under resource scarcity. *Swiss Med Wkly* 2020; 150:w20229.
28. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The incubation period of coronavirus disease 2019 (COVID-19) from

- publicly reported confirmed cases: estimation and application. *Ann. Intern. Med.* 2020; 172(9):577. <https://doi.org/107326/M20-0504>.
29. To KK-W, Tsang OT-Y, Yip CC-Y, Chan K-H, Wu T-C, Chan JM-C, et al. Consistent detection of 2019 novel coronavirus in saliva. *Clin.Infect.Dis.* 2020;71(15):841. <https://doi.org/10.1093/cid/ciaa149>.
30. Spagnuolo G, De Vito D, Rengo S, Tatullo M. COVID-19 outbreak: an overview on dentistry. *Multidiscipl Digit Publishing Inst.* 2020; 17(6):2094. <https://doi.org/10.3390/ijerph17062094>.
31. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann. Intern. Med.* 2020; 172(9):577-82. <https://doi.org/10.7326/M20-0504>.
32. Negahdaripour M. The battle against COVID-19: where do we stand now Iranian J Med Sci. 2020; 45(2):81. <https://doi.org/10.30476/ijms.2020.46357>.
33. 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):1-6. <https://doi.org/10.1038/s41368-020-0075-9>.
34. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *J Hosp Infect.* 2020; 104(3):246-51. <https://doi.org/10.1016/j.jhin.2020.01.022>.
35. Sampson V. Oral hygiene risk factor. *Br Dent J.* 2020; 228(8):569. <https://doi.org/10.1038/s41415-020-1545-3>.
36. Ren Y, Rasubala L, Malmstrom H, Eliav E. Dental care and oral health under the clouds of COVID-19. *JDR Clin Transl Res.* 2020; 5(3):202. <https://doi.org/10.1177/2380084420924385>.
37. Estai M, Kanagasingam Y, Xiao D, Vignarajan J, Huang B, Kruger E, et al. A proof-of-concept evaluation of a cloud-based store-and-forward telemedicine app for screening for oral diseases. *J Telemed.Telecare.* 2016; 22(6):319-25. <https://doi.org/10.1177/1357>.
38. Santacroce L, Passarelli PC, Passarelli G, Charitos IA, Rella E, D'Addona A. COVID-19 and Oral diseases: how can we manage hospitalized and quarantined patients while reducing risks? 2020. <https://doi.org/10.29333/ejgm/7945>.