BOHR International Journal of Current research in Dentistry
2022, Vol. 1, No. 1, pp. 34–38
DOI: 10.54646/bijcrid.2022.06
www.bohrpub.com

REVIEW

Diagnosis and protection of COVID-19 in stomatology

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Received: 28 June 2022; **Accepted:** 04 July 2022; **Published:** 17 August 2022

In late 2019, a novel coronavirus of uncertain etiology caused outbreaks in Wuhan, China, and quickly spread to other provinces and countries. Some researchers isolated the pathogen, which they named the 2019 novel coronavirus disease (2019-nCoV). The common symptoms of patients infected with SARS-CoV-2, such as sore throat, high fever, diarrhea, and dyspnea. Besides that, researchers also recorded oral symptoms, including ulcers, herpes, and tongue pain. At the same time, dental practitioners, as a high-risk infection occupation, always contact close patients. It is very important to prevent infection. The review aims to look back at the progress of the coronavirus disease 2019 (COVID-19) associated with stomatology, to be studied, diagnosed, and prevented from the disease from the oral aspect.

Keywords: COVID-19, oral, diagnostic, aged

1. Introduction

In 2019, we found pneumonia from an unknown source in China, and it has broken out in many places around the world. This is a new zoonosis that can be isolated from human airway epithelial cells and is named 2019-nCoV (1). The virus is an enveloped RNA virus (2), which possesses high infectivity and can cause fatal respiratory diseases. Because the clinical characteristics of COVID-19 are not significant and it is highly infectious, early diagnosis and prevention become critical to control the rapid spread of the outbreak. The common screening symptoms of the disease include fever, cough, sore throat, dyspnea, diarrhea, etc. (3). Furthermore, studies have shown that the main host cell receptor of SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2) (4). The damage to various organs is linked to the distribution of ACE2 receptors in human systems. Therefore, ACE2 receptor-distributed cells may become the host cells of the virus, causing an inflammatory response in related organs and tissues. ACE2 higher expression in oral mucosa may indicate that oral mucosa is a potential target of COVID-19, which may lead to oral mucosa-associated infections, including ulcers, salivary gland inflammation, and so on so that oral medical staff can make an early diagnosis of the patients through the oral cavity to achieve early prevention. Moreover, it is inevitable to generate fog as well as aerosol, which exposes doctors and patients to a high-risk environment during dental diagnosis and treatment, so protective treatment is very crucial. The current research on COVID-19 related to oral disease is less reported, and it is easy to be ignored. This review mainly summarizes the research progress on suspicious symptoms, protective measures, and detection schemes through a literature search, which attracts the attention of dental practitioners.

2. Symptoms and signs of COVID-19

Angiotensin-converting enzyme 2 is the target receptor for coronaviruses to enter host cells, which are potential targets of SARS-CoV-2. At present, many studies have reported some oral symptoms associated with COVID-19, including dry mouth, strange taste, oral mucosal lesions, and salivary gland inflammation. ACE2 may exist in oral tissues (5),

but the correlation between new crown patients and oral symptoms is controversial.

2.1. Taste dysfunction

Taste dysfunction is a common symptom of inpatients and most outpatients. Although other viral infections also have altered taste functions, the incidence rate is considerably lower than that of COVID-19. It is reported that 88.8% of taste disorders (308 of 342 cases) occur in patients with a positive diagnosis of SARS-CoV-2 (6). In a short case report, a couple was diagnosed as having SARS-CoV-2 shortly after developing taste and olfactory dysfunction (7). Moreover, among 88 patients diagnosed with COVID-19, 20.3% had symptoms of taste or olfactory disorders before admission. The incidence of this symptom in women was higher than that in men (8). Furthermore, the first symptom of COVID-19 may be azoospermia, smell, and taste disorders (9). There are currently two hypotheses about potential mechanisms that are reasonable: First, the virus directly attacks olfactory neurons and damages their epithelium (10). Second, the expression of ACE2 receptors was higher in the tongue than in the other oral mucosa (5). Finally, the SARS-CoV-2 infection is expanding all over the world, which is a challenge to the medical system and medical resources. Sometimes, taste and smell can also be included in a screening condition. If these symptoms appear, patients can consider immediate home isolation.

2.2. Oral mucosal lesions

Recently, few authors have reported that SARS-CoV-2-infected patients had common oral symptoms and signs, but the expression of ACE2 in the oral mucosa indicates the oral cavity may be a high-risk site for COVID-19. A case report described an elderly male infected with COVID-19 who complained of pain from the palate, sore throat, and sore tongue, as well as other systemic symptoms such as fever, cough, and diarrhea. A complete intraoral examination found a large number of ulcers and blisters that resembled herpetic recurrent lesions and was subsequently diagnosed with COVID-19 (11). Likewise, in the other case reported 24 days after hospitalization, the internal examination found white plaque and several yellowish ulcers on the tongue dorsum. A few days after leaving the ICU, when the patient's systemic symptoms improved, the oral symptoms quickly recovered (12). Moreover, a study discovered the oral symptoms and signs, including ulcers that resembled simplex herpes lesions on their lips and tongue dorsum, and denied that they had a history of recurrent ulcer disease, among 8 patients diagnosed with SARS-CoV-2 (13).

Although no oral tissue samples were obtained from patients with infected COVID-19 in the actual study, the author found that the evolution of oral lesions paralleled the clinical symptoms of COVID-19 (13). It is very important to know whether SARS-CoV-2 destroys the oral mucosa epithelium, then causes an oral ulcer or plaque, and what the new pathogenic mechanism is. Furthermore, we could assume whether oral lesions are the first symptom caused by COVID-19 infection.

2.3. Sialadenitis

A report stated that the expression of ACE2 was higher in salivary glands epithelial cells than in lung cells, explaining that salivary glands may also be a potential target of COVID-19 (14). Therefore, we should not ignore the potential infection from saliva. The virus damaged the gland, leading to salivary gland inflammation, including submandibular gland inflammation and parotitis. Furthermore, it was reported that SARS-CoV-2 could be detected in saliva before lung lesions (15). In conclusion, the virus in patients with asymptomatic carriers may originate from saliva generated by the salivary gland. Many researchers hypothesized that salivary gland infection could cause changes in salivary flow rate and composition, resulting in taste changes and dry mouth (16).

3. Oral manifestations in the elderly with underlying diseases

Mueller et al. (17) found that hospitalized patients infected with SARS-CoV-2 were over 65 years old, accounting for 80% of cases, and the mortality of elderly patients is also higher than that of young people. Some studies show that many basic diseases in elderly patients with cardiovascular diseases, hypertension, diabetes, and chronic obstructive pulmonary disease (COPD) are the major risk factors for the increase of COVID-19 and the main life-threatening risk factors (18). The cytokines and microorganisms released by an oral infection can cause distal organ inflammation, so oral health is associated with general health. Local oral disease may promote the severity of COVID-19 in older people. In a recent study, hypertension, obesity, and diabetes were identified as the three most potential adverse outcomes in COVID-19 patients requiring hospitalization (19). The elderly and obese patients are prone to oral diseases, especially gingivitis and periodontitis, because obesity will change the composition of periodontal microorganisms and increase pathogens. Obesity can reduce immunity, cause serious damage to organs and tissues, and cause complications of a variety of systemic diseases (20). Compared with normal weight, the adipose tissue of obese patients secretes pro-inflammatory factors and adipokines, which will aggravate the inflammatory effects of periodontitis and SARS-CoV-2 infection (21). Studies have found that obese people are likely to be able to be infected with COVID-19, among whom co-diseased patients with periodontitis and obesity may increase the risk of infection in obese patients

(22). In addition, it has been reported that the level of the chronic inflammatory marker C-reactive protein is increased not only in hospitalized patients with COVID-19 but is also expressed in patients with periodontitis, even in obese patients with periodontitis. With the increase in age, the prevalence of obesity and periodontal disease will increase, which increases the prevalence and death risk of new crowns.

It was also reported that 12% of the 140 patients with COVID-19 were diabetic. Scholars believe that elderly patients with diabetes are more likely to infect with the virus, even as a predictor of morbidity and mortality from periodontal disease and COVID-19 (23). Studies have found that the expression of ACE2 is significantly increased in diabetic patients because patients with diabetes and hypertension will increase angiotensin II type I receptor blockers (ARBs) and ACE inhibitors (24). Moreover, COVID-19 may cause inflammation through ACE2 imbalance and cause complications of diabetes. Meanwhile, viruses entering cells can delay death, evade host immunity, and increase the replication and secretion of chemokines. When infected with SARS-CoV-2, the immune response and interferon will decrease, and pro-inflammatory factors will increase, causing a cytokine storm, and leading to serious local tissue damage, such as periodontitis.

Hypertension is a common senile disease and one of the comorbidities of infection with SARS-CoV-2. It has been reported that comorbid hypertension is the highest risk factor in 1,099 hospitalized patients with a new crown infection (24). ACE inhibitors and angiotensin receptor blockers (ARBs) are used to treat hypertensive patients, both of which will increase ACE2 expression (25). Therefore, increased ACE2 expression in hypertension and periodontitis may indicate an increased risk of SARS-CoV-2 infection.

Cancer is also considered to be one of the risk factors for SARS-CoV-2 infection and aggravation because of its systemic immune suppression. When a systemic immune disorder is accompanied by an increase in cytokines and chemokines, it promotes inflammation, accelerates the serious progress of COVID-19, and leads to a local inflammatory response in the oral cavity, especially periodontitis. When the host is immunosuppressed, the interaction between the virus and host epithelial cells will destroy the integrity of the tissue and cause local lesions, such as necrotizing gingivitis, periodontitis, and dry mouth.

Oral diseases caused by systemic basic diseases of COVID-19 comorbidity, oral local inflammatory comorbidity COVID-19 will also cause systemic lesions. For example, persistent periodontal disease will cause the release of inflammatory cytokines, enter the systemic circulation, induce systemic inflammation, and aggravate the viral infection of COVID-19. There are many systemic diseases among the elderly. Due to the poor oral hygiene environment, the oral bacterial load increases, which destroys the symbiotic relationship between oral microorganisms. Bacteria can be colonized in distal organs through blood and even spread to the respiratory tract through the inhalation of oral liquid during breathing, increasing the risk of pneumonia or respiratory diseases (26). Other scholars hypothesized that gram-negative periodontal bacteria from the mouth may lead to lipopolysaccharide-induced lung cell aging and accelerate SARS-CoV-2 replication (26).

Therefore, it is very crucial to pay attention to the oral health of the elderly, specifically the elderly in the intensive care unit. Improving oral health can reduce complications and the COVID-19 incidence of distal organs. Although there is no clear causal relationship between the oral cavity, systemic diseases, and COVID-19 in the elderly, oral-related inflammation can cause microbial ecological imbalance, host stress response, and immune imbalance to stimulate the severity of COVID-19.

4. Department of stomatology protection during COVID-19

Due to the highly infectious and worldwide epidemic, COVID-19 is a new challenge for the stomatology department. There are several characteristics of oral treatment, such as long treatment times, close contact between patients and doctors, the water mist and aerosol formed by saliva and blood, as well as the secretions of patients during the operation of dental instruments. The aerosol can spread up to 2.1 m, and splash into the face, eyes, or blood of medical staff or other patients (27). Furthermore, the liquids, materials, and contaminated dental instruments contacted by dental professionals may also be the route of virus transmission. Sometimes, a dental clinic is one of the most concentrated places for patients. It is possible that patients conceal their illnesses or potentially infectious diseases, which may cause a big outbreak. Therefore, protection has become very indispensable in the department of stomatology.

4.1. Personal protective equipment department of stomatology

Personal protective equipment in the department of stomatology is a high-exposure occupation during the novel coronavirus disease of 2019, so occupation protection is very important. (1) Researchers investigated the protection status of medical staff in the department of stomatology through questionnaires. The results showed that 80.71% of the 1,229 medical staff used ordinary masks. The wearing rate of N95 masks was only 0.56%. Only 67.61% of the medical staff changed masks in 4–6 h. In high-risk conditions, a respirator has an 85% chance of not being infected with the virus (28). In the past few months, Ma et al. (27) analyzed the effect of N95 masks, family masks, and surgical masks on virus isolation and showed that N95 masks had greater reliability. (2) Gowns and gloves: In a dental setting with a severe infection rate, to increase the protection function,

the professionals should use disposable protective clothing. Medically disposable protective clothing should cover the head, trunk, and ankle and protect all parts of the body. Furthermore, it should not be able to penetrate the virus-carrying saliva and blood when splashed on the protective clothing during a dental operation. Professionals are prone to cross-infection in practice, so they must wear protective gloves and change them for each patient. Besides this, gloves should be replaced when contacting the cleaning area. (3) Hand hygiene: the first measure to reduce cross-transmission of the virus in a dental environment (29). Washing hands with soapy water and alcohol is particularly important to control the spread of respiratory diseases, including SARS (30). Due to the transmission characteristics of the 2019-nCoV virus, a study suggests the "two before and three after" technique as standard hand hygiene procedure. Doctors must wash their hands before examining the patient, before dental practices, after contact with the patient, after touching the environment without previous disinfection, and after touching the oral mucosa and skin of a patient. Furthermore, WHO recommends that professionals should frequently wash their hands before and after any direct or indirect contact with the patient (31).

4.2. Prevention and control of hospital

The dental clinic has always been a high-density place with a high flow of people, so it is very important to do a good job in the prevention and control of nosocomial infection during this time. Otherwise, it is easier to increase the risk of infection. Through a review of the literature, we summarized the following points regarding the prevention and control of nosocomial infection. First, we advocated for orderly consultation and diagnosis before treatment, including by telephone or remote video consultation and diagnosis, to preliminarily screen whether patients could go to the outpatient clinic and formulate a treatment plan and preventive nursing. It also includes emergency priorities to reduce the number of outpatient visits. The department of stomatology in many countries advocates the principle of oral emergency priority. During the outbreak of this disease in early 2020, China only opened an oral emergency to deal with some acute toothache, acute space infection, tooth trauma, and so on. Similarly, according to the *British Medical Journal*, ibuprofen will not be used to treat toothache, but paracetamol will be selected as a new analgesic to treat some simple toothache. The main reason is that ibuprofen can interfere with the function of the human immune system (32). Furthermore, a survey before visiting time survey was conducted by the New Zealand Dental Association and other associations, which included whether COVID-19 was positive or respiratory symptoms (cough, shortness of breath, sore throat, travel outpatient history, and body temperature) were noted to help dentists understand whether or not COVID-19 might have been exposed to an earthquake. If the temperature exceeds 37.5°C and is accompanied by respiratory disease-related symptoms, the dental visit will be delayed for 14 days (33). At the time you make the appointment, to reduce the number of oral microorganisms in saliva, the researchers suggest that 0.2% povidone-iodine or 1% hydrogen peroxide gargles be used before dental practice (34). In addition, since the bacterial aerosols are the largest at 1m from the headrest, it is found that rubber dam isolation can effectively reduce the contaminated gas produced by dental treatments (35). In the meantime, WHO suggests that sodium hypochlorite should be used to disinfect public areas and appliances in the dental clinic (31).

5. Discussion

Although many countries have already developed and started to use an effective COVID-19 vaccine, SARS-CoV-2 is spreading globally. Even in a short time, experts assess that the epidemic will continue. Early detection, diagnosis, isolation, and treatment are necessary to implement outbreak control measures. We urgently need to seek a safe, sensitive, and highly efficient method to detect the rival. In addition, dental clinics, which have a high density of patients, have more transmission routes. Therefore, practicing dentists should not ignore any oral symptoms of the development and changes of patients who tested positive for COVID-19 during the period. The review has some limitations. There is a limited number of primary reports and data about dental research related to COVID-19. Likewise, the studies of the pathology and mechanism of oral symptoms of patients infected with COVID-19 are still unclear. What a pity that the vaccines for SARS-CoV-2 are entering various regions and countries, but few scholars have reported changes in oral protection after the entry of vaccines. In short, more scholars in the field of stomatology are needed to fully research the oral symptoms, manifestations, and pathogenesis of COVID-19 infection in the future and to timely evaluate and treat them to improve the quality of life of patients.

Author contributions

MY: data curation and writing – original draft, including preparation, creation, and presentation of the published work, and specifically writing the initial draft. YC: formal analysis and application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data. MW: writing – original draft, preparation, creation, and presentation of the published work by those from the original research group, specifically critical review, commentary, or revision, including pre- or post-publication stages. JL: oversight and leadership responsibility for the research activity's execution. All authors contributed to the article and approved the submitted version.

Funding

This study was supported by the Construction Projects of Medical Biomaterial Research and Development Talent Base in Guizhou Province and Zunyi City (Nos. 3 and 69) and the Science and Technology Project of Guizhou Province (5772-006).

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