Universidad Europea
LAUREATE INTERNATIONAL UNIVERSITIES

TRABAJO DE FIN DE GRADO

Grado en Odontología

COVID-19 AND DENTISTRY

Madrid, curso 2020/2021

Número identificativo **138**

RESUMEN

Antecedentes: El nuevo coronavirus, Sars-CoV-2, detectado en China en diciembre de 2019 originó la pandemia mundial COVID-19 que ha afectado a más de 70 millones de pacientes. El virus es altamente infeccioso por contaminación aérea. Por ello, los dentistas son considerados como profesionales de alto riesgo de contaminación. Deben ser conscientes de los riesgos de transmisión y seguir las recomendaciones oficiales para protegerse como a sus pacientes. Además, las células humanas huéspedes del virus se encuentran en muchos órganos vitales, pero también en el medio oral, lo que implica posibles afecciones orales de COVID-19.

Objetivo: Esta revisión de literatura pretende explicar cómo el nuevo coronavirus afecta a la salud bucodental y a la práctica diaria de la odontología.

Métodos: Usamos bases de datos PubMed, SciELO y Wiley Online Library con las palabras clave “covid-19”, “dentistry”, “sars-cov-2”, “coronavirus”, “oral”, “manifestation”, “dental”, “periodontitis” y “aerosols”. También se examinaron publicaciones de organizaciones cientificas y webs de Odontostomatología. Sólo se incluyeron estudios realizados en humanos, escritos en inglés y español.

Discusión: Los casos clínicos y series sobre las manifestaciones orales de la COVID-19 son escasos. Sus autores mencionan lesiones intraorales de muchas formas y localización diferentes que pueden deberse a la inmunodepresión originada por infección viral. Se necesita más evidencia científica para concluir sobre la semiología oral de la COVID-19. Las recomendaciones mundiales incluyen el uso de equipos de protección individual para los trabajadores y la desinfección frecuente de las superficies potencialmente contaminadas como medidas preventivas contra la transmisión del Sars-CoV-2. Los profesionales y especialistas de la odontología se ven obligados a cambiar sus protocolos y a desarrollar habilidades en telediagnóstico para garantizar una actividad más segura.

Conclusión: Las profesiones odontológicas se ven muy afectadas por la aparición del Sars-CoV-2 y necesitan evolucionar y adaptarse a la nueva situación planteada por la pandemia del COVID-19. Es necesario adoptar medidas preventivas para proporcionar una atención sanitaria bucodental más segura y realizar exámenes intraorales de los pacientes afectados por COVID-19 para diagnosticar y tratar las manifestaciones orales provocadas por esta enfermedad.

ABSTRACT

Background: The new coronavirus, Sars-CoV-2, detected in China in December 2019 originated the global COVID-19 pandemic that affected more than 70 million of patients. The virus is highly infective through airborne contamination. Therefore, dentists are considered high risk professionals for contamination. They should be aware of transmission risks and follow official recommendations to protect themselves and their patients. Furthermore, human host cells for the virus are found in many vital organs but also in oral medium, which leads to investigate on possible oral affectations of COVID-19.

Objective: This literature review aims to explain how the novel coronavirus disease outbreak impacts oral health and daily dental practice.

Methods: We searched PubMed, SciELO and Wiley Online Library databases using the following keywords "covid-19", "dentistry", "sars-cov-2", "coronavirus", "oral", "manifestation", "dental", "periodontitis" and "aerosol". Scientific organizations and odontostomatology websites were also screened for publications. Only human studies written in English and Spanish.

Discussion: Case reports and series on COVID-19 oral manifestations are scarce. They mention many different types and locations of intraoral lesions that can be due to the immunodepression originated by the viral infection. More evidence is needed in the future to conclude on COVID-19 oral semiology. Worldwide recommendations and guidelines include wearing personal protective equipment or frequent disinfection of touched areas of the dental clinic as preventive measures against Sars-CoV-2 transmission. Dental professionals and specialists are obligated to change their protocols and develop teledentistry skills to ensure a safer activity.

Conclusion: Dental professions are highly affected by the Sars-CoV-2 emergence and needs to evolve and adapt to the new situation brought up by the COVID-19 pandemic. Preventive measures need to be taken to provide safe oral healthcare and intraoral examination of patients

with COVID-19 should be carried out in order to diagnose and treat oral manifestations of the disease.

INDEX

1. INTRODUCTION

1.1 COVID-19 novel disease emergence and Sars-CoV-2

Emergence of a new disease

At the end of year 2019, several cases of a new severe acute pulmonary disease of unknown etiology were reported in Wuhan City, in the Hubei province of China. During the following months, the number of cases increased considerably and many affected individuals died. The disease spread all throughout Europe and then worldwide, constraining the World Health Organization (WHO) to declare an official pandemic alert on the 11th of March of 2020(1,2). In an official situation report published in February 2020, the condition was named Coronavirus Disease 2019 (COVID-19) by the WHO(3). The pandemic which started from December 2019 has caused over 109 million laboratory-confirmed infections and over 2.4 million death cases worldwide by March 2021(4).

Etiology of COVID-19

The pathogen responsible for the respiratory syndrome has been rapidly identified as a virus belonging to the *Coronoviridae* viruses' family as the severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS-CoV)(1,5,6). Consequently, it was first named "2019 Novel Corona Virus" (2019-nCoV) before being renamed few months later as Sars-CoV-2 standing for "Severe acute respiratory syndrome Corona Virus 2", name under which it is broadly known today by the scientific community(1,7). As the other coronaviruses, it is highly infective, and especially through an airborne mode of transmission(1).

According to the latest epidemiological and genetic studies performed, the Sars-CoV-2 human infection is a zoonosis, due to a single transmission from an animal. The subsequent rapid human-to-human transmission of the coronavirus has been at the origin of the COVID-19 epidemic(1,5,8). According to Zhou et al., the Sars-CoV-2 may be originating from a bat as many other coronaviruses, but the existence of an intermediate animal host between bat and human is highly suggested(5,6,9). A scheme of the emergent Sars-CoV-2 virus and its principal features is presented on **Figure 1**.

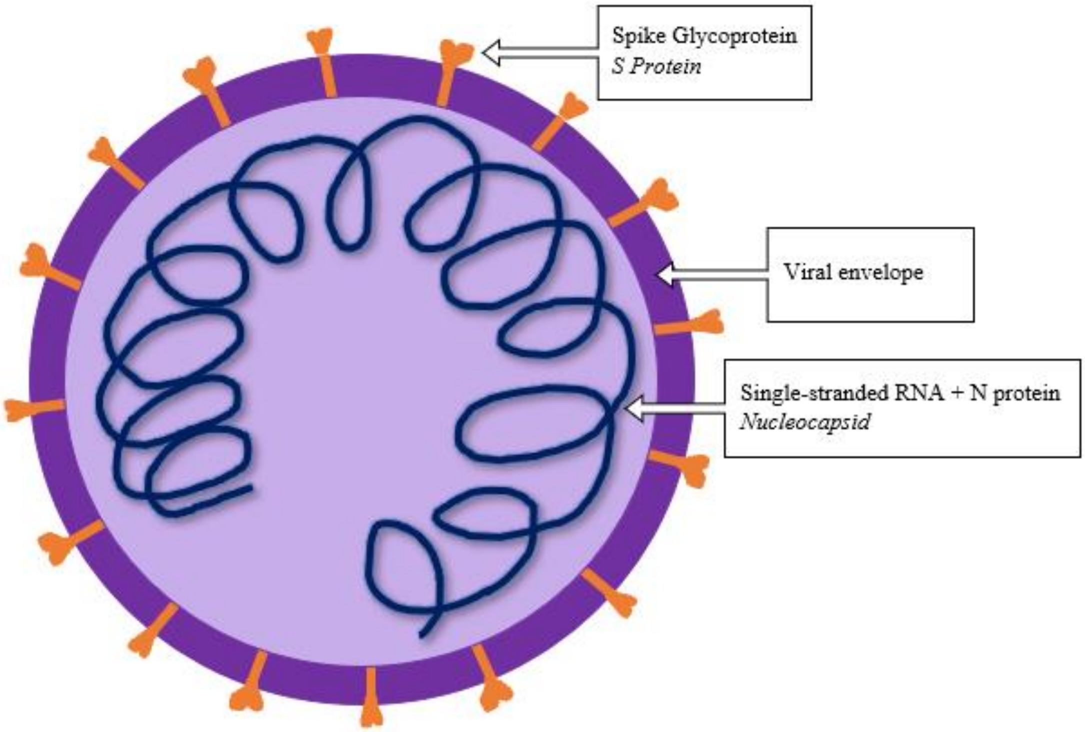


Figure 1- Sars-CoV-2. Original figure based on BioDigital platform.

Sars-CoV-2 virus pathogenicity

The Sars-CoV-2 is an RNA virus causing COVID-19 disease(10). Viruses are parasites, which means that to live and replicate, they previously need to infect a host cell. The Sars-CoV-2 encodes for membrane proteins like the spike glycoprotein (S protein) that allow its adhesion with specific receptors on host cell's surface(1,7,10). The S-protein presents a strong interaction with the angiotensin-converting enzyme II (ACE-2)(9) and the Sars-CoV-2 may use ACE-2 as receptor to enter host cells(1,5,7,10). These findings suggest that ACE-2 expressing cells are likely to act as targets for the virus. In the human body, ACE-2 are found in alveolar cells of lungs, enterocytes, myocardial and urothelial cells, and epithelial cells of esophagus and kidney(1,11). The presence of ACE-2 expressing cells in the oral cavity has also been studied with the expression of ACE-2 molecules present in oral environment being higher in the floor of the mouth, the oral tongue, and its base compared to other oral tissues(11). The Sars-CoV-2 pathway of infection is mainly by airborne and direct contacts with contaminated surfaces before touching eyes, mouth or nose(1). Airborne infection is made possible through flügge droplets released by talking, coughing, and exhaling. They are from oropharyngeal and nasopharyngeal origin and associated with saliva(12). **Figure 2** shows the speed and distance that can be reach by aerosols and droplets. Sars-CoV-2 virus seems to demonstrate a variable incubation period that extends from 3 to 14 days(1).

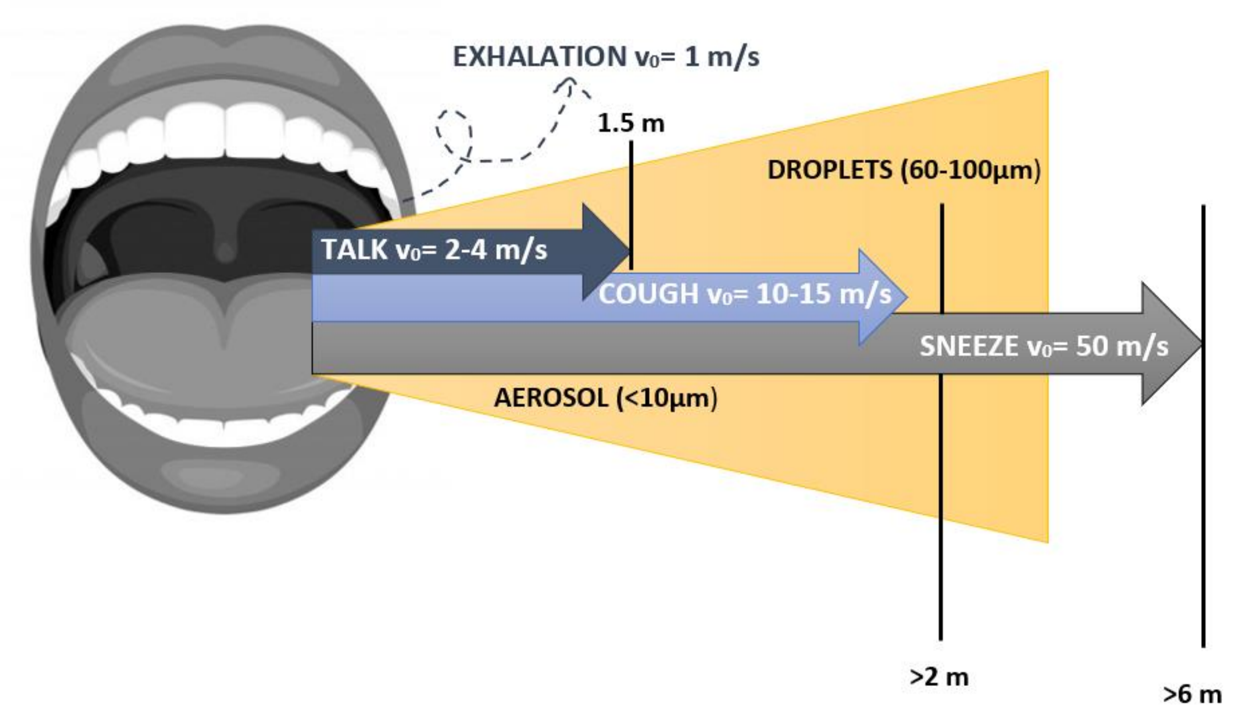


Figure 2- Aerosol and droplets distance of projection while coughing, sneezing, talking and exhaling. Original figure with data extracted from references (1,13,14).

1.2 COVID-19 manifestations and diagnosis

COVID-19 general manifestations

Infected humans by Sars-CoV-2 will exhibit variable symptomatology depending on the host's immune system, health status, and age(15,16). It ranges from the absence of symptoms to a potentially lethal interstitial bilateral pneumonia(1). Common symptoms of the illness are fever, dry cough, extreme fatigue, asthenia, myalgia, and even dyspnea(1,11,17). Headache, dizziness, abdominal pain, diarrhea, and vomiting have also been reported with a lower prevalence(11). Unfortunately, in some cases, there is a worsening of symptoms leading to a severe respiratory impairment due to alveolar damage and a need for hospitalization and assisted ventilation. According to an early study conducted on 99 patients in Wuhan City (epicenter of the epidemic), the most severe form occurred in 15% to 25% of the cases with confirmed pneumonia(6). In addition, a higher risk of thrombosis has been detected through blood analysis in some COVID-19 patients(17,18). Among patients presenting mild to moderate pneumonia, mucocutaneous manifestations have also been reported, being palmoplantar and oral involvements the most frequently encountered conditions(19).

COVID-19 diagnosis

The principal challenge in the clinical diagnosis of the COVID-19 disease is that reported symptoms are not specific. In order to help in the differential diagnosis, the Kansas Department of Health and Environment published a poster gathering symptoms of COVID-19, the usual winter cold, flu, and allergies to compare them(20). As seen on **Table 1**, seasonal flu is the disease that shares most symptoms with COVID-19. However, the common appearance of shortness of breath, anosmia (loss of smell) and ageusia (loss of taste) among COVID-19 affected patients is considered more specific of the disease although it can be confounding with allergies(1,20). The diagnosis of COVID-19 is also based on epidemiological findings as involving patients that have had previous contacts with infected individuals 14 days before symptoms appearance(1). Additionally, it has been reported that more severe (lethal) forms of the disease are likely to occur in ≥40 years old patients with comorbidities(21,22).

SYMPTOMS	COVID-19	COLD	FLU	ALLERGIES
FEVER	X		X	
GENERAL ACHES	X		X	
FATIGUE	X		X	X
COUGH	X	X	X	
SHORTNESS OF BREATH	X			X
LOSS OF APETITE	X		X	
NAUSEA AND VOMITING	X		X	
ABDOMINAL PAIN	X		X	
DIARRHEA	X		X	
ANOSMIA OR AGEUSIA	X			X
CHILLS	X		X	
RHINORREA	X	X	X	X
NASAL CONGESTION		X	X	X
SORE THROAT	X	X	X	
SNEEZING		X	X	X

Table 1- Comparative table of adult symptoms of COVID-19, cold, flu and allergies where X indicates the possible of common presence of the symptom among the pathologies. Original table with data extracted from the Kansas Department of Health and Environment (20).

A meta-analysis has been carried out by Chinese medical doctors to study comorbidities as a risk for COVID-19(15). They concluded that hypertension, diabetes, chronic obstructive pulmonary disease (COPD), cardiovascular and cerebrovascular diseases are the pathologies that are major risk factors for patients with COVID-19.

Blood test analysis is useful in the detection of Sars-CoV-2 infection because the results may include a low white blood cells and lymphocytes count together with a high level of serum C-reactive protein (CRP)(21). Another diagnostic test for COVID-19 is the nucleic acid amplification (NAAT) of upper respiratory tract samples using the reverse transcription polymerase chain reaction (RT-PCR)(1,21). The disadvantage of this method is its low sensitivity because if the viral load is low, it might give easily a false negative result. However, it remains the gold standard method.

In order to improve correct COVID-19 diagnosis and detection in hospitalized patients, some authors highly recommend the use of chest computed tomography (CT) as a complementary test. Indeed, it is already the diagnostic method used for other pulmonary diseases such as viral pneumonia of which it provides a high detection rate. CT scans can reveal the disease progression(21): during the early stage of the disease, pure ground glass opacities are likely to be observed whereas multiple ground glass opacities in a crazy-paving pattern are seen in the progressive stage. In the most advanced stage, the lung whiteout effect and diffuse exudative lesions are detected.

1.3 COVID-19 treatment perspectives

The actual treatment for mild forms of COVID-19 is based on treating symptomatology with analgesics and antipyretics. During all past year 2020, researchers and pharmacological laboratories throw themselves body and soul into the creation of a new vaccine, competent against COVID-19. Various strategies and candidates have been tested first *in vitro* to evaluate their effectivity and toxicity. Some testings *in vivo* have also been conducted but it presents ethical issues. Experimental therapies may be offered to some candidates only in the context of clinical trials and under informed consent(22). Among the candidates, antiviral agents such as the combination Lopinavir/Ritonavir (protease inhibitor) and Remdesivir (nucleotide analogue) were tested *in vitro* and *in vivo* and showed an efficiency against the Sars-CoV-2 (22–24).

1.4 COVID-19 challenges in dental practice

Most of dental treatments (periodontal, surgical, restorative and endodontic) are considered aerosols-generating procedures. The aerosol production at the office is mainly made via air-driven rotatory instruments, ultrasonic devices and airborne-particle abrasion units(25). Besides, the amount of aerosols produced is deemed superior than the permissible level and may be induced as far as 2m from patients' head(2). A study revealed that the saliva of more than 91% of patients with COVID-19 contain the Sars-CoV-2 virus(8). Likewise, many authors refer that dental practitioners are more prone to be contaminated by airborne transmitted microorganisms(2,25–27). Besides, the Occupational Safety and Health Administration evaluated dentists as "very high exposure risk" for COVID-19 occupational risk pyramid(25,28). Among dental professionals, it has been reported that endodontists are especially vulnerable because cameral access and pulp extirpation are believed to generate greater aerosols than surgical and restorative procedures(26). The virus might be viable in air suspensions for hours after dispersion and it can also last up to 72h after its application on plastic and stainless steel materials(29). During dental work practice, infected droplets and aerosol from patients 'saliva can reach equipment surfaces. Therefore, both instruments and worktops at the dental clinic should be considered as potential sources for Sars-CoV-2 transmission and contamination of any person located near the dental chair(1,25). It is more than ever of great importance to take preventive and protective measures.

COVID-19 disease has emerged recently and its influence on oral health, care and hygiene is still little-known by dentists. Also, the global pandemic and the three-months lockdown period changed the actual way of practicing dentistry and certainly also the profession in a more permanent manner. Renowned associations as the American Dental Association called for dental professionals to keep themselves informed about the disease and its effects on themselves and patients(30). The expectations for post-COVID-19 dental practice include safer working conditions for dentists and reinsuring practice for all patients' care. To comply those goals, official agencies for public health along with various authors published studies and recommendations for all the dental community.

2. OBJECTIVES

The purpose of this work is to provide dental caregivers and non-dental related professionals with consistent data about how COVID-19 impacted the field of dentistry.

Main objective:

1. To determine the effect of novel disease COVID-19 on oral health and dental practice.

Secondary objective:

2. To review COVID-19 oral manifestations and diagnosis.

3. METHODS

Articles were searched using PubMed, Wiley Online Library and SciELO databases including the search terms “covid-19”, “dentistry”, “sars-cov-2”, “coronavirus”, “oral”, “manifestation”, “dental”, “periodontitis” and “aerosols”. Official websites of the Center of Disease Control and Prevention, World Health Organization and the International Journal of Odontostomatology were also screened for published articles, recommendations, and guidelines. Original data from bibliographic sources of those articles have also been searched. Only human studies and reviews written in English and Spanish were used.

4. DISCUSSION

4.1 COVID-19 oral manifestations

4.1.1 Oral findings among COVID-19 patients

It has been suggested that the oral cavity could be a perfect niche for Sars-CoV-2 infection due to its special affinity for ACE2 receptors containing cells such as those of the oral mucosa, salivary glands and tongue(11,31). Various hypotheses were emitted on the pathway for the virus to enter the oral cavity(12). Firstly, it could be due to the exchange of droplets with already infected upper and lower respiratory tract organs. Secondly, it is suggested that infected blood can access the oral environment through the crevicular fluid that contains proteins derived from the serum. And finally, infected major and minor salivary glands may produce infected saliva which is later released in the oral cavity by salivary ducts. It is therefore not surprising that previously mentioned COVID-19 symptoms include alterations of taste sensations, smell and integrity of oral tissues. Ageusia and anosmia, the absence of taste and smell sensations respectively, was considered the first or only symptomatology present in COVID-19 patients(32). The association of oral lesions with COVID-19 disease has been studied and results were gathered in the table presented in **Table 2**. To date, few studies are available and they are cases reports, small series, and letters to editor. Nevertheless, they are relevant since they allow to assert the presence of oral lesions in COVID-19 patients the same way it can be found in other viral infections.

Concerning the type of lesions, ulcers are the most commonly mentioned. They were observed on tongue(33), on lip(34), hard palate(35) and on buccal mucosa(36). Together with herpetic and bullous lesions, ulcers are known to be associated with viral processes(31,35). Another oral symptom reported by patients was xerostomia or hyposalivation(18). The affectation of salivary glands by Sars-CoV-2 infection is suggested by the literature and their

Authors	Study type	Patients with OI (n)	Age (years)	Sars-CoV-2 infection	Results
Cebeci Kahraman et al.(37)	Case report	1	51	Confirmed	Erythematous hard palate with petechiae Soft palate pustular enanthema
Chaux-Bodard et al.(33)	Case report	1	45	Confirmed	Tongue ulcer
Ciccarese et al.(34)	Case report	1	19	Confirmed	Palatal and gingival petechiae and macules Erosions, ulcerations and crust on lip
Cruz-Tapia et al.(38)	Case series	4	47.2 (mean)	Confirmed	Erythematous bullous lesion on hard palate (1/4) Diffuse purple macule and plaque on palatal mucosa (1/4) Purple bullous lesion on ventral tongue (1/4) Multiple irregular erythematous macules on hard palate (1/4)
Díaz-Rodriguez et al.(18)	Case series	3	58 (mean)	Confirmed	Burning sensation (2/3) Commissural cheilitis (1/3) Xerostomia (1) Tongue depapillation (2/3) Glossitis with patchy depapillations (1/3) Aphtous stomatitis (1/3)
Jimenez-Cauhe et al.(39)	Case series	3	66.7 (mean)	Confirmed	Palatal petechiae and macular lesions (n=3)
Martín Carreras et al.(35)	Case series	3	59.7 (mean)	Suspected (n=2) or confirmed (n=1)	Lip blisters and desquamative gingivitis (1/3) Ulcers with erythematous halo on hard palate (2/3)

Table 2- Comparative table of studies results searching for oral manifestations among COVID-19 (or suspected) patients.

OI = oral involvement.

Authors	Study type	Patients with OI (n)	Age (years)	Sars-CoV-2 infection	Results
Nuño-Gonzalez et al.(19)	Case series	78	55.7 (mean)	Confirmed or COVID-19 associated bilateral pneumonia	Lingual papillitis (11.5%) Glossitis with lateral indentations (6.6%) Aphthous stomatitis (6.9%) Burning sensation (5.3%) Glossitis with patchy depapillations (3.9%) Mucositis (3.9%)
Soares et al.(36)	Case report	1	48	Confirmed	Multiple erythematous macules on lip, tongue and hard palate Ulcer in buccal mucosa

Table 2 (CONTINUED)- Comparative table of studies results searching for oral manifestations among COVID-19 (or suspected) patients.

OI = oral involvement.

.

alteration may lead to a decrease of salivary flow(40). Saliva is a biofluid rich in water, ions and proteins that plays an important role in immunity. Hyposalivation alters the equilibrium of the oral microbiota and contributes to immunosuppression(40). Thereby, it is believed that the appearance of ulcerous lesions and dysgeusia may be direct consequences of xerostomia by favorizing viral adhesion and colonization of oral tissues(31).

If most of oral lesions appeared to be located in keratinized tissue at the level of attached gingiva and hard palate, non-keratinized tissue is also affected. Macules and blisters were found in inner lip and ventral tongue(35,36). Palatal petechiae and erythematous macules were frequently reported and kindred to erythema multiform-like lesions(34,36–39). An example can be seen in **Figure 3B**. Aphtous stomatitis, glossitis with patchy depapillations (**Figure 3A**) and burning mouth sensation seem also present among patients infected by Sars-CoV-2 or suspected with COVID-19(18,19). Oropharyngeal candidiasis was studied on 1059 COVID-19 patients and found in 5% of them(41). Species identification revealed that 71% was due to C. albicans and that lymphopenia was the most common risk factor(41). The presence of fungal opportunistic infections is explained by the lowering of immune defenses among infected patients(31). Additionally, oral hygiene plays a role in the development of those infections as exogenous bacteria present in dental plaque increase the risk of oral flora imbalance(40). Also, a bad oral hygiene can be considered as a contributory factor to posterior complications of viral infections by increasing the risk of bacterial exchange with all the respiratory system(16,31). A possible association of COVID-19 with variable inflammatory reactions has been suggested to explain a vasculitis leading to the presence of an irregular ulcer on tongue(33) (**Figure 3C**).

Except in one case(34), the mean age of patients presenting oral symptoms was 45 years old and older. It is broadly known that it exists a correlation between the age and the consumption of pharmacological drugs. Yet, oral manifestations can appear as adverse effects of some treatments. The link between the presence of oral manifestations and adverse effects of drugs gave rise to some doubts about a possible bias(31,40). Thus, COVID-19 impact on oral health depends essentially on the patient's susceptibility and immune status, the pharmacological treatment he receives and the virus pathogenicity. At last, some authors remind that oral lesions could be the result of other factors such as stress due to social restrictions, work pressure and/or economic situation during COVID-19 pandemic lockdown.

Figure 3- **A.** Glossitis with patchy depapillations in a patient with suspected COVID-19(19). **B.** Multiple pinpoint ulcers with erythematous halo on left hard palate of confirmed COVID-19 patient(35). **C.** Irregular ulcer on tongue observed in a confirmed COVID-19 patient(33).

4.1.2 Periodontitis and COVID-19

Periodontal disease etiological factors include the presence of bacteria, *Prevotella intermedia* being the major etiological specie for severe periodontal lesions, bad oral hygiene and systemic diseases. They may appear in COVID-19 patients due to intra-oral bacterial co-infections. Indeed, periodontopathic bacteria were found present in the metagenome of Sars-CoV-2 infected patients with high reads for *P. intermedia*(16). Patel et al. reported a case of necrotizing periodontal disease in a 35-year-old patient with suspected Sars-CoV-2 infection(42). The reported signs and symptoms were necrotizing interdental papillae, severe halitosis, generalized erythematous inflamed and bleeding gingiva accompanied by intense gingival pain, and a history of 3 days prior fever. Both gingival and general symptoms completely resolved after 5 days antibiotic treatment with 400mg metronidazole 3 times/day which indicates that bacterial co-infections may influence the severity of COVID-19 disease(42). Periodontitis and COVID-19 share potentially exacerbating factors such as diabetes or cardiovascular diseases, and the probability of an association between these two has been investigated(43). Results show that periodontitis was positively associated with higher COVID-19 complications risk, intensive care unit admission, need for assisted ventilation, blood levels of biomarkers and death(43). As poor oral hygiene is an important risk factor for periodontal disease and it seem to be related with COVID-19 severe consequences, it is of great importance that COVID-19 patients keep a proper oral hygiene to limit the risk of post-viral complications(16).

4.1.3 Limitations

The bibliography used to write this section is limited to observational studies like case series and reports. All authors mentioned the difficulty to conclude their investigations and they agree that there is not enough evidence to strongly establish a cause-effect relationship between encountered oral conditions and the Sars-CoV-2 infection(18,44). The principal brought up reason would be the lack of oral cavity examination among infected patients by dentists or other professionals entitled to adequately diagnose oral conditions(44). Another mentioned cause is the decrease of number of patients attending dental facilities due to lockdowns, dental activity cessation worldwide for months in 2020 and its limitation to prioritize emergencies. The need for a complete oral examination of patients affected with COVID-19 is highly suggested in order to find out whether oral lesions are correlated with Sars-CoV-2. Further studies with higher scientific evidence strength are expected in the future to deal with this hypothesis. Furthermore, it lacks information about the nature and exact cause of oral pathologies reported and only few studies performed histological examination of oral biopsied lesions(36).

4.2 Practical guidelines to prevent transmission in dental clinic

Due to COVID-19 disease global pandemic, the WHO declared in August 2020 that non-essential dental care or “routine” care, should be postponed in order to avoid the virus transmission and propagation(45). ADA disagrees strongly with the WHO explaining that dentistry is essential health care, playing a crucial part in the evaluation, diagnosis and prevention of oral conditions that can affect systemic health(30). However, it is worth noting that protective measures must be used and changes in the way of practicing must be applied by dental workers if they want to be able to practice safely. Indeed, the transmission risk is difficult to evaluate since an asymptomatic Sars-CoV-2 carrier can contribute to spread the virus and the incubation period of the disease occurs within twelve days after exposure(46). ADA recommendation echoes the interim guidance of the Center for Disease Control and Prevention (CDC) for dentists that include two main prevention and infection control levels to follow during the pandemic(47,48): the infection prevention for routine dental care delivery and the dental care management of suspected or confirmed Sars-CoV-2 infected patients.

4.2.1 Measures to take in dental facility

A new reorganization of the dental healthcare facility is preconized(47). First of all, it includes an easy access to alcohol-based hand rub (at the entrance of the clinic, in the waiting room etc.), a body temperature checking of all patients attending the facility and the delivery of a questionnaire to be filled up, asking for COVID-19 symptoms and any probable recent exposure to the virus. This questionnaire should include information about epidemiological and clinical history of patients to classify them as low, intermediate or high transmission risk(49). The fever screening has to be accompanied with quick dental diagnosis to attend dental-related fever cases such as intraoral swelling or periapical pathologies. Any other patient presenting COVID-19 symptoms are asked to go home immediately, seek medical attention and to follow a strict quarantine procedure. The reorganization of the facility also consists of installing visual alerts -that can be posters for example- displaying instructions in easy language about how to perform appropriate hand hygiene, signs reminding the mandatory use of facemask, physical barriers like glass shield at the receptionist area, and two meters distancing of chairs in the waiting room. An appropriate ventilation system should be installed to maintain a negative pressure in the operating room or in the absence of this system, office windows should be open to allow a good circulation of the air(50). As well, it is highly recommended to remove any toys, magazines or other touched objects that may be present in the waiting areas. Superficial disinfection of potentially contaminated areas like the dental chair for example, should be cleaned between patients with 0.1% sodium hypochlorite, 0.5% hydrogen peroxide or 70% ethanol solutions(49). A schedule reorganization is finally proposed in order to minimize appointment overlapping.

4.2.2 Personal protective equipment

According to the FDA (U.S Food and Drugs Administration), are referred as personal protective equipment (PPE), “any equipment designed to protect the wearer from injury or the spread of infection or illness" such as protective clothing, helmets, gloves, face shields, eye protection, and facemasks. Concerning PPE used in dentistry during COVID-19 pandemic, the first measure is that all of the persons older than 2 years old and present in the facility should wear a facemask that covers nose and mouth, including workers in break rooms(47). Obviously, during the dental treatment the patient is allowed to remove it but has to put it back on immediately after leaving the dental chair. Apart from masks, foot and head covers, eye protection with goggles or face shields, surgical gowns and of course, single-use gloves are included in the PPE(8,47,48). N95 masks or equivalent are prioritized for healthcare professionals during their daily activity as they allow to minimize the risk of infection by offering a greater filtration power(2,51) (**Table 3**).

MASK TYPE	INFECTION RISK
 N95 mask	Minimized
 N95 equivalent mask: FFP2, KN/KP95	Minimized
 Surgical mask (Level 3)	May be elevated, depending on hazard

Table 3- Comparative table of mask types according to the infection risk. Data extracted from reference (51)

4.2.3 Changes in protocols to perform dental treatments

Before, during and after dental treatment, performing an adequate hand hygiene remains the first important measure to take. While using rotatory instruments, the use of rubber-dams, and 4-handed techniques with high velocity suction is advised in order to minimize aerosols(7,48,49). Likewise, some less aerosol-generating procedures alternatives are proposed. Manual scaling has to be prioritized rather than using ultrasonic devices(48) and hand curetting of caries whenever possible. Concerning the management of emergencies in the dental clinic, the preference goes to a pharmacological management of pain and infection, incisions and drainage(2). According to Patel et al., emergencies are the most often from endodontic nature. They proposed a pharmacological protocol depending on the diagnosis of the referred pain, which is exposed in **Table 4**.

DIAGNOSIS	PHARMACOLOGICAL MANAGEMENT	
	FIRST LINE	*SECOND LINE*
Symptomatic irreversible pulpitis ***Symptomatic apical periodontitis***	• IBUPROFEN 400-600mg + APAP 325-500mg OR • NAPROXEN SODIUM 220mg + APAP 500mg	• DEXAMETHASONE 0.07-0.09mg/kg • Consider placing long lasting local anesthetic or bupivacaine for immediate relief
Acute apical abscess	Intraoral and extraoral swelling: • AUGMENTIN 500mg/ CLINDAMYCIN 300mg AND • IBUPROFEN 400-600mg + APAP 325-500mg	

Table 4- Pharmacological treatment guidelines for endodontic emergencies- Original table with data extracted from(2). APAP= acetaminophen

Furthermore, it has been reported that non-surgical extractions could be performed instead of aerosol-generating treatment, but this approach is not-conservative and the possibility to correctly restore the tooth has to be evaluated(2). The use of extraoral radiography techniques such as Cone Beam Computed Tomography (CBCT) and panoramic X-rays is recommended instead of periapical radiographs that can provoke hypersalivation, coughing and nausea reflex(7,49). Various authors reported the use of disinfecting mouthwashes before the dental treatment(49,52,53). The evidence preconize the use of oxidative solutions such as 0.23% iodopovidone and 0.5-1% hydrogen peroxide for a 15 seconds to one minute mouthwash thanks to their antiviral capacity and apparent safety for oral tissues(49,52). Before oral examination or treatment, patients should be invited to mouthwash with iodopovidone or hydrogen peroxide as they help to reduce the viral load in the saliva. Besides, some authors reported that chlorhexidine mouthwashes do not seem to be effective to kill the virus(8,50). Finally, the use of one-use only instruments and devices is justified in the context of the pandemic(49).

Aside from all previous recommendations, dental healthcare providers are invited to regularly update themselves about local obligations and recommendations of the region in which they are practicing. It is stated that with appropriate PPE, hygiene measures and evaluation of the balance transmission risk/need for urgent care, dental care should continue to be delivered even under global pandemic conditions.

4.3 Odontopediatrics and COVID-19

COVID-19 disease in children is unlikely to provoke lower respiratory tract infection compared to adults. Pediatric patients are usually asymptomatic or presenting mild symptoms, immunosuppression or underlying diseases being predictors of severity(50,54). A study conducted in China on children (<19 years old) with confirmed or suspected Sars-CoV-2 infection revealed that 90% of them did present mild form of the disease or no symptoms at all(54,55). However, they may be carriers of the virus to older people, including their dentist. If the pediatric dentist should follow the general guidelines for dental practitioners enumerated in part **4.2**, young patients are also encouraged to wear protective coveralls. In this regard, their experience at the dental clinic may be improved as they are more comfortable and less fearful being dressed like the dental staff(50).

One of the actual challenges in pediatric dentistry is to maintain the access to preventive dental care which represents a high proportion of the pediatric dentist activity(50). It is relevant, indeed, because the combination of dental care privation together with the stressful situation brought up by COVID-19 global pandemic might negatively affect children oral health. It is believed that a change in habits and diet may be observed during the following months, and pediatric patients may rapidly fall into moderate to high caries risk, being in need of appropriate treatment and fluoride application every 3 or 6 months. Teledentistry was reported as a useful alternative to face-to-face appointments(50,54). During these visio chats, the pediatric dentist can talk with parents and children to give oral hygiene instructions, and interestingly, new technologies-based meetings are fun for young patients and may help to increase observance. Also, some preventive treatments such as the application of fluoride varnish can be performed by the parents under the supervision of the dentist. Some odontopediatrics treatments were reported to be safe during COVID-19 pandemic, as they are considered low transmission risk while performed following the previous recommendations and under rubber dam use. Among them, the sealing of early carious lesions with fissure sealants placement, atraumatic restorative treatment, selective caries removal and the Hall technique were reported(54). The Hall technique has been brought up as it constitutes an atraumatic approach where a metallic crown is placed over a selectively caries-excavated tooth to restore it.

4.4 Dental education during COVID-19 pandemic

Since the beginning of the global pandemic, dental schools and clinical practices are also widely affected. They were regularly suspended depending on each country situation regarding COVID-19 number of contagions and have been in need to manage increasing anxiety among students and patients(56). Online lectures, preclinical simulation laboratory activities, case studies and resolving tutorials were part of adopted measures to avoid unnecessary accumulation of students, teachers and patients together in close spaces(7,56). Problem-based learning approaches has been shown to enable students to understand important concepts based on critical thinking(56). Dental schools are therefore invited to re-evaluate their competency-based education and to permanently incorporate e-learning in their curricula which could be of use if further pandemics arise. To improve psychomotor skills of students that cannot perform practices in clinic, haptic technology such as the Simodont (Nissin) is proposed(56). However, and despite the implemented efforts from dental education administrations, the lack of direct patient care which is a key component of the dental curriculum, may directly impact newly graduated dentists for the beginning of their professional life. Interestingly, webinars and online courses are booming. They are of great utility to promote self-learning and up-to-date about last developments in the field of dentistry for all the dental community(7). They also encourage cases and techniques exchanges between dental professionals all over the world and students. The number of articles and publications also increased last year (2020) as authors have had more time and resources to write and study during lockdowns.

4.5 The future of dental profession

Despite the prevention measures adopted worldwide, the number of COVID-19 cases does not decrease and the pandemic is not likely to end soon, forcing dentistry field to adapt itself to the everchanging actual situation. After more than one year living during a global pandemic, the hope of a setting back is closer than ever and especially thanks to the development and testing of promising COVID-19 vaccine(57). However, the dental practitioner should be able to adapt itself to any other future crisis. Possibly, and according to what has been observed in multiple publications and reports from different health associations across the world, carrying out a remote diagnosis of patient's general and oral health conditions through tele-dentistry, wearing PPE like masks and overalls, performing a temperature control, footwear and hand disinfection, among others, will be common procedures in future clinical dental practice(58). In this complex context, the development of new preventive tools, better aspiration systems, more efficient disinfection agents and more comfortable PPE will probably arise.

The dentist of the future, post COVID-19 pandemic will require new abilities, starting by the global observation of the patient in the reality of its biopsychosocial environment to use that information as a tool to facilitate oral health education(58). The correct and indispensable use of PPE as well as new technology abilities might probably also be part of the post-COVID-19 dentist's skills. Therefore, it is of the utmost importance that higher education institutions, dental schools and faculties act quickly and proactively in the re-evaluation of their educative programs to include new protective measures and technology savvy for undergraduate and postgraduate students. In conclusion, the pandemic could revolutionize the dentistry field, promoting the use of minimally invasive treatments or the development of new tools to perform a virus-proof dental activity for example.

Tele-dentistry

Seldomly used before 2020, telehealth services are one of the changes in healthcare delivery that has known a real breakthrough during the COVID-19 pandemic. It is promoted to provide assistance to patients while minimizing the risk of contagion for medical staff(59). In odontology, a telephone screen-based triage protocol of patients can be a useful tool within the scope of the epidemic(47). It consists on calling all patients needing dental care to screen any COVID-19 symptoms and to assess the urgency of their dental situation. This method permits to filter scheduled patients that would need to be seen at the office urgently and the ones for which the treatment can be delayed without damage for their health conditions. According to the CDC, the in-office treatment of patients that present symptoms of COVID-19 or being at risk of Sars-CoV-2 infection should be postponed whenever possible until the end of their isolation period(47). The pre-appointment call is also a way to remind patients to not forget preventive measures such as attending the dental clinic alone (with the exceptions of children, elderly and disabled that can be accompanied), the mandatory body temperature checking and use of a facemask inside the facility.

Moreover, video conferencing in dentistry allows patient to dentist interactions for quick diagnosis, counseling and oral health recommendations, follow-ups, drugs prescriptions and dose adjustments if needed(59). Educational videos can also be uploaded in social media to remain our patients the importance of oral health(50). It is of precious help to keep social distancing and mainly for isolated patients or patients with limited mobility. However, telehealth is more used in medicine than in dentistry because dental care usually requires physical interventions inside the oral cavity. It remains restrictive, especially when it comes to perform intraoral examinations or complementary diagnostical testing like radiographs or vitality checkups for example. Finally, it is important to note that offering tele-dentistry depends on the comfort of patients and dentist with new technologies and that they both own a computer or tablet with internet access.

6. RESPONSABILITY

WHO guidelines for the prevention of COVID-19 in the dental clinic clearly indicate that PPE like surgical mask, gown and gloves should be discarded and that high touched surfaces such as door handles, chairs, phones, computer, and reception desks should be cleaned after every patient(45). We may question ourselves on the impact that the daily use of disposable equipment and chemical disinfection products can have on the environment. Additionally, it is interesting for the healthcare provider to weight the pros and cons between providing certain treatments and the risk he may take to be infected and posteriorly transmit the virus to his relatives. This constitutes a moral decision that post-COVID-19 dentists should consider.

Dental clinic workflow found itself deeply affected by the global pandemic context because the production chain, communication with prosthetic laboratories and the number of patients attending the clinic was troubled. Therefore, dental teams should take new measures, include changes in their working protocols and adapt themselves to the reality that our everchanging world and society have brought to us.

7. CONCLUSIONS

1. Dental professions are considered high risk activities for Sars-CoV-2 transmission due to the specificity of their procedures that include face-to-face visits, exposition to blood and saliva and aerosols-generating treatments.
2. Recommendations have been established to limit that risk and dentists are invited to take measures in dental facilities as well as during dental treatments, to prioritize emergencies visits and the use of teledentistry is highly promoted.
3. The future of the dental profession is altered and urgently requires an adaptation of the healthcare provider to our society needs for post-pandemic times.
4. Face-to-face intraoral examination of COVID-19 patients is relevant as the disease seems to cause the apparition of a wide range of lesions inside the oral cavity, taking various presentations, leading to general and local implications. Still, it lacks evidence on whether if the oral manifestations reported are part of COVID-19 semiology, if they are due to the immunodepression generated by the Sars-CoV-2 infection, or by COVID-19 treatments.

REFERENCES

1. Checchi V, Bellini P, Bencivenni D, Consolo U. COVID-19 Dentistry-related aspects: a literature overview. International Dental Journal. 2021;7:21-26.

2. Patel B, Eskander M, Ruparel N. To drill or not to rill: management of endodontic emergencies and in-process patients during the COVID-19 pandemic. Journal of Endodontics. 2020;46:1559-1569.

3. World Health Organization. Novel Coronavirus(2019-nCoV). 2020.

4. WHO Coronavirus (COVID-19) Dashboard [Internet]. Covid19.who.int. 2021. Available from: https://covid19.who.int/

5. Zhou P, Yang X, Wang X, Hu B, Zhang L, Zhang W et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579:270-273.

6. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395:507-513.

7. Meng L, Hua F, Bian Z. Coronavirus Disease 2019 (COVID-19): emerging and future challenges for dental and oral medicine. Journal of Dental Research. 2020;99:481– 487.

8. Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. International Journal of Oral Science. 2020;12.

9. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Science China Life Sciences. 2020;63:457-460.

10. Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science. 2020;367:1444-1448.

11. 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. International Journal of Oral Science. 2020;12(1).

12. Sabino-Silva R, Jardim A, Siqueira W. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. Clinical Oral Investigations. 2020;24:1619-1621.

13. Xie X, Li Y, Chwang A, Ho P, Seto W. How far droplets can move in indoor environments – revisiting the Wells evaporation–falling curve. Indoor Air. 2007;17:211-225.

14. Kwon S, Park J, Jang J, Cho Y, Park D, Kim C et al. Study on the initial velocity distribution of exhaled air from coughing and speaking. Chemosphere. 2012;87:1260-1264.

15. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. Aging. 2020;12:6049-6057.

16. Sampson V, Kamona N, Sampson A. Could there be a link between oral hygiene and the severity of SARS-CoV-2 infections? British Dental Journal. 2020;228:971-975.

17. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al. Clinical characteristics of 138 hospitalized patients wwith 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323:1061.

18. Díaz Rodríguez M, Jimenez Romera A, Villarroel M. Oral manifestations associated with COVID-19. Oral Diseases. 2020;1-3.

19. Nuno-Gonzalez A, Martin-Carrillo P, Magaletsky K, Martin Rios M, Herranz Mañas C, Artigas Almazan J et al. Prevalence of mucocutaneous manifestations in 666 patients with COVID-19 in a field hospital in Spain: oral and palmoplantar findings. British Journal of Dermatology. 2020;184:184-185.

20. Kansas Department of Health and Environment. Symptoms in adults: Covid-19 vs. cold vs. flu vs. allergies. 2020.

21. Dai W, Zhang H, Yu J, Xu H, Chen H, Luo S et al. CT Imaging and differential diagnosis of COVID-19. Canadian Association of Radiologists' Journal. 2020;20:1-6.

22. Cevik M, Bamford C, Ho A. COVID-19 pandemic—a focused review for clinicians. Clinical Microbiology and Infection. 2020;26:842-847.

23. Scavone C, Brusco S, Bertini M, Sportiello L, Rafaniello C, Zoccoli A et al. Current pharmacological treatments for COVID-19: What's next? British Journal of Pharmacology. 2020;177:4813-4824.

24. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A. Compassionate use of remdesivir for patients with severe Covid-19. The New England Journal of Medicine. 2020;382:2327-2336.

25. Mupparapu M. Editorial: Aerosol reduction urgency in post-COVID-19 dental practice. Quintessence international. 2020;51:525-526.

26. Manarte-Monteiro P, Carvalho A, Pina C, Oliveira H, Manso M. Air quality assessment during dental practice: aerosols bacterial counts in an universitary clinic. Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial. 2013;54:2-7.

27. Rivera C. Los aerosoles dentales a propósito de la pandemia por COVID-19. International journal of odontostomatology. 2020;14:519-522.

28. US Department of Labor. Guidance on preparing workplaces for COVID-19. Occupational Safety and Health Administration; 2020.

29. Van Doremalen N, Bushmake T, Morris D. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. The New England Journal of Medicine. 2020;382:1564-1567.

30. American Dental Association. American dental association responds to world health organization recommendation: dentistry is essential health care [Internet]. 2020. Available from: https://www.ada.org/en/press-room/news-releases/2020-archives/august/american-dental-association-dentistry-is-essential-health-care

31. Nemeth-Kohanszky M, Matus-Abásolo C, Carrasco-Soto R. Manifestaciones orales de la infección por COVID-19. International journal of odontostomatology. 2020;14:555-560.

32. Vaira L, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: common findings in COVID -19 patients. The Laryngoscope. 2020;130:1787-1787.

33. Chaux-Bodard A, Deneuve S, Desoutter A. Oral manifestation of Covid-19 as an inaugural symptom?. Journal of Oral Medicine and Oral Surgery. 2020;26:18.

34. Ciccarese G, Drago F, Boatti M, Porro A, Muzic S, Parodi A. Oral erosions and petechiae during SARS-CoV-2 infection. Journal of Medical Virology. 2020;93:129-132.

35. Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez A, Jané-Salas E, Somacarrera Pérez M. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. Oral Diseases. 2020;27:710-712.

36. Soares C, Carvalho R, Carvalho K, Carvalho M, Almeida O. Letter to Editor: Oral lesions in a patient with Covid-19. Medicina Oral Patología Oral y Cirugia Bucal. 2020;563-564.

37. Cebeci Kahraman F, Çaşkurlu H. Mucosal involvement in a COVID -19-positive patient: a case report. Dermatologic Therapy. 2020;33.

38. Cruz Tapia R, Peraza Labrador A, Guimaraes D, Matos Valdez L. Oral mucosal lesions in patients with SARS-CoV-2 infection. Report of four cases. Are they a true sign of COVID-19 disease?. Special Care in Dentistry. 2020;40:555-560.

39. Jimenez-Cauhe J, Ortega-Quijano D, Carretero-Barrio I, Suarez-Valle A, Saceda-Corralo D, Moreno-Garcia del Real C et al. Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings. Clinical and Experimental Dermatology. 2020;45:892-895.

40. Pedrosa M, Sipert C, Nogueira F. Salivary Glands, saliva and oral findings in COVID-19 infection. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2020;20.

41. Salehi M, Ahmadikia K, Mahmoudi S, Kalantari S, Jamalimoghadamsiahkali S, Izadi A et al. Oropharyngeal candidiasis in hospitalised COVID-19 patients from Iran: species identification and antifungal susceptibility pattern. Mycoses. 2020;63:771-778.

42. Patel J, Woolley J. Necrotizing periodontal disease: oral manifestation of COVID-19. Oral Diseases. 2020;27:768-769.

43. Marouf N, Cai W, Said K, Daas H, Diab H, Chinta V et al. Association between periodontitis and severity of COVID-19 infection: a case–control study. Journal of Clinical Periodontology. 2021.

44. Cornejo-Ovalle M, Espinoza-Santander I. COVID-19 y manifestaciones orales. International Journal of Odontostomatology. 2020;14:538-539.

45. World Health Organization. Considerations for the provision of essential oral health services in the context of COVID-19 [Internet]. 2020:1-5. Available from: https://www.who.int/publications/i/item/who-2019-nCoV-oral-health-2020.1

46. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. The England Journal of Medicine. 2020;382:1199-1207.

47. Centers for Disease Control and Prevention. Interim infection prevention and control guidance for dental settings during the coronavirus disease 2019 (COVID-19) Pandemic [Internet]. 2020. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/dental-settings.html

48. American Dental Association. CDC Guidance for dental settings Echoes ADA guidance [Internet]. 2020. Available from: https://www.ada.org/en/press-room/news-releases/2020-archives/may/cdc-guidance-for-dental-settings-echoes-ada-guidance

49. Falcón-Guerrero B, Falcón-Pasapera G. Medidas para prevenir el COVID-19 en el consultorio dental. International Journal of Odontostomatology. 2020;14:468-473.

50. Bahramian H, Gharib B, Baghalian A. COVID-19 considerations in pediatric dentistry. JDR Clinical & Translational Research. 2020;5:307-311.

51. American Dental Association. Interim mask and face shield guidance. 2020.

52. Méndez J, Villasanti U. Uso de peróxido de hidrógeno como enjuague bucal previo a la consulta dental para disminuir la carga viral de COVID-19. Revisión de la literatura. International Journal of Odontostomatology. 2020;14:544-547.

53. Santos-López M, Jaque D, Fuentes E, González-Quintanilla D. Mouthwashes and nasal sprays as a way to prevent the spread of SARS-CoV-2. International Journal of Odontostomatology. 2020;14:513-518.

54. Mallineni S, Innes N, Raggio D, Araujo M, Robertson M, Jayaraman J. Coronavirus disease (COVID-19): characteristics in children and considerations for dentists providing their care. International Journal of Paediatric Dentistry. 2020;30:245-250.

55. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. The Lancet Infectious Diseases. 2020;20:911-919.

56. Iyer P, Aziz K, Ojcius D. Impact of COVID-19 on dental education in the United States. Journal of Dental Education. 2020;84:718-722.

57. Voysey M, Pollard A. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet. 2020;396:1486-1487.

58. Pérez V, Díaz J, Rojas S, Onetto J. El odontopediatra del futuro para tiempos post COVID-19. International journal of interdisciplinary dentistry. 2020;13:57-58.

59. Centers for Disease Control and Prevention. Using telehealth to expand access to essential health services during the COVID-19 pandemic [Internet]. 2020. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/telehealth.html

International Dental Journal
doi: 10.1111/idj.12601

COVID-19 dentistry-related aspects: a literature overview

Vittorio Checchi, Pierantonio Bellini, Davide Bencivenni and Ugo Consolo

Unit of Dentistry and Oral-Maxillo-Facial Surgery, Department of Surgery, Medicine, Dentistry and Morphological Sciences with Transplant Surgery, Oncology and Regenerative Medicine Relevance, University of Modena and Reggio Emilia, Modena, Italy.

A new coronavirus (Sars-CoV-2) was detected in China at the end of 2019 and has since caused a worldwide pandemic. This virus is responsible for an acute respiratory syndrome (COVID-19), distinguished by a potentially lethal interstitial bilateral pneumonia. Because Sars-CoV-2 is highly infective through airborne contamination, the high infection risk in the dental environment is a serious problem for both professional practitioners and patients. This literature overview provides a description of the clinical aspects of COVID-19 and its transmission, while supplying valuable information regarding protection and prevention measures.

Key words: *Coronavirus, 2019-nCoV, Sars-CoV-2, COVID-19, cross infections, personal protective equipment, dental environment*

INTRODUCTION

At the end of 2019, the first cases of a pulmonary disease of unknown aetiology were detected in Wuhan City, China. In the following months, this new pathogen spread throughout Europe and then worldwide; in March 2020, the World Health Organization (WHO) officially declared a pandemic alert.

This new virus, highly infective especially through airborne transmission, is responsible for an acute respiratory syndrome, distinguished by an often asymptomatic, but potentially lethal, interstitial bilateral pneumonia[1]. This virus, initially named 2019-nCoV and subsequently renamed Sars-CoV-2, belongs to the *Coronoviridae* family, along with the Middle East respiratory syndrome (MERS-CoV) and the severe acute respiratory syndrome (SARS-CoV) viruses[2]. The most updated epidemiological and genetic studies performed on infected Chinese patients revealed that this pandemic originated from a zoonosis, after a single transmission event between an animal and a human, followed by subsequent, rapid interhuman diffusion[1,3].

Sars-CoV-2 expresses membrane proteins that permit adhesion between it and specific receptors expressed on the surface of host tissue cells[4]. The most common receptor involved in the virus–cell interaction is angiotensin-converting enzyme 2 (ACE-2), which is present at high concentrations in lungs, myocardial cells and kidney, as well as on oral mucosa (especially of the salivary glands and tongue)[5,6]. These structures have been considered as early targets of Sars-CoV-2, with infection causing a disease in humans known as Corona Virus Disease 19 (COVID-19)[7].

The main infection pathways of Sars-CoV-2 are air and direct contact[1]. Airborne infection occurs through droplets released by coughing, sneezing, exhalation or speech[1,8]; direct-contact infection occurs through contact with contaminated surfaces and subsequent touching of the eyes, nose or mouth[8] (*Figure 1*). Saliva also plays a crucial role in the spread of infection, through both airborne and direct-contact pathways[1].

The incubation period of Sars-CoV-2 varies between 3 and 14 days; however, a 24-day incubation period has also been reported[9]. In most instances, the infection brought on by this new coronavirus is asymptomatic or causes few symptoms[2]. Infected patients mainly exhibit night fever, dry cough, sore throat and asthenia; patients with more severe disease can exhibit dyspnea. The most severe symptoms occur in 15%–25% of infected patients, with a relevant impairment of respiratory function that leads to hospitalisation and assisted ventilation[2]. From a clinical perspective, this infection presents as a bilateral interstitial pneumonia, detected radiographically as bilateral ground-glass opacity[10,11].

COVID-19 diagnosis is based on clinical symptoms (e.g., asthenia, dyspnea, headache and hyperpyrexia) and epidemiological aspects, particularly involving

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/Pe03mD.

CLINICAL RESEARCH

To Drill or Not to Drill: Management of Endodontic Emergencies and In-Process Patients during the COVID-19 Pandemic

Biraj Patel, BDS, Michael A. Eskander, DDS, PhD, and Nikita B. Ruparel, MS, DDS, PhD

ABSTRACT

Introduction: Dental professionals are at high risk of contracting coronavirus disease 2019 (COVID-19) infection because of their scope of practice with aerosol-generating procedures. Recommendation by the Centers for Disease Control and Prevention to suspend elective dental procedures and avoid aerosol-generating procedures posed significant challenges in the management of patients presenting with endodontic emergencies and uncertainty of outcomes for endodontic procedures initiated, but not completed, before shutdown. The purpose of this study was to evaluate the success of palliative care on endodontic emergencies during the COVID-19 pandemic and to evaluate the stability of teeth with long-term $Ca(OH)_2$ placement because of delays in treatment completion. **Methods:** Patients presenting for endodontic emergencies during COVID-19 Shelter-in-Place orders received palliative care, including pharmacologic therapy and/or non–aerosol-generating procedural interventions. Part I of the study evaluated the effectiveness of palliative care, and need for aerosol-generating procedures or extractions was quantified. Part II of the study evaluated survivability and rate of adverse events for teeth that received partial or full root canal debridement and placement of calcium hydroxide before shutdown. **Results:** Part I: Twenty-one patients presented with endodontic emergencies in 25 teeth during statewide shutdown. At a follow-up rate of 96%, 83% of endodontic emergencies required no further treatment or intervention after palliative care. Part II: Thirty-one teeth had received partial or full root canal debridement before statewide shutdown. Mean time to complete treatment was 13 weeks. At a recall rate of 100%, 77% of teeth did not experience any adverse events due to delays in treatment completion. The most common adverse event was a fractured provisional restoration (13%), followed by painful and/or infectious flare-up (6.4%), which were managed appropriately and therefore seemed successful. Only 1 tooth was fractured and nonrestorable (3%), leading to a failed outcome of tooth extraction. The remaining 4 outcome failures (13%) were due to patient unwillingness to undergo school-mandated COVID testing or patient unwillingness to continue treatment because of perceived risk of COVID infection. **Conclusions:** Palliative care for management of endodontic emergencies is a successful option when aerosol-generating procedures are restricted. This treatment approach may be considered in an effort to reduce risk of transmission of COVID-19 infection during subsequent shutdowns. Prolonged $Ca(OH)_2$ medicament because of COVID-19 related delays in treatment completion appeared to have minimal effect on survival of teeth. *(J Endod 2020;46:1559–1569.)*

KEY WORDS

Aerosol-generating procedure; COVID-19; endodontic emergencies; long-term calcium hydroxide; palliative care

SIGNIFICANCE

Palliative care for management of endodontic emergencies is a successful option when aerosol-generating procedures are restricted.

From the Department of Endodontics, University of Texas Health Science Center at San Antonio, San Antonio, Texas

Address requests for reprints to Dr Nikita B. Ruparel, Department of Endodontics, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78229.
E-mail address: ruparel@uthscsa.edu
0099-2399/$ - see front matter

https://doi.org/10.1016/j.joen.2020.08.008

Novel Coronavirus(2019-nCoV)
Situation Report – 22

Data as reported by 11 February 2020*

HIGHLIGHTS

- No new countries reported cases of 2019-nCoV in the past 24 hours.

- An advanced team is currently in Beijing to prepare an international mission and to determine the questions the international team will want to learn more about: from characteristics of the virus to public health response China put in place to try to contain the virus. The group of international experts, with a range of specializations, will work with Chinese counterparts on increasing understanding of the outbreak to guide global response efforts. Since being notified of the outbreak on 31 December, the WHO Country Office in China, supported by the regional and international offices, has worked to support China, and indeed the world, to scale up the response. A small mission was sent to Wuhan mid-January, and the Director-General visited in January.

- Following WHO best practices for naming of new human infectious diseases, which were developed in consultation and collaboration with the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO), WHO has named the disease COVID-19, short for "coronavirus disease 2019."

SITUATION IN NUMBERS
total and new cases in last 24 hours

Globally
43 103 confirmed (2560 new)

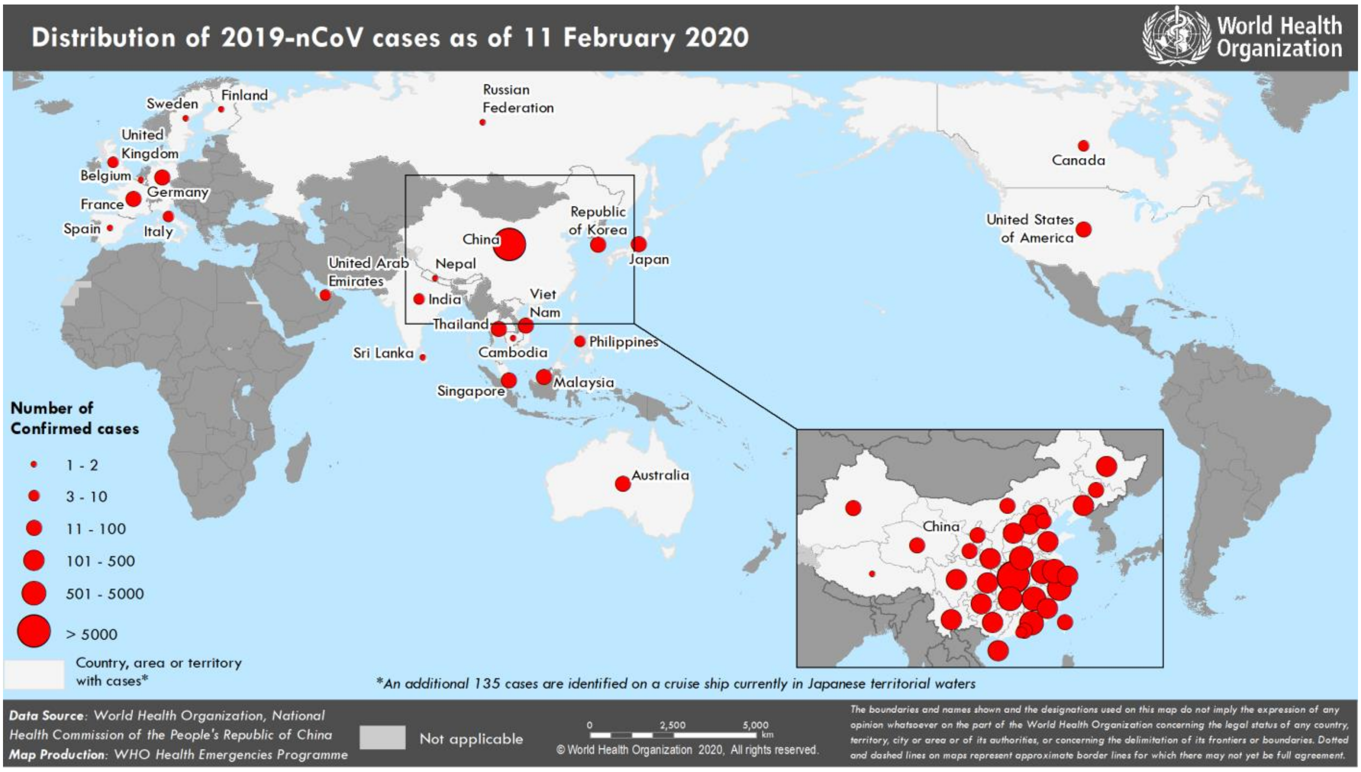
China
42 708 confirmed (2484 new)
7333 severe (849 new)
1017 deaths (108 new)

Outside of China
395 confirmed (76 new)
24 countries
1 death

WHO RISK ASSESSMENT

China	Very High
Regional Level	High
Global Level	High

Figure 1. Countries, territories or areas with reported confirmed cases of 2019-nCoV, 11 February 2020



*The situation report includes information provided by national authorities as of 10 AM Central European Time

World Health Organization

Search by Country, Territory, or Area

Covid-19 Response Fund

Donate

WHO Coronavirus (COVID-19) Dashboard

Overview | Data Table | Explore

Cases

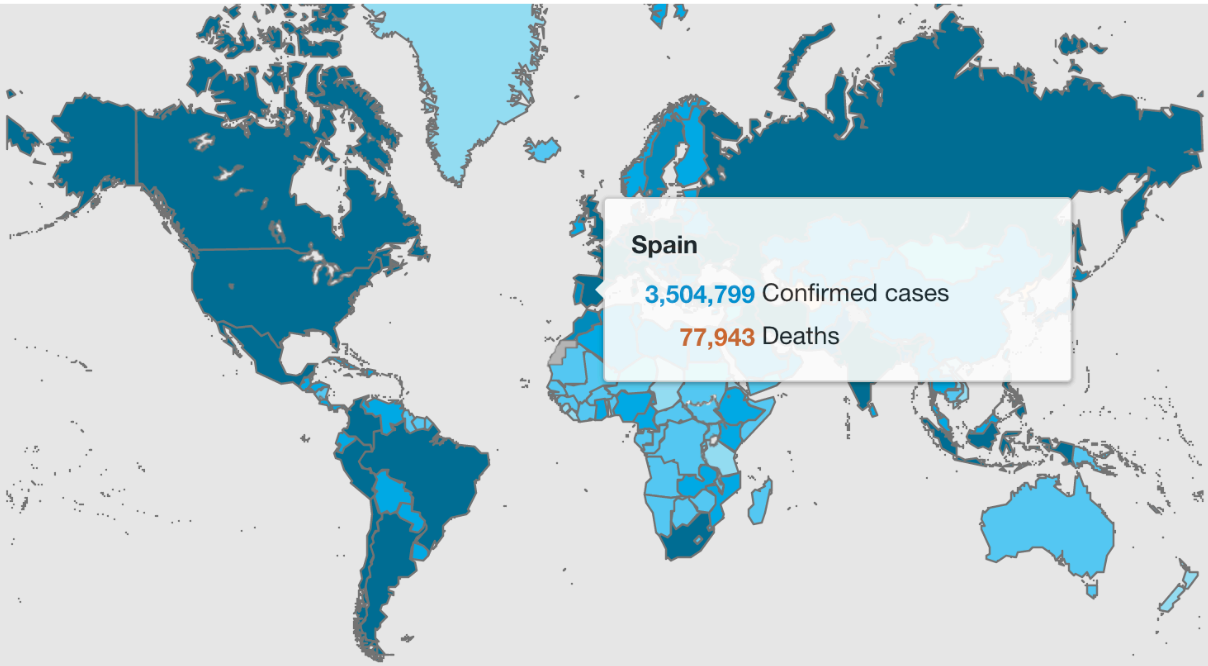
Total

692,879 new cases

149,910,744 confirmed cases

3,155,168 deaths

968,452,196 vaccine doses administered



Download Map Data

Globally, as of **11:59am CEST, 30 April 2021**, there have been **149910744 confirmed cases** of COVID-19, including **3155168 deaths**, reported to WHO. As of **29 April 2021**, a total of **968452196 vaccine doses** have been administered.

Article

A pneumonia outbreak associated with a new coronavirus of probable bat origin

https://doi.org/10.1038/s41586-020-2012-7

Received: 20 January 2020

Accepted: 29 January 2020

Published online: 3 February 2020

Open access

Peng Zhou[1,5], Xing-Lou Yang[1,5], Xian-Guang Wang[2,5], Ben Hu[1], Lei Zhang[1], Wei Zhang[1], Hao-Rui Si[1,3], Yan Zhu[1], Bei Li[1], Chao-Lin Huang[2], Hui-Dong Chen[2], Jing Chen[1,3], Yun Luo[1,3], Hua Guo[1,3], Ren-Di Jiang[1,3], Mei-Qin Liu[1,3], Ying Chen[1,3], Xu-Rui Shen[1,3], Xi Wang[1,3], Xiao-Shuang Zheng[1,3], Kai Zhao[1,3], Quan-Jiao Chen[1], Fei Deng[1], Lin-Lin Liu[4], Bing Yan[1], Fa-Xian Zhan[4], Yan-Yi Wang[1], Geng-Fu Xiao[1] & Zheng-Li Shi[1]*

Since the SARS outbreak 18 years ago, a large number of severe acute respiratory syndrome-related coronaviruses (SARSr-CoV) have been discovered in their natural reservoir host, bats[1–4]. Previous studies indicated that some of those bat SARSr-CoVs have the potential to infect humans[5–7]. Here we report the identification and characterization of a novel coronavirus (2019-nCoV) which caused an epidemic of acute respiratory syndrome in humans in Wuhan, China. The epidemic, which started from 12 December 2019, has caused 2,050 laboratory-confirmed infections with 56 fatal cases by 26 January 2020. Full-length genome sequences were obtained from five patients at the early stage of the outbreak. They are almost identical to each other and share 79.5% sequence identify to SARS-CoV. Furthermore, it was found that 2019-nCoV is 96% identical at the whole-genome level to a bat coronavirus. The pairwise protein sequence analysis of seven conserved non-structural proteins show that this virus belongs to the species of SARSr-CoV. The 2019-nCoV virus was then isolated from the bronchoalveolar lavage fluid of a critically ill patient, which can be neutralized by sera from several patients. Importantly, we have confirmed that this novel CoV uses the same cell entry receptor, ACE2, as SARS-CoV.

Coronavirus has caused two large-scale pandemic in the last two decades, SARS and MERS (Middle East respiratory syndrome)[8,9]. It was generally believed that SARSr-CoV, mainly found in bats, might cause future disease outbreak[10,11]. Here we report on a series of unidentified pneumonia disease outbreaks in Wuhan, Hubei province, central China. Started from a local seafood market, the outbreak has grown substantial to infect 2050 people in China with 56 deaths and to infect 35 people in 11 other countries up to January 26, 2020[12]. Typical clinical symptoms of these patients are fever, dry cough, dyspnea, headache, and pneumonia. Disease onset may result in progressive respiratory failure due to alveolar damage (as observed by transverse chest CT images) and even death. The disease was determined as viral induced pneumonia by clinicians according to clinical symptoms and other criteria including body temperature rising, lymphocytes and white blood cells decreasing (sometimes normal for the later), new pulmonary infiltrates on chest radiography, and no obvious improvement upon three days antibiotics treatment. It appears most of the early cases had contact history with the original seafood market, but the disease progressed to human-to-human transmission now.

Samples from seven patients with severe pneumonia (six are seafood market sellers or delivers), who were enrolled in intensive unit cares at the beginning of the outbreak, were sent to WIV laboratory for pathogen diagnosis (Extended Data Table 1). As a CoV lab, we first used pan-CoV PCR primers to test these samples[13], considering the outbreak happened in winter and in a market, same environment as SARS. We found five PCR positive. A sample (WIV04) collected from bronchoalveolar lavage fluid (BALF) was analysed by metagenomics analysis using next-generation sequencing (NGS) to identify potential etiological agents. Of the 10,038,758 total reads, or 1582 total reads obtained after human genome filtering, 1378 (87.1%) matched sequences of SARSr-CoV (Fig. 1a). By *de novo* assembly and targeted PCR, we obtained a 29,891-bp CoV genome that shared 79.5% sequence identity to SARS-CoV BJ01 (GenBank accession number AY278488.2). High genome coverage was obtained by remapping the total reads to this genome (Extended Data Figure 1). This sequence has been submitted to GISAID (accession no. EPI_ISL_402124). Following the name by WHO, we tentatively call it novel coronavirus 2019 (2019-nCoV). Four more full-length genome sequences of 2019-nCoV (WIV02, WIV05, WIV06, and WIV07) (GISAID accession nos. EPI_ISL_402127-402130) that were above 99.9% identical to each other were subsequently obtained from other four patients using NGS and PCR (Extended Data Table 2).

The virus genome consists of six major open reading frames (ORFs) common to coronaviruses and a number of other accessory genes (Fig. 1b). Further analysis indicates that some of the 2019-nCoV genes shared less than 80% nt sequence identity to SARS-CoV. However, the seven conserved replicase domains in ORF1ab that were used for

[1]CAS Key Laboratory of Special Pathogens, Wuhan Institute of Virology, Center for Biosafety Mega-Science, Chinese Academy of Sciences, Wuhan, People's Republic of China. [2]Wuhan Jinyintan Hospital, Wuhan, China. [3]University of Chinese Academy of Sciences, Beijing, People's Republic of China. [4]Hubei Provincial Center for Disease Control and Prevention, Wuhan, People's Republic of China. [5]These authors contributed equally: Peng Zhou, Xing-Lou Yang, Xian-Guang Wang. *e-mail: zlshi@wh.iov.cn

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study

Nanshan Chen, Min Zhou*, Xuan Dong*, Jieming Qu*, Fengyun Gong, Yang Han, Yang Qiu, Jingli Wang, Ying Liu, Yuan Wei, Jia'an Xia, Ting Yu, Xinxin Zhang, Li Zhang*

Summary

Background **In December, 2019, a pneumonia associated with the 2019 novel coronavirus (2019-nCoV) emerged in Wuhan, China. We aimed to further clarify the epidemiological and clinical characteristics of 2019-nCoV pneumonia.**

Methods **In this retrospective, single-centre study, we included all confirmed cases of 2019-nCoV in Wuhan Jinyintan Hospital from Jan 1 to Jan 20, 2020. Cases were confirmed by real-time RT-PCR and were analysed for epidemiological, demographic, clinical, and radiological features and laboratory data. Outcomes were followed up until Jan 25, 2020.**

Findings **Of the 99 patients with 2019-nCoV pneumonia, 49 (49%) had a history of exposure to the Huanan seafood market. The average age of the patients was 55·5 years (SD 13·1), including 67 men and 32 women. 2019-nCoV was detected in all patients by real-time RT-PCR. 50 (51%) patients had chronic diseases. Patients had clinical manifestations of fever (82 [83%] patients), cough (81 [82%] patients), shortness of breath (31 [31%] patients), muscle ache (11 [11%] patients), confusion (nine [9%] patients), headache (eight [8%] patients), sore throat (five [5%] patients), rhinorrhoea (four [4%] patients), chest pain (two [2%] patients), diarrhoea (two [2%] patients), and nausea and vomiting (one [1%] patient). According to imaging examination, 74 (75%) patients showed bilateral pneumonia, 14 (14%) patients showed multiple mottling and ground-glass opacity, and one (1%) patient had pneumothorax. 17 (17%) patients developed acute respiratory distress syndrome and, among them, 11 (11%) patients worsened in a short period of time and died of multiple organ failure.**

Interpretation **The 2019-nCoV infection was of clustering onset, is more likely to affect older males with comorbidities, and can result in severe and even fatal respiratory diseases such as acute respiratory distress syndrome. In general, characteristics of patients who died were in line with the MuLBSTA score, an early warning model for predicting mortality in viral pneumonia. Further investigation is needed to explore the applicability of the MuLBSTA score in predicting the risk of mortality in 2019-nCoV infection.**

Funding **National Key R&D Program of China.**

Lancet 2020; 395: 507–13

Published **Online** January 29, 2020 https://doi.org/10.1016/S0140-6736(20)30211-7

*Contributed equally

Tuberculosis and Respiratory Department (Prof N Chen MD, X Dong PhD, Y Wei MD, J Xia MD, T Yu MD, Prof L Zhang MD), **Infection Disease Department** (F Gong MD, J Wang MD), **Science and Education Department** (Y Han PhD), **and The Office of Drug Clinical Trial Institution** (Y Liu MD), **Wuhan Jinyintan Hospital, Wuhan, China; Department of Respiratory and Critical Care Medicine, Ruijin Hospital** (Prof M Zhou MD, Prof J Qu MD), **Institute of Respiratory Diseases** (Prof M Zhou, Prof J Qu), **Research Laboratory of Clinical Virology, Ruijin Hospital and Ruijin Hospital North** (Prof X Zhang MD), **and Clinical Research Center, Ruijin Hospital North** (Prof X Zhang), **Shanghai Jiaotong University School of Medicine, Shanghai, China; and State Key Laboratory of Virology, Wuhan Institute of Virology, Center for Biosafety Mega-Science, Chinese Academy of Sciences, Wuhan, China** (Prof Y Qiu PhD, Y Han)

Correspondence to: Prof Li Zhang, Tuberculosis and Respiratory Department, Wuhan Jinyintan Hospital, Dongxihu District, Wuhan 430023, China **zhangli080806@163.com**

or

Prof Xinxin Zhang, Research Laboratory of Clinical Virology, Ruijin Hospital and Ruijin Hospital North, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China **zhangx@shsmu.edu.cn**

Introduction

Since Dec 8, 2019, several cases of pneumonia of unknown aetiology have been reported in Wuhan, Hubei province, China.[1–3] Most patients worked at or lived around the local Huanan seafood wholesale market, where live animals were also on sale. In the early stages of this pneumonia, severe acute respiratory infection symptoms occurred, with some patients rapidly developing acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications. On Jan 7, a novel coronavirus was identified by the Chinese Center for Disease Control and Prevention (CDC) from the throat swab sample of a patient, and was subsequently named 2019-nCoV by WHO.[4]

Coronaviruses can cause multiple system infections in various animals and mainly respiratory tract infections in humans, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[5–7] Most patients have mild symptoms and good prognosis. So far, a few patients with 2019-nCoV have developed severe pneumonia, pulmonary oedema, ARDS, or multiple organ failure and have died. All costs of 2019-nCoV treatment are covered by medical insurance in China.

At present, information regarding the epidemiology and clinical features of pneumonia caused by 2019-nCoV is scarce.[1–3] In this study, we did a comprehensive exploration of the epidemiology and clinical features of 99 patients with confirmed 2019-nCoV pneumonia admitted to Jinyintan Hospital, Wuhan, which admitted the first patients with 2019-nCoV to be reported on.

Methods

Study design and participants

For this retrospective, single-centre study, we recruited patients from Jan 1 to Jan 20, 2020, at Jinyintan Hospital in Wuhan, China. Jinyintan Hospital is a hospital for adults (ie, aged ≥14 years) specialising in infectious diseases. According to the arrangements put in place by

Journal of Dental Research
2020, Vol. 99(5) 481–487

DOI: 10.1177/0022034520914246
journals.sagepub.com/home/jdr

Coronavirus Disease 2019 (COVID-19): Emerging and Future Challenges for Dental and Oral Medicine

L. Meng[1], F. Hua[2], and Z. Bian[1]

Abstract

The epidemic of coronavirus disease 2019 (COVID-19), originating in Wuhan, China, has become a major public health challenge for not only China but also countries around the world. The World Health Organization announced that the outbreaks of the novel coronavirus have constituted a public health emergency of international concern. As of February 26, 2020, COVID-19 has been recognized in 34 countries, with a total of 80,239 laboratory-confirmed cases and 2,700 deaths. Infection control measures are necessary to prevent the virus from further spreading and to help control the epidemic situation. Due to the characteristics of dental settings, the risk of cross infection can be high between patients and dental practitioners. For dental practices and hospitals in areas that are (potentially) affected with COVID-19, strict and effective infection control protocols are urgently needed. This article, based on our experience and relevant guidelines and research, introduces essential knowledge about COVID-19 and nosocomial infection in dental settings and provides recommended management protocols for dental practitioners and students in (potentially) affected areas.

Keywords: virology, infection control, dental public health, dental education, transmission, dental practice management

Introduction

On January 8, 2020, a novel coronavirus was officially announced as the causative pathogen of COVID-19 by the Chinese Center for Disease Control and Prevention (Li et al. 2020). The epidemics of coronavirus disease 2019 (COVID-19) started from Wuhan, China, last December and have become a major challenging public health problem for not only China but also countries around the world (Phelan et al. 2020). On January 30, 2020, the World Health Organization (WHO) announced that this outbreak had constituted a public health emergency of international concern (Mahase 2020). The novel coronavirus was initially named 2019-nCoV and officially as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of February 26, COVID-19 has been recognized in 34 countries, with a total of 80,239 laboratory-confirmed cases and 2,700 deaths (WHO 2020b).

Due to the characteristics of dental settings, the risk of cross infection may be high between dental practitioners and patients. For dental practices and hospitals in countries/regions that are (potentially) affected with COVID-19, strict and effective infection control protocols are urgently needed. This article, based on our experience and relevant guidelines and research, introduces the essential knowledge about COVID-19 and nosocomial infection in dental settings and provides recommended management protocols for dental practitioners and students in (potentially) affected areas.

What Is COVID-19?

Viral Etiology

According to recent research, similar to SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-CoV-2 is zoonotic, with Chinese horseshoe bats (*Rhinolophus sinicus*) being the most probable origin (Chan et al. 2020; Lu et al. 2020) and pangolins as the most likely intermediate host (The Chinese Preventive Medicine Association 2020).

Epidemiologic Characteristics

Mode of Transmission. Based on findings of genetic and epidemiologic research, it appears that the COVID-19 outbreak

[1]The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Key Laboratory of Oral Biomedicine Ministry of Education, School and Hospital of Stomatology, Wuhan University, Wuhan, China
[2]Center for Evidence-Based Stomatology, School and Hospital of Stomatology, Wuhan University, Wuhan, China

Corresponding Author:
Z. Bian, The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Key Laboratory of Oral Biomedicine Ministry of Education, School and Hospital of Stomatology, Wuhan University, Luoyu Road 237, Wuhan, Hubei 430079, China.
Email: bianzhuan@whu.edu.cn

International Journal of Oral Science www.nature.com/ijos

REVIEW ARTICLE OPEN

Transmission routes of 2019-nCoV and controls in dental practice

Xian Peng[1], Xin Xu[1], Yuqing Li[1], Lei Cheng[1], Xuedong Zhou[1] and Biao Ren[1]

A novel β-coronavirus (2019-nCoV) caused severe and even fetal pneumonia explored in a seafood market of Wuhan city, Hubei province, China, and rapidly spread to other provinces of China and other countries. The 2019-nCoV was different from SARS-CoV, but shared the same host receptor the human angiotensin-converting enzyme 2 (ACE2). The natural host of 2019-nCoV may be the bat *Rhinolophus affinis* as 2019-nCoV showed 96.2% of whole-genome identity to BatCoV RaTG13. The person-to-person transmission routes of 2019-nCoV included direct transmission, such as cough, sneeze, droplet inhalation transmission, and contact transmission, such as the contact with oral, nasal, and eye mucous membranes. 2019-nCoV can also be transmitted through the saliva, and the fetal–oral routes may also be a potential person-to-person transmission route. The participants in dental practice expose to tremendous risk of 2019-nCoV infection due to the face-to-face communication and the exposure to saliva, blood, and other body fluids, and the handling of sharp instruments. Dental professionals play great roles in preventing the transmission of 2019-nCoV. Here we recommend the infection control measures during dental practice to block the person-to-person transmission routes in dental clinics and hospitals.

International Journal of Oral Science (2020)12:9 ; https://doi.org/10.1038/s41368-020-0075-9

INTRODUCTION

An emergent pneumonia outbreak originated in Wuhan City, in the late December 2019[1]. The pneumonia infection has rapidly spread from Wuhan to most other provinces and other 24 countries[2,3]. World Health Organization declared a public health emergency of international concern over this global pneumonia outbreak on 30th January 2020.

The typical clinical symptoms of the patients who suffered from the novel viral pneumonia were fever, cough, and myalgia or fatigue with abnormal chest CT, and the less common symptoms were sputum production, headache, hemoptysis, and diarrhea[4–6]. This new infectious agent is more likely to affect older males to cause severe respiratory diseases[7,8]. Some of the clinical symptoms were different from the severe acute respiratory syndrome (SARS) caused by SARS coronavirus (SARS-CoV) that happened in 2002–2003, indicating that a new person-to-person transmission infectious agent has caused this emergent viral pneumonia outbreak[8,9]. Chinese researchers have quickly isolated a new virus from the patient and sequenced its genome (29,903 nucleotides)[10]. The infectious agent of this viral pneumonia happenening in Wuhan was finally identified as a novel coronavirus (2019-nCOV), the seventh member of the family of coronaviruses that infect humans[11]. On 11th February 2020, WHO named the novel viral pneumonia as "Corona Virus Disease (COVID19)", while the international Committee on Taxonomy of Viruses (ICTV) suggested this novel coronavirus name as "SARS-CoV-2" due to the phylogenetic and taxonomic analysis of this novel coronavirus[12].

CHARACTERISTICS OF 2019 NOVEL CORONAVIRUS

Coronaviruses belong to the family of *Coronaviridae*, of the order *Nidovirales*, comprising large, single, plus-stranded RNA as their genome[13,14]. Currently, there are four genera of coronaviruses: α-CoV, β-CoV, γ-CoV, and δ-CoV[15,16]. Most of the coronavirus can cause the infectious diseases in human and vertebrates. The α-CoV and β-CoV mainly infect the respiratory, gastrointestinal, and central nervous system of humans and mammals, while γ-CoV and δ-CoV mainly infect the birds[13,17–19].

Usually, several members of the coronavirus cause mild respiratory disease in humans; however, SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV) explored in 2002–2003 and in 2012, respectively, caused fatal severe respiratory diseases[20–22]. The SARS-CoV and MERS-CoV belong to the β-CoV[23,24]. 2019-nCoV explored in Wuhan also belongs to the β-CoV according to the phylogenetic analysis based on the viral genome[10,11]. Although the nucleotide sequence similarity is less than 80% between 2019-nCoV and SARS-CoV (about 79%) or MERS-CoV (about 50%), 2019-nCoV can also cause the fetal infection and spread more faster than the two other coronaviruses[7,9,11,25–27]. The genome nucleotide sequence identity between a coronavirus (BatCoV RaTG13) detected in the bat *Rhinolophus affinis* from Yunnan Province, China, and 2019-nCoV, was 96.2%, indicating that the natural host of 2019-nCoV may also be the *Rhinolophus affinis* bat[11]. However, the differences may also suggest that there is an or more intermediate hosts between the bat and human. A research team from the South China Agricultural University has invested more than 1 000 metagenomic samples

[1]State Key Laboratory of Oral Diseases & National Clinical Research Center for Oral Diseases & Department of Cariology and Endodontics, West China Hospital of Stomatology, Sichuan University, Chengdu, China
Correspondence: Xuedong Zhou (zhouxd@scu.edu.cn) or Biao Ren (renbiao@scu.edu.cn)

Received: 15 February 2020 Revised: 18 February 2020 Accepted: 19 February 2020
Published online: 03 March 2020

SCIENCE CHINA
Life Sciences

•LETTER TO THE EDITOR•

March 2020 Vol.63 No.3: 457–460
https://doi.org/10.1007/s11427-020-1637-5

Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission

Xintian Xu[1†], Ping Chen[2,5†], Jingfang Wang[3†], Jiannan Feng[4], Hui Zhou[2], Xuan Li[2*], Wu Zhong[4*] & Pei Hao[1,5*]

[1]*Key Laboratory of Molecular Virology and Immunology, Institut Pasteur of Shanghai, Center for Biosafety Mega-Science, Chinese Academy of Sciences, Shanghai 200031, China;*
[2]*Key Laboratory of Synthetic Biology, CAS Center for Excellence in Molecular Plant Sciences, Chinese Academy of Sciences, Shanghai 200032, China;*
[3]*Key Laboratory of Systems Biomedicine, Ministry of Education, Shanghai Center for Systems Biomedicine, Shanghai Jiao Tong University, Shanghai 200240, China;*
[4]*National Engineering Research Center for the Emergence Drugs, Beijing Institute of Pharmacology and Toxicology, Beijing 100850, China;*
[5]*The Joint Program in Infection and Immunity: a. Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou 510623, China; b. Institute Pasteur of Shanghai, Chinese Academy of Sciences, Shanghai 200031, China*

Received January 16, 2020; accepted January 20, 2020; published online January 21, 2020

Citation: Xu, X., Chen, P., Wang, J., Feng, J., Zhou, H., Li, X., Zhong, W., and Hao, P. (2020). Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci 63, 457–460. https://doi.org/10.1007/s11427-020-1637-5

Dear Editor,

The occurrence of concentrated pneumonia cases in Wuhan city, Hubei province of China was first reported on December 30, 2019 by the Wuhan Municipal Health Commission (WHO, 2020). The pneumonia cases were found to be linked to a large seafood and animal market in Wuhan, and measures for sanitation and disinfection were taken swiftly by the local government agency. The Centers for Disease Control and Prevention (CDC) and Chinese health authorities later determined and announced that a novel coronavirus (CoV), denoted as Wuhan CoV, had caused the pneumonia outbreak in Wuhan city (CDC, 2020). Scientists from multiple groups had obtained the virus samples from hospitalized patients (Normile, 2020). The isolated viruses were morphologically identical when observed under electron microscopy.

One genome sequence (WH-Human_1) of the Wuhan CoV was first released on Jan 10, 2020, and subsequently five additional Wuhan CoV genome sequences were released (Zhang, 2020; Shu and McCauley, 2017) (Table S1 in Supporting Information). The current public health emergency partially resembles the emergence of the SARS outbreak in southern China in 2002. Both happened in winter with initial cases linked to exposure to live animals sold at animal markets, and both were caused by previously unknown coronaviruses. As of January 15, 2020, there were more than 40 laboratory-confirmed cases of the novel Wuhan CoV infection with one reported death. Although no obvious evidence of human-to-human transmission was reported, there were exported cases in Hong Kong China, Japan, and Thailand.

Under the current public health emergency, it is imperative to understand the origin and native host(s) of the Wuhan

†Contributed equally to this work
*Corresponding authors (Pei Hao, email: phao@ips.ac.cn; Wu Zhong, email: zhongwu@bmi.ac.cn; Xuan Li, email: lixuan@sippe.ac.cn)

RESEARCH ARTICLE

CORONAVIRUS

Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2

Renhong Yan[1,2], Yuanyuan Zhang[1,2]*, Yaning Li[3]*, Lu Xia[1,2], Yingying Guo[1,2], Qiang Zhou[1,2]†

Angiotensin-converting enzyme 2 (ACE2) is the cellular receptor for severe acute respiratory syndrome–coronavirus (SARS-CoV) and the new coronavirus (SARS-CoV-2) that is causing the serious coronavirus disease 2019 (COVID-19) epidemic. Here, we present cryo–electron microscopy structures of full-length human ACE2 in the presence of the neutral amino acid transporter B^0AT1 with or without the receptor binding domain (RBD) of the surface spike glycoprotein (S protein) of SARS-CoV-2, both at an overall resolution of 2.9 angstroms, with a local resolution of 3.5 angstroms at the ACE2-RBD interface. The ACE2-B^0AT1 complex is assembled as a dimer of heterodimers, with the collectrin-like domain of ACE2 mediating homodimerization. The RBD is recognized by the extracellular peptidase domain of ACE2 mainly through polar residues. These findings provide important insights into the molecular basis for coronavirus recognition and infection.

Severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) is a positive-strand RNA virus that causes severe respiratory syndrome in humans. The resulting outbreak of coronavirus disease 2019 (COVID-19) has emerged as a severe epidemic, claiming more than 2000 lives worldwide between December 2019 and February 2020 (*1*, *2*). The genome of SARS-CoV-2 shares about 80% identity with that of SARS-CoV and is about 96% identical to the bat coronavirus BatCoV RaTG13 (*2*).

In the case of SARS-CoV, the spike glycoprotein (S protein) on the virion surface mediates receptor recognition and membrane fusion (*3*, *4*). During viral infection, the trimeric S protein is cleaved into S1 and S2 subunits and S1 subunits are released in the transition to the postfusion conformation (*4*–*7*). S1 contains the receptor binding domain (RBD), which directly binds to the peptidase domain (PD) of angiotensin-converting enzyme 2 (ACE2) (*8*), whereas S2 is responsible for membrane fusion. When S1 binds to the host receptor ACE2, another cleavage site on S2 is exposed and is cleaved by host proteases, a process that is critical for viral infection (*5*, *9*, *10*). The S protein of SARS-CoV-2 may also exploit ACE2 for host infection (*2*, *11*–*13*). A recent publication reported the structure of the S protein of SARS-CoV-2 and showed that the ectodomain of the SARS-CoV-2 S protein binds to the PD of ACE2 with a dissociation constant (K_d) of ~15 nM (*14*).

Although ACE2 is hijacked by some coronaviruses, its primary physiological role is in the maturation of angiotensin (Ang), a peptide hormone that controls vasoconstriction and blood pressure. ACE2 is a type I membrane protein expressed in lungs, heart, kidneys, and intestine (*15*–*17*). Decreased expression of ACE2 is associated with cardiovascular diseases (*18*–*20*). Full-length ACE2 consists of an N-terminal PD and a C-terminal collectrin-like domain (CLD) that ends with a single transmembrane helix and a ~40-residue intracellular segment (*15*, *21*). The PD of ACE2 cleaves Ang I to produce Ang-(1-9), which is then processed by other enzymes to become Ang-(1-7). ACE2 can also directly process Ang II to give Ang-(1-7) (*15*, *22*).

Structures of the claw-like ACE2-PD alone and in complex with the RBD or the S protein of SARS-CoV have revealed the molecular details of the interaction between the RBD of the S protein and PD of ACE2 (*7*, *8*, *23*, *24*). Structural information on ACE2 is limited to the PD domain. The single transmembrane (TM) helix of ACE2 makes it challenging to determine the structure of the full-length protein.

ACE2 also functions as the chaperone for membrane trafficking of the amino acid transporter B^0AT1, also known as SLC6A19 (*25*), which mediates uptake of neutral amino acids into intestinal cells in a sodium-dependent manner. Mutations in B^0AT1 may cause Hartnup disorder, an inherited disease with symptoms such as pellagra, cerebellar ataxia, and psychosis (*26*–*28*). Structures have been determined for the SLC6 family members *d*DAT (*Drosophila* dopamine transporter) and human SERT (serotonin transporter, SLC6A4) (*29*, *30*). It is unclear how ACE2 interacts with B^0AT1. The membrane trafficking mechanism for ACE2 and B^0AT1 is similar to that of the LAT1-4F2hc complex, a large neutral–amino acid transporter complex that requires 4F2hc for its plasma membrane localization (*31*). Our structure of LAT1-4F2hc shows that the cargo LAT1 and chaperone 4F2hc interact through both extracellular and transmembrane domains (*32*). We reasoned that the structure of full-length ACE2 may be revealed in the presence of B^0AT1.

Here, we report cryo–electron microscopy (cryo-EM) structures of the full-length human ACE2-B^0AT1 complex at an overall resolution of 2.9 Å and a complex between the RBD of SARS-CoV-2 and the ACE2-B^0AT1 complex, also with an overall resolution of 2.9 Å and with 3.5-Å local resolution at the ACE2-RBD interface. The ACE2-B^0AT1 complex exists as a dimer of heterodimers. Structural alignment of the RBD-ACE2-B^0AT1 ternary complex with the S protein of SARS-CoV-2 suggests that two S protein trimers can simultaneously bind to an ACE2 homodimer.

Structural determination of the ACE2-B^0AT1 complex

Full-length human ACE2 and B^0AT1, with Strep and FLAG tags on their respective N termini, were coexpressed in human embryonic kidney (HEK) 293F cells and purified through tandem affinity resin and size exclusion chromatography. The complex was eluted in a single monodisperse peak, indicating high homogeneity (Fig. 1A). Details of cryo-sample preparation, data acquisition, and structural determination are given in the materials and methods section of the supplementary materials. A three-dimensional (3D) reconstruction was obtained at an overall resolution of 2.9 Å from 418,140 selected particles. This immediately revealed the dimer of heterodimers' architecture (Fig. 1B). After applying focused refinement and C2 symmetry expansion, the resolution of the extracellular domains improved to 2.7 Å, whereas the TM domain remained at 2.9-Å resolution (Fig. 1B, figs. S1 to S3, and table S1).

The high resolution supported reliable model building. For ACE2, side chains could be assigned to residues 19 to 768, which contain the PD (residues 19 to 615) and the CLD (residues 616 to 768), which consists of a small extracellular domain, a long linker, and the single TM helix (Fig. 1C). Between the PD and TM helix is a ferredoxin-like fold domain; we refer to this as the neck domain (residues 616 to 726) (Fig. 1C and fig. S4). Homodimerization is entirely mediated by ACE2, which is sandwiched by B^0AT1. Both the PD and neck domains contribute to dimerization, whereas each B^0AT1 interacts with the neck and TM helix in the adjacent ACE2 (Fig. 1C). The extracellular region is highly glycosylated, with seven and five glycosylation sites on each ACE2 and B^0AT1 monomer, respectively.

[1]Key Laboratory of Structural Biology of Zhejiang Province, Institute of Biology, Westlake Institute for Advanced Study, 18 Shilongshan Road, Hangzhou 310024, Zhejiang Province, China. [2]School of Life Sciences, Westlake University, 18 Shilongshan Road, Hangzhou 310024, Zhejiang Province, China. [3]Beijing Advanced Innovation Center for Structural Biology, Tsinghua-Peking Joint Center for Life Sciences, School of Life Sciences, Tsinghua University, Beijing 100084, China.
*These authors contributed equally to this work.
†Corresponding author. Email: zhouqiang@westlake.edu.cn

International Journal of Oral Science www.nature.com/ijos

ARTICLE OPEN

High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa

Hao Xu[1], Liang Zhong[1], Jiaxin Deng[1], Jiakuan Peng[1], Hongxia Dan[1], Xin Zeng[1], Taiwen Li[1] and Qianming Chen[1]

It has been reported that ACE2 is the main host cell receptor of 2019-nCoV and plays a crucial role in the entry of virus into the cell to cause the final infection. To investigate the potential route of 2019-nCov infection on the mucosa of oral cavity, bulk RNA-seq profiles from two public databases including The Cancer Genome Atlas (TCGA) and Functional Annotation of The Mammalian Genome Cap Analysis of Gene Expression (FANTOM5 CAGE) dataset were collected. RNA-seq profiling data of 13 organ types with para-carcinoma normal tissues from TCGA and 14 organ types with normal tissues from FANTOM5 CAGE were analyzed in order to explore and validate the expression of ACE2 on the mucosa of oral cavity. Further, single-cell transcriptomes from an independent data generated in-house were used to identify and confirm the ACE2-expressing cell composition and proportion in oral cavity. The results demonstrated that the ACE2 expressed on the mucosa of oral cavity. Interestingly, this receptor was highly enriched in epithelial cells of tongue. Preliminarily, those findings have explained the basic mechanism that the oral cavity is a potentially high risk for 2019-nCoV infectious susceptibility and provided a piece of evidence for the future prevention strategy in dental clinical practice as well as daily life.

International Journal of Oral Science (2020)12:8 ; https://doi.org/10.1038/s41368-020-0074-x

INTRODUCTION

Since December 2019, an increasing number of patients with pneumonia occurred in Wuhan, Hubei province, China, which attracted much attention not only within China but across the world[1,2]. The novel pneumonia was named as Corona Virus Disease 19 (COVID-19) by World Health Organization (WHO) (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf?sfvrsn=fb6d49b1_2), the common symptoms of COVID-19 at illness onset were fever, fatigue, dry cough, myalgia, and dyspnea[3]. In addition, some patients might suffer from headache, dizziness, abdominal pain, diarrhea, nausea, and vomiting[3]. Onset of disease may lead to progressive respiratory failure due to alveolar damage and even death[4].

Scientists then isolated a novel coronavirus from human airway epithelial cells, which was named 2019-nCoV[5]. Lu et al.[6] found that 2019-nCoV was closer to bat-SL-CoVZC45 and bat-SL-CoVZXC21 at the whole-genome level, and the external subdomain of the 2019-nCoV receptor-binding domain (RBD) was more similar to that of severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV). Study of Zhou et al.[4] indicated that the angiotensin-converting enzyme II (ACE2) is likely the cell receptor of 2019-nCoV, which were also the receptor for SARS-CoV and HCoV-NL63[7,8]. Zhou et al.[4] also proved that 2019-nCoV does not use other coronavirus receptors, aminopeptidase N, and dipeptidyl peptidase 4. The study of Xu et al.[9] found that the RBD domain of the 2019-nCoV S-protein supports strong interaction with human ACE2 molecules. These findings suggest that the ACE2 plays an important role in cellular entry, thus ACE2-expressing cells may act as target cells and are susceptible to 2019-nCoV infection[10].

The expression and distribution of the ACE2 in human body may indicate the potential infection routes of 2019-nCoV. Through the developed single-cell RNA sequencing (scRNA-Seq) technique and single-cell transcriptomes based on the public database, researchers analyzed the ACE2 RNA expression profile at single-cell resolution. High ACE2 expression was identified in type II alveolar cells (AT2) of lung[10–12], esophagus upper and stratified epithelial cells, absorptive enterocytes from ileum and colon[12], cholangiocytes[13], myocardial cells, kidney proximal tubule cells, and bladder urothelial cells[10]. These findings indicated that those organs with high ACE2-expressing cells should be considered as potential high risk for 2019-nCoV infection[10].

In order to investigated the potential routes of 2019-nCov infection on the mucosa of oral cavity, we explored whether the ACE2 is expressed and the ACE2-expressing cell composition and proportion in oral cavity based on the public bulk RNA-seq profiles from two public databases and single-cell transcriptomes from an independent data generated in-house. The result showed that the ACE2 could be expressed in the oral cavity, and was highly enriched in epithelial cells. Moreover, among different oral sites, ACE2 expression was higher in tongue than buccal and gingival tissues. These findings indicate that the mucosa of oral cavity may be a potentially high risk route of 2019-nCov infection.

[1]State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, Chinese Academy of Medical Sciences Research Unit of Oral Carcinogenesis and Management, West China Hospital of Stomatology, Sichuan University, Chengdu, Sichuan, China
Correspondence: Taiwen Li (litaiwen@scu.edu.cn) or Qianming Chen (qmchen@scu.edu.cn)
These authors contributed equally: Hao Xu, Liang Zhong, Jiaxin Deng

Received: 13 February 2020 Revised: 15 February 2020 Accepted: 15 February 2020
Published online: 24 February 2020

Clinical Oral Investigations
https://doi.org/10.1007/s00784-020-03248-x

LETTER TO THE EDITOR

Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis

Robinson Sabino-Silva [1,2] • Ana Carolina Gomes Jardim [3] • Walter L. Siqueira [1]

Received: 15 February 2020 / Accepted: 17 February 2020

Summary

A novel coronavirus (COVID-19) is associated with human-to-human transmission. The COVID-19 was recently identified in saliva of infected patients. In this point-of-view article, we discuss the potential of transmission via the saliva of this virus. The COVID-19 transmission via contact with droplets and aerosols generated during dental clinical procedures is expected. There is a need to increase investigations to the detection of COVID-19 in oral fluids and its impact on the transmission of this virus, which is crucial to improve effective strategies for prevention, especially for dentists and healthcare professionals that perform aerosol-generating procedures. Saliva can have a pivotal role in the human-to-human transmission, and non-invasive salivary diagnostics may provide a convenient and cost-effective point-of-care platform for the fast and early detection of COVID-19 infection.

Current point of view

The present outbreak of the 2019 coronavirus strain (COVID-19) constitutes a public health emergency of global concern [1]. International centers for disease control and prevention are monitoring this infectious disease outbreak; symptoms of COVID-19 infection include fever, cough, and acute respiratory disease, with severe cases leading to pneumonia, kidney failure, and even death. The severe respiratory illness caused by the COVID-19 was first detected in Wuhan, Hubei, China, and infections have spread worldwide [2]. Currently, the available COVID-19 genome sequences from clinical samples suggest that this viral emergence is related to bat coronaviruses [3]. Although the coronavirus infection in humans frequently presents with mild severity, the betacoronavirus infection of either the severe acute respiratory syndrome coronavirus (SARS-CoV) [4] or the Middle East respiratory syndrome coronavirus (MERS-CoV) [5] resulted in higher mortality rates [6]. Given the novelty of COVID-19, some characteristics of the virus remain yet unknown. The COVID-19 outbreak serves as both a reminder and an opportunity to assist. Considering that COVID-19 was recently identified in saliva of infected patients [7], the COVID-19 outbreak is a reminder that dental/oral and other health professionals must always be diligent in protecting against the spread of infectious disease, and it provides a chance to determine if a non-invasive saliva diagnostic for COVID-19 could assist in detecting such viruses and reducing the spread.

The Chinese Centre for Disease Control and Prevention isolated the COVID-19. It published the viral genome sequence data immediately in international database banks GenBank and the Global Initiative on Sharing All Influenza Data (GISAID) [8, 9]. This action enabled laboratories in several countries to develop unique PCR tests focusing on the diagnosis of COVID-19 [8, 10]. Currently, the COVID-19 transmission routes are still to be determined, but human-to-human transmission has been confirmed [10, 11]. The laboratory diagnostic tests should be performed using nasopharyngeal, oropharyngeal, and blood samples. Expectorated sputum and other specimens in severe respiratory disease should be considered as lower respiratory tract samples [2, 12, 13]. Several potential scenarios of COVID-19 transmission have been described. The transmission via contact with droplets from talking, coughing, sneezing (related to human respiratory activities), and aerosols generated during clinical procedures is expected, as it would be for other respiratory

Robinson Sabino-Silva, Ana Carolina Gomes Jardim and Walter L. Siqueira contributed equally to this work.

✉ Walter L. Siqueira
walter.siqueira@usask.ca

1 College of Dentistry, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

2 Department of Physiology, Institute of Biomedical Sciences, Federal University of Uberlandia, Uberlandia, Minas Gerais, Brazil

3 Laboratory of Virology, Institute of Biomedical Sciences, Federal University of Uberlandia, Uberlandia, Minas Gerais, Brazil

Published online: 20 February 2020

Indoor Air 2007; 17: 211–225
www.blackwellpublishing.com/ina
Printed in Singapore. All rights reserved

INDOOR AIR
doi:10.1111/j.1600-0668.2006.00469.x

How far droplets can move in indoor environments – revisiting the Wells evaporation–falling curve

Abstract A large number of infectious diseases are believed to be transmitted between people via large droplets and by airborne routes. An understanding of evaporation and dispersion of droplets and droplet nuclei is not only significant for developing effective engineering control methods for infectious diseases but also for exploring the basic transmission mechanisms of the infectious diseases. How far droplets can move is related to how far droplet-borne diseases can transmit. A simple physical model is developed and used here to investigate the evaporation and movement of droplets expelled during respiratory activities; in particular, the well-known Wells evaporation–falling curve of droplets is revisited considering the effect of relative humidity, air speed, and respiratory jets. Our simple model considers the movement of exhaled air, as well as the evaporation and movement of a single droplet. Exhaled air is treated as a steady-state non-isothermal (warm) jet horizontally issuing into stagnant surrounding air. A droplet is assumed to evaporate and move in this non-isothermal jet. Calculations are performed for both pure water droplets and droplets of sodium chloride (physiological saline) solution (0.9% w/v). We calculate the droplet lifetimes and how droplet size changes, as well as how far the droplets travel in different relative humidities. Our results indicate that a droplet's size predominately dictates its evaporation and movement after being expelled. The sizes of the largest droplets that would totally evaporate before falling 2 m away are determined under different conditions. The maximum horizontal distances that droplets can reach during different respiratory activities are also obtained. Our study is useful for developing effective prevention measures for controlling infectious diseases in hospitals and in the community at large.

X. Xie[1], Y. Li[1], A. T. Y. Chwang[1], P. L. Ho[2], W. H. Seto[3]
[1]Department of Mechanical Engineering, The University of Hong Kong, Hong Kong, China, [2]Department of Microbiology, The University of Hong Kong, Hong Kong, China, [3]Department of Microbiology, Queen Mary Hospital, Hong Kong, China

Key words: Droplet evaporation; Droplet movement; Infection transmission; Respiratory jet; Large droplet.

Dr Yuguo Li
Department of Mechanical Engineering
The University of Hong Kong
Pokfulam Road
Hong Kong
China
Tel.: +1 852 2859 2625
Fax: +1 852 2858 5415
e-mail: liyg@hku.hk

Received for review 26 February 2006. Accepted for publication 14 September 2006.

Practical Implications

Our study reveals that for respiratory exhalation flows, the sizes of the largest droplets that would totally evaporate before falling 2 m away are between 60 and 100 μm, and these expelled large droplets are carried more than 6 m away by exhaled air at a velocity of 50 m/s (sneezing), more than 2 m away at a velocity of 10 m/s (coughing) and less than 1 m away at a velocity of 1 m/s (breathing). These findings are useful for developing effective engineering control methods for infectious diseases, and also for exploring the basic transmission mechanisms of the infectious diseases. There is a need to examine the air distribution systems in hospital wards for controlling both airborne and droplet-borne transmitted diseases.

Introduction

Among the various transmission routes of infection, droplets and airborne routes are the most interesting with respect to building ventilation and indoor air filtration. Examples of pathogens that can be transmitted by large droplets but are not considered as true airborne infections include SARS coronavirus (SARS CoV), whooping cough (*Bordetella pertussis*), influenza virus, adenovirus, rhinovirus, *Mycoplasma pneumoniae*, group A streptococcus, and bacterial meningitis (*Neisseria meningitidis*). Virtually, all pathogens where replication and/or colonization occurs in the upper respiratory tract (URT) could have the potential of being transmitted by large droplets (Chin, 2000). Siegel et al. (2004) state that only tuberculosis (mycobacterium tuberculosis), measles (rubeola virus), and chickenpox [varicella zoster virus (VZV)] could be considered as true airborne infectious diseases, although claims of such a small number of airborne transmittable diseases are debatable. For example, although a WHO consensus document concludes that SARS is mainly transmitted by large droplets, some detailed investigations concluded that some outbreaks might be airborne (Li et al., 2005; Yu et al., 2004).

Chemosphere 87 (2012) 1260–1264

Contents lists available at SciVerse ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Study on the initial velocity distribution of exhaled air from coughing and speaking

Soon-Bark Kwon [a], Jaehyung Park [a], Jaeyoun Jang [a], Youngmin Cho [a], Duck-Shin Park [a], Changsoo Kim [b], Gwi-Nam Bae [c], Am Jang [d,*]

[a] Subway IAQ Research Corps., Korea Railroad Research Institute, Gyeonggi-do, South Korea
[b] Dept. of Preventive Medicine, Yonsei University, Seoul, South Korea
[c] Global Environment Center, Korea Institute of Science and Technology, Seoul, South Korea
[d] Dept. of Civil & Environmental Engineering, Sungkyunkwan University, Suwon, Gyeonggi-do, South Korea

ARTICLE INFO

Article history:
Received 7 November 2011
Received in revised form 27 December 2011
Accepted 20 January 2012
Available online 18 February 2012

Keywords:
Airborne pathogens
Angle
Bioaerosols
Particle Image Velocimetry (PIV)
Velocity

ABSTRACT

Increasing concerns about the spread of airborne pathogens such as severe acute respiratory syndrome (SARS) and novel swine-origin influenza A (H1N1) have attracted public attention to bioaerosols and protection against them. The airborne pathogens are likely to be expelled from coughing or speaking, so the physical data of the exhaled particles plays a key role in analyzing the pathway of airborne viruses. The objective of this study was to analyze the initial velocity and the angle of the exhaled airflow from coughing and speaking of 17 males and 9 females using Particle Image Velocimetry (PIV) and acrylic indoor chamber. The results showed that the average initial coughing velocity was 15.3 m/s for the males and 10.6 m/s for the females, while the average initial speaking velocity was 4.07 m/s and 2.31 m/s respectively. The angle of the exhaled air from coughing was around 38° for the males and 32° for the females, while that of the exhaled air from speaking was around 49° and 78° respectively. Also, the linear relation between the tested subject's height and their coughing and speaking velocity was shown in this study.

1. Introduction

The necessity of understanding the infection mechanism of airborne transmission is proven from the epidemic cases reported by WHO such as SARS (severe acute respiratory syndrome) in 2003 and H1N1 (novel swine-origin influenza A) in 2009 (WHO, 2004, 2010). Olsen et al. (2003) reported the transmission of SARS on an aircraft by interviewing passengers and crew members who were on the spot and noted that passengers who were seated in the same row with the index patient had higher risk. Especially, higher number of infected passengers seated in front of the index patient than behind him possibly implied the airborne transmission through respiratory activities such as coughing and sneezing. Efficiency of respiratory transmission of H1N1 virus was tested by conducting animal experiments using ferrets (Maines et al., 2009; Munster et al., 2009; Perez et al., 2009). Prediction on the transmission airborne contaminants including SARS inside an enclosed space such as an airliner cabin (Mazumdar and Chen, 2009) and a hospital ward (Qian et al., 2009) have been made, providing a reasonable prediction for applications when the infection occurred and the virus was transmitted to a person staying at the same location in an enclosed space.

Airborne transmission refers to the passage of microorganisms from a source to a person through aerosols, causing possible illness of the person in consequence of infection. Aerosolized disease transmission can be classified into two groups (Gralton et al., 2011); one is the droplet transmission, which is defined as disease transmission through the expelled particles that are likely to settle down quickly due to their size. The other is aerosol transmission, which is defined as disease transmission through the expelled particles that range relatively smaller in size. Such aerosols can be transmitted over short and long distances. Short-range transmission occurs across the short distance (less than 1 m) from person to person and can be moderated by using of personal protective equipment such as gloves and facemasks with precautions to avoid the usual contact transmission from touching of the eyes, nose and mouth. Long range transmission occurs between distant locations and is primarily governed by air flows generated from ventilation systems or movement of people (Tang et al., 2006). Wang and Chow (2011) reported that human walking disturbs the local velocity field influencing the droplet dispersion and the increase of walking speed could effectively cut down the number of suspended droplets ranged 0.5–20 μm.

Large droplets can evaporate to become small droplets that can further evaporate, eventually becoming droplet nuclei suspended for prolonged periods (Parienta et al., 2011), if this evaporation process is fast enough to occur before the droplets settle down. Morawska et al. (2009) showed that evaporation to the equilibrium droplet size occurred within 0.8 s for particles between 0.5 and 20 μm. Redrow et al. (2011) also demonstrated that a 10 μm sputum droplet evaporated to become a droplet nucleus (3.5 μm) in

* Corresponding author. Tel./fax: +82 31 290 7526.
E-mail address: amjang@skku.edu (A. Jang).

0045-6535/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.chemosphere.2012.01.032

Research Paper

Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis

Bolin Wang[1], Ruobao Li[2], Zhong Lu[3], Yan Huang[3]

[1]Weifang Medical University, Weifang 261031, China
[2]Department of Human Anatomy, Weifang Medical University, Weifang 261031, China
[3]Department of Oncology, Affiliated Hospital of Weifang Medical University, Weifang 261031, China

Correspondence to: Yan Huang; **email:** Yanhuangdr@163.com
Keywords: COVID-19, comorbidity, meta-analysis, risk
Abbreviations: COVID-19: coronavirus disease 2019; 2019-nCoV: 2019 novel coronavirus; COPD: chronic obstructive pulmonary disease
Received: March 12, 2020 **Accepted:** March 28, 2020 **Published:** April 8, 2020

ABSTRACT

Currently, the number of patients with coronavirus disease 2019 (COVID-19) has increased rapidly, but relationship between comorbidity and patients with COVID-19 still not clear. The aim was to explore whether the presence of common comorbidities increases COVID-19 patients' risk. A literature search was performed using the electronic platforms (PubMed, Cochrane Library, Embase, and other databases) to obtain relevant research studies published up to March 1, 2020. Relevant data of research endpoints in each study were extracted and merged. All data analysis was performed using Stata12.0 software. A total of 1558 patients with COVID-19 in 6 studies were enrolled in our meta-analysis eventually. Hypertension (OR: 2.29, P<0.001), diabetes (OR: 2.47, P<0.001), chronic obstructive pulmonary disease (COPD) (OR: 5.97, P<0.001), cardiovascular disease (OR: 2.93, P<0.001), and cerebrovascular disease (OR:3.89,P=0.002) were independent risk factors associated with COVID-19 patients. The meta-analysis revealed no correlation between increased risk of COVID-19 and liver disease, malignancy, or renal disease. Hypertension, diabetes, COPD, cardiovascular disease, and cerebrovascular disease are major risk factors for patients with COVID-19. Knowledge of these risk factors can be a resource for clinicians in the early appropriate medical management of patients with COVID-19.

INTRODUCTION

Coronavirus Disease 2019(COVID-19) is a viral respiratory disease caused by the 2019 novel coronavirus (2019-nCoV), which has caused the pneumonia epidemic in the world [1–3]. As of March 5, 2020, a total of 96539 cases with laboratory-confirmed COVID-19 infection have been detected in the world reported by the World Health Organization (WHO). In China, there have been 80567 accumulated confirmed cases of COVID-19, and 5952 of them were existing severe patients. Given the rapid spread and high mortality rate of COVID-19, it is absolutely necessary to evaluate the possible risk factors affecting the progression of disease in COVID-19 patients.

Previous studies show that COVID-19 patients with comorbidity may lead to a poor prognosis [5]. Identifying the most important risk groups is essential when making decisions anti-2019-nCoV therapy. To date, there has been no systematic review that comprehensively explores whether the presence of common comorbidities increase COVID-19 patients' risk, to guide clinical practice better. Therefore, we performed a meta-analysis of the available studies to explore relationship between comorbidity and patients with COVID-19.

Could there be a link between oral hygiene and the severity of SARS-CoV-2 infections?

Victoria Sampson,*[1] Nawar Kamona[2] and Ariane Sampson[3]

Key points

Describes what COVID-19 is and the associated risk factors for developing complications.	Investigates whether bacteria contribute to COVID-19 complications by causing bacterial superinfections.	Examines whether there is a link between the oral microbiome and COVID-19 complications.

Abstract

On 30 January 2020, the World Health Organisation 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 in often seemingly healthy individuals. This paper investigates the potential link between SARS-CoV-2 and bacterial load, questioning whether bacteria may play a role in bacterial superinfections and complications such as pneumonia, acute respiratory distress syndrome and sepsis. The connection between COVID-19 complications and oral health and periodontal disease is also examined, as the comorbidities at highest risk of COVID-19 complications also cause imbalances in the oral microbiome and increase the risk of periodontal disease. We explore the connection between high bacterial load in the mouth and post-viral complications, and how improving oral health may reduce the risk of complications from COVID-19.

Introduction

On 31 December 2019, the World Health Organisation (WHO) was informed of a cluster of 27 cases of pneumonia with no known cause linked to a wet animal wholesale market in Wuhan City, China.[1] By 7 January 2020, the causative virus was identified as SARS-CoV-2, which causes the disease COVID-19, and was declared a global emergency by the WHO on 30 January 2020.

Zhu *et al.* (2020) were able to identify and characterise SARS-CoV-2 using unbiased sequencing samples from infected patients with pneumonia.[2] The viral genome revealed SARS-CoV-2 to be 75–80% identical to severe acute respiratory syndrome coronavirus (SARS-CoV) and several bat coronaviruses. Prior to this discovery, six coronaviruses were known to cause human disease. Four viruses (229E, OC43, NL63 and HKU1) are prevalent and cause common cold symptoms. The two other strains are SARS-CoV and Middle East respiratory syndrome Coronavirus (MERS-CoV), both of which are zoonotic in origin and fatal. SARS-CoV-2 has joined as the seventh member of the family of coronaviruses that infect humans.[2] No specific treatment is yet accessible; however, management involves restriction of travel, patient isolation and the support of medical supervision.[3]

COVID-19 affects people in different ways, with patients exhibiting a range of symptoms and severity. While risk factors such as age, gender and comorbidities have been highlighted as increasing the risk of complications and mortality, there is still a high proportion of patients with no identified risk factors who suffer from severe side effects and complications. As much as 10–15% of people under 60 years old with no risk factors are exhibiting moderate to severe reactions to COVID-19.[1] While COVID-19 has a viral origin, it is suspected that in severe cases, bacterial superinfections may contribute to causing complications such as pneumonia and acute respiratory distress syndrome (ARDS). We explore the connection between high bacterial load in the mouth and post-viral complications, and how improving oral health may reduce the risk of complications from COVID-19.

Symptoms

The clinical symptoms of COVID-19 appear after an incubation period of approximately 5.2 days[4] and range from fever (98.6%), fatigue (69.6%), dry cough (59.4%), myalgia (34.8%) and sore throat (17.4%).[5] Diarrhoea has also been shown to be a key distinguishing symptom of COVID-19 compared with SARS-CoV and MERS-CoV.[6,7]

COVID-19 infections can present with mild, moderate or severe illness. The severity of the illness, the rate of decline and the risk of mortality are significantly dependent on risk factors highlighted by Zhou *et al.* (2020) in the largest retrospective cohort study among

[1]Dentistry, 38 Devonshire Street, London, W1G 6QB, UK; [2]Centre for Nutrition Education & Lifestyle Management, London, RG40 1DH, UK; [3]Orthodontics, Cambridge University Hospital Trust, Cambridge, CB1 0QQ, UK.
*Correspondence to: Victoria Sampson
Email address: drvictoriasampson@hotmail.com

Refereed Paper.
Accepted 21 May 2020
https://doi.org/10.1038/s41415-020-1747-8

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China

Dawei Wang, MD; Bo Hu, MD; Chang Hu, MD; Fangfang Zhu, MD; Xing Liu, MD; Jing Zhang, MD; Binbin Wang, MD; Hui Xiang, MD; Zhenshun Cheng, MD; Yong Xiong, MD; Yan Zhao, MD; Yirong Li, MD; Xinghuan Wang, MD; Zhiyong Peng, MD

Viewpoint
Related article
Audio

IMPORTANCE In December 2019, novel coronavirus (2019-nCoV)–infected pneumonia (NCIP) occurred in Wuhan, China. The number of cases has increased rapidly but information on the clinical characteristics of affected patients is limited.

OBJECTIVE To describe the epidemiological and clinical characteristics of NCIP.

DESIGN, SETTING, AND PARTICIPANTS Retrospective, single-center case series of the 138 consecutive hospitalized patients with confirmed NCIP at Zhongnan Hospital of Wuhan University in Wuhan, China, from January 1 to January 28, 2020; final date of follow-up was February 3, 2020.

EXPOSURES Documented NCIP.

MAIN OUTCOMES AND MEASURES Epidemiological, demographic, clinical, laboratory, radiological, and treatment data were collected and analyzed. Outcomes of critically ill patients and noncritically ill patients were compared. Presumed hospital-related transmission was suspected if a cluster of health professionals or hospitalized patients in the same wards became infected and a possible source of infection could be tracked.

RESULTS Of 138 hospitalized patients with NCIP, the median age was 56 years (interquartile range, 42-68; range, 22-92 years) and 75 (54.3%) were men. Hospital-associated transmission was suspected as the presumed mechanism of infection for affected health professionals (40 [29%]) and hospitalized patients (17 [12.3%]). Common symptoms included fever (136 [98.6%]), fatigue (96 [69.6%]), and dry cough (82 [59.4%]). Lymphopenia (lymphocyte count, 0.8 × 10^9/L [interquartile range {IQR}, 0.6-1.1]) occurred in 97 patients (70.3%), prolonged prothrombin time (13.0 seconds [IQR, 12.3-13.7]) in 80 patients (58%), and elevated lactate dehydrogenase (261 U/L [IQR, 182-403]) in 55 patients (39.9%). Chest computed tomographic scans showed bilateral patchy shadows or ground glass opacity in the lungs of all patients. Most patients received antiviral therapy (oseltamivir, 124 [89.9%]), and many received antibacterial therapy (moxifloxacin, 89 [64.4%]; ceftriaxone, 34 [24.6%]; azithromycin, 25 [18.1%]) and glucocorticoid therapy (62 [44.9%]). Thirty-six patients (26.1%) were transferred to the intensive care unit (ICU) because of complications, including acute respiratory distress syndrome (22 [61.1%]), arrhythmia (16 [44.4%]), and shock (11 [30.6%]). The median time from first symptom to dyspnea was 5.0 days, to hospital admission was 7.0 days, and to ARDS was 8.0 days. Patients treated in the ICU (n = 36), compared with patients not treated in the ICU (n = 102), were older (median age, 66 years vs 51 years), were more likely to have underlying comorbidities (26 [72.2%] vs 38 [37.3%]), and were more likely to have dyspnea (23 [63.9%] vs 20 [19.6%]), and anorexia (24 [66.7%] vs 31 [30.4%]). Of the 36 cases in the ICU, 4 (11.1%) received high-flow oxygen therapy, 15 (41.7%) received noninvasive ventilation, and 17 (47.2%) received invasive ventilation (4 were switched to extracorporeal membrane oxygenation). As of February 3, 47 patients (34.1%) were discharged and 6 died (overall mortality, 4.3%), but the remaining patients are still hospitalized. Among those discharged alive (n = 47), the median hospital stay was 10 days (IQR, 7.0-14.0).

CONCLUSIONS AND RELEVANCE In this single-center case series of 138 hospitalized patients with confirmed NCIP in Wuhan, China, presumed hospital-related transmission of 2019-nCoV was suspected in 41% of patients, 26% of patients received ICU care, and mortality was 4.3%.

JAMA. doi:10.1001/jama.2020.1585
Published online February 7, 2020.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Zhiyong Peng, MD, Department of Critical Care Medicine, Zhongnan Hospital of Wuhan University, Wuhan 430071, Hubei, China (Pengzy5@hotmail.com).

Section Editor: Derek C. Angus, MD, MPH, Associate Editor, *JAMA* (angusdc@upmc.edu).

Received: 4 June 2020 | Revised: 5 July 2020 | Accepted: 7 July 2020
DOI: 10.1111/odi.13555

LETTER TO THE EDITOR

ORAL DISEASES WILEY

Oral manifestations associated with COVID-19

The appearance in December of a new coronavirus has caused an unprecedented pandemic in the modern era. Undoubtedly, the disease produced by the novel coronavirus and its consequences have posed a challenge for health authorities worldwide. The way of contagion through direct contact and through saliva in the form of small drops and the production of aerosols have facilitated the rapid spread worldwide.

In Spain, the authorities declared the confinement for the majority of population in March 14; therefore, most of dental clinics were closed except for emergencies. Dentists were considered at high risk due to two factors: All procedures are obviously performed in the mouth with direct contact with saliva and the exposure to aerosols produced by rotatory instruments. Many articles have been published regarding the spread of the virus and the role that saliva plays in its transmission and diagnosis (Chen et al., 2020; Li et al., 2020; Sabino-Silva, Jardim, & Siqueira, 2020; Xu et al., 2020a,2020b; Zhong et al., 2020).

In relationship to extrapulmonary manifestations, several authors have reported cases with cutaneous manifestations in which maculo-papular, acral, urticariform, vesicular, and vascular obstruction-type manifestations are the most common (Estebanez et al., 2020; Galván Casas et al., 2020; Landa, Mendieta-Eckert, Fonda-Pascual, & Aguirre, 2020; Recalcati, 2020).

During this period, despite the implications of saliva for virus transmission and the possibility of salivary glands as a reservoir, few oral manifestations have been reported. Oral dryness, vesiculobullous lesions, aphthous-like lesions, dysgeusia, and anosmia are the most common oral signs reported (Martín Carreras-Presas, Amaro Sánchez, López-Sánchez, Jané-Salas, & Somacarrera Pérez, 2020; Xu et al., 2020a,2020b).

In this paper, we present 3 cases in which we have a confirmation for SARS-CoV-2 with oral manifestations.

A 43-year-old woman tested positive for SARS-CoV-2 for 56 days, period in which several PCRs were performed. Patient developed fever, malaise, dysgeusia and anosmia, diarrhea, and pneumonia, and blood laboratories suggested risk of thrombosis. She was isolated and remained in quarantine during this period with regular follow-ups by doctors over the phone. In the last 2 weeks, she reported aphthous-like lesions, burning sensation, and tongue depapillation that progressed as observed in Figure 1. Image was sent through SMS with informed consent and data protection for sending

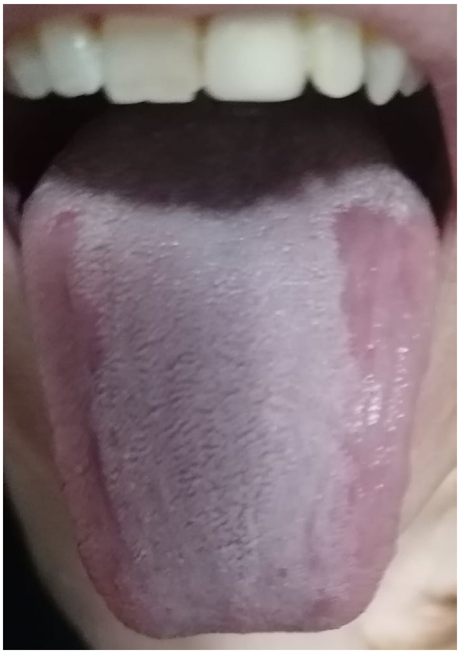


FIGURE 1 Bilateral atrophy of the surface of the tongue located in the lateral sides. Lateral dorsum appears depapillated with a symmetrical distribution

FIGURE 2 Commissural cheilitis. Notice the fissure and bleeding located in the commissure

DR ALMUDENA NUNO-GONZALEZ (Orcid ID : 0000-0001-7252-1647)
DR ANDER MAYOR IBARGUREN (Orcid ID : 0000-0003-1585-5995)

Article type : Research Letter

Prevalence of mucocutaneous manifestations, oral and palmoplantar findings in 666 patients with COVID-19 in a field hospital in Spain

Dear Editor:

Coronavirus disease 2019 (Covid-2019) has been associated with several cutaneous manifestations(1–3). A temporary field hospital was implemented during the pandemic peak in Madrid, Spain, to attend COVID-19 patients with mild to moderate pneumonia.

A team of dermatologists working as medical volunteers performed a cross-sectional study between April 10 and April 25, 2020 to evaluate cutaneous findings of such patients.

A total of 666 COVID-19 patients fulfilled the inclusion criteria (either positive RT-PCR testing for SARS-CoV-2 or bilateral pneumonia). The mean age was 55.67 years; with a slight female predominance (58%). Remarkably, 47.1% were from-Latin America.

Globally, 304 (45.65%) of our patients presented one or more mucocutaneous manifestations. Oral cavity findings were seen in 78 (25.65%) cases, including transient lingual papillitis (11.5%), glossitis with lateral indentations (6.6%)(Figure 1A), aphthous stomatitis (6.9%), glossitis with patchy depapillation (3.9%) (Figure 1B) and mucositis (3.9%). Burning sensation was reported in 5.3% of patients and taste disturbances (dysgeusia) was commonly associated.

Palmoplantar involvement was observed in 121 patients (39.8%) and included diffuse desquamation in 77 patients (25.3%), often favouring the weight bearing areas and reddish-to-brown acral macules on palms and soles in 46 (15.1%)(Figure 1C and 1D). Mild pruritus was occasionally reported. Fungal cultures of plantar desquamation performed in 9 patients ruled out superficial mycoses. Histological study from the acral macules was performed in 4 patients, showing a mild to moderate lymphocytic infiltrate surrounding the blood vessels and the eccrine

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/BJD.19564

Kansas Department of Health and Environment

Symptoms in Adults

COVID-19 vs. COLD vs. FLU vs. ALLERGIES

SYMPTOMS	COVID-19* (Gradual onset)	COLD (Sudden onset)	FLU (Sudden onset)	ALLERGIES (Varies)
Fever	Common (measured at 100 F or higher)	Rare	High (100-102 F), can last 3-4 days	No
General aches, pains	Common, sometimes severe	Slight	Common, often severe	No
Fatigue, weakness	Common (can lead to unexplained falls in elderly)	Slight	Common, often severe	Sometimes
Extreme exhaustion	Common	Never	Common (starts early)	No
Cough	Common	Mild to moderate	Common, can become severe	Sometimes
Shortness of breath	Common	Rare	Rare	Common
Chest pain	Common	Rare	Common	No
Poor appetite	Common	Sometimes	Common	No
Nausea, vomiting, abdominal pain	Common	Rare	Sometimes	No
Diarrhea	Common	No	Sometimes	No
Loss of smell or taste	Often	Rare (congestion could impact smell)	No	Possible (congestion could impact smell)
Chills	Sometimes	Rare	Common	No
Headache	Sometimes	Rare	Intense	Sometimes
Sore throat	Sometimes	Common	Common	No
Runny nose	Sometimes	Common	Sometimes	Common
Stuffy nose	Rare	Common	Sometimes	Common
Sneezing	Rare	Common	Sometimes	Common

For more information: www.coronavirus.kdheks.gov

Sources: KDHE, CDC, CSTE, WHO, NIH, National Institute of Allergy and Infectious Diseases, American College of Allergy, Asthma and Immunology.

Revised 9/22/20

Canadian Association of Radiologists' Journal
1-6

DOI: 10.1177/0846537120913033
journals.sagepub.com/home/caj
SAGE

CT Imaging and Differential Diagnosis of COVID-19

Wei-cai Dai, MD[1,2], Han-wen Zhang, MD[3], Juan Yu, MD, PhD[3], Hua-jian Xu, MD[3], Huan Chen, MD[3], Si-ping Luo, MM[3], Hong Zhang, MM[3], Li-hong Liang, MM[3], Xiao-liu Wu, BMT[3], Yi Lei, MD[3], and Fan Lin, MD, PhD[3]

Abstract

Since the beginning of 2020, coronavirus disease 2019 (COVID-19) has spread throughout China. This study explains the findings from lung computed tomography images of some patients with COVID-19 treated in this medical institution and discusses the difference between COVID-19 and other lung diseases.

Résumé

Depuis le début de l'année 2020, la maladie à coronavirus 2019 (COVID-19) s'est répandue dans toute la Chine. Cette étude analyse les résultats tirés des images de TDM pulmonaire de certains patients atteints de COVID-19 traités dans cet établissement médical et examine la différence entre le COVID-19 et d'autres maladies pulmonaires.

Keywords

COVID19, CT, pneumonia, lung diseases, 2019n-CoV

Introduction

Since December 2019, cases of coronavirus disease 2019 (COVID-19) have been emerging in Wuhan, Hubei Province, China, and the epidemic has swiftly spread to other parts of China and beyond.[1] As of February 25, there were a total of 77 779 cases of diagnosed COVID-19, 2824 cases of suspected COVID-19, 27 361 cured cases, and 2666 deaths from it in China, and there were 2464 cases of diagnosed COVID-19, 189 cured cases, and 43 deaths outside China. Compared with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), COVID-19 has lower mortality, a stronger occult nature, and a greater transmission capacity.[2] Like the former two, COVID-19 can be transmitted through the respiratory tract and by contact and has evidence of human–human transmission. Another possible transmission route, fecal–oral transmission, has not been confirmed.

In the initial screening, computed tomography (CT) examination is needed for the auxiliary diagnosis.[3] The diagnosis is then confirmed by the positive results of the nucleic acid amplification test (NAAT) of the respiratory tract or blood specimens using reverse transcription real-time fluorescence polymerase chain reaction (RT-PCR).[2] However, this diagnosis method is highly limited: (1) When the viral load is low, the detection rate is low, leading to false-negative results. (2) Only a positive diagnosis can be made, but the severity of COVID-19 and its progression cannot be judged (in contrast, CT imaging can reveal disease progression). (3) The supply of the reagents cannot keep up with the demand, and the quality of new products of major companies awaits to be studied and improved. (4) It takes 1 day or longer to obtain the results after sampling. For these reasons, Chinese researchers strongly recommend CT imaging as the main basis for the diagnosis of COVID-19 in the current situation.[4] An academician of the American Society for Radiation Oncology called for the immediate establishment of a CT-based diagnostic method for COVID-19 and improvement of the detection rate of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[5] If a patient with clinically suspected COVID-19 has negative NAAT results but positive imaging results, the patient should be isolated and treated as soon as possible. The advantage of CT examination in the

[1] Guangzhou Medical University, Guangzhou, China
[2] Imaging Department, Fifth People's Hospital of Longgang District, Shenzhen, China
[3] Department of Radiology, The First Affiliated Hospital of Shenzhen University, Health Science Center, Shenzhen Second People's Hospital, Shenzhen, China

Corresponding Authors:
Yi Lei, MD and Fan Lin, MD, PhD, Department of Radiology, The First Affiliated Hospital of Shenzhen University, Health Science Center, Shenzhen Second People's Hospital, 3002 SunGangXi Road, Shenzhen 518035, China.
Emails: 13602658583@163.com; foxetfoxet@gmail.com

Clinical Microbiology and Infection 26 (2020) 842–847

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

COVID-19 pandemic—a focused review for clinicians

M. Cevik [1,*], C.G.G. Bamford [2], A. Ho [3]

[1] Division of Infection and Global Health Research, School of Medicine, University of St Andrews, UK
[2] Wellcome–Wolfson Institute for Experimental Medicine, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK
[3] MRC-University of Glasgow Centre for Virus Research, University of Glasgow, Glasgow, UK

ARTICLE INFO

Article history:
Received 8 April 2020
Received in revised form
19 April 2020
Accepted 21 April 2020
Available online 25 April 2020

Editor: L Leibovici

Keywords:
Coronavirus
COVID-19
Novel coronavirus
SARS-CoV-2

ABSTRACT

Background: The COVID-19 pandemic caused by SARS-CoV-2 remains a significant issue for global health, economics and society. A wealth of data has been generated since its emergence in December 2019, and it is vital for clinicians to keep up with this data from across the world at a time of uncertainty and constantly evolving guidelines and clinical practice.
Objectives: Here we provide an update for clinicians on the recent developments in the virology, diagnostics, clinical presentation, viral shedding, and treatment options for COVID-19 based on current literature.
Sources: We considered published peer-reviewed papers and non-peer-reviewed pre-print manuscripts on COVID19 and related aspects with an emphasis on clinical management aspects.
Content: We describe the virological characteristics of SARS-CoV-2 and the clinical course of COVID-19 with an emphasis on diagnostic challenges, duration of viral shedding, severity markers and current treatment options.
Implications: The key challenge in managing COVID-19 remains patient density. However, accurate diagnosis as well as early identification and management of high-risk severe cases are important for many clinicians. For improved management of cases, there is a need to understand test probability of serology, qRT-PCR and radiological testing, and the efficacy of available treatment options that could be used in severe cases with a high risk of mortality. **M. Cevik, Clin Microbiol Infect 2020;26:842**

Introduction

The first cases of atypical pneumonia of unidentified aetiology were reported on December 30, 2019, from Wuhan, China. By January 7, 2020, a novel betacoronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified, while the disease has been named COVID-19. COVID-19 has now been declared a pandemic, affecting nearly every country, with over 2.3 million confirmed cases and >160 000 deaths. The initial clinical case series from China largely comprised hospitalized patients with severe pneumonia. Further data suggested that approximately 80% of the patients have mild disease, 20% require hospital admission, and approximately 5% require intensive care admission [1]. Mortality rates are higher among people over 60 years of age and with coexisting conditions (most commonly hypertension, diabetes and cardiovascular disease). Here we provide an update for clinicians on the recent developments in virology, diagnostics, clinical presentation, and treatment options for COVID-19 based on current literature.

Virology

Metagenomic sequencing and targeted real-time polymerase chain reaction (qRT-PCR) assays identified a novel human CoV (SARS-CoV-2) in bronchoalveolar lavage fluid taken from the initial patient cluster in Wuhan [2]. Infectious SARS-CoV-2 has been cultured on monkey Vero, human Huh7 and primary human airway epithelial cells [3], where it is cytopathic. Furthermore, serum antibodies (IgM and IgG) from cases neutralized SARS-CoV-2 in cell culture and detected virus-infected cells by indirect immunofluorescence [3].

Phylogenetic analysis reveals that SARS-CoV-2 is closely related to SARS-CoV (~80% similar) in the *Sarbecovirus* subfamily (genus

* Corresponding author. M. Cevik, Division of Infection and Global Health Research, School of Medicine, University of St Andrews, Fife, KY16 9TF. UK.
E-mail address: mc349@st-andrews.ac.uk (M. Cevik).

https://doi.org/10.1016/j.cmi.2020.04.023
1198-743X/

Received: 8 April 2020 | Revised: 16 April 2020 | Accepted: 17 April 2020

DOI: 10.1111/bph.15072

Themed Issue: The Pharmacology of COVID-19

REVIEW ARTICLE

Current pharmacological treatments for COVID-19: What's next?

Cristina Scavone[1] | Simona Brusco[1] | Michele Bertini[1] | Liberata Sportiello[1] | Concetta Rafaniello[1] | Alice Zoccoli[2] | Liberato Berrino[1] | Giorgio Racagni[3] | Francesco Rossi[1,2] | Annalisa Capuano[1]

[1]Department of Experimental Medicine, Università degli studi della Campania "Luigi Vanvitelli", Naples, Italy

[2]Clinical Innovation Office, Università Campus Bio-medico, Rome, Italy

[3]Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy

Correspondence
Cristina Scavone, Department of Experimental Medicine, Università degli studi della Campania "Luigi Vanvitelli", Naples, Italy.
Email: cristina.scavone@unicampania.it

Since December 2019 SARS-Cov-2 was found responsible for the disease COVID-19, which has spread worldwide. No specific therapies/vaccines are yet available for the treatment of COVID-19. Drug repositioning may offer a strategy and a number of drugs have been repurposed, including lopinavir/ritonavir, remdesivir, favipiravir and tocilizumab. This paper describes the main pharmacological properties of such drugs administered to patients with COVID-19, focusing on their antiviral, immune-modulatory and/or anti-inflammatory actions. Where available, data from clinical trials involving patients with COVID-19 are reported. Preliminary clinical trials seem to support their benefit. However, such drugs in COVID-19 patients have peculiar safety profiles. Thus, adequate clinical trials are necessary for these compounds. Nevertheless, while waiting for effective preventive measures i.e. vaccines, many clinical trials on drugs belonging to different therapeutic classes are currently underway. Their results will help us in defining the best way to treat COVID-19 and reducing its symptoms and complications.

LINKED ARTICLES: This article is part of a themed issue on The Pharmacology of COVID-19. To view the other articles in this section visit http://onlinelibrary.wiley.com/doi/10.1111/bph.v177.21/issuetoc

Abbreviations: AAK1, protein kinase 1 associated with AP2; AIFA, Italian Medicine Agency; ARDS, acute respiratory distress syndrome; BEST-RCT and BEST-CP, clinical trials on bevacizumab; CamoCO-19, clinical trial on camostat mesilate; CD147, cluster of differentiation 147; ChiCTR2000030906 and NCT04283461, studies on vaccines; ChiCTR200030254, clinical trial on favipiravir; COLCORONA, clinical trial on colchicine; EMA, European Medicine Agency; FDA, Food and Drug Administration; HIV, human immunodeficiency virus; IL-6R, IL-6 receptor; IP-10, IFN-γ-induced protein 10; MERS-CoV, Middle East Respiratory Syndrome Coronavirus; PD-1, programmed cell death protein 1; PD-L1, programmed death–Ligand 1; RdRp, RNA-dependent RNA polymerase; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TMPRSS2, Transmembrane Serine Protease 2; VEGF, growth factor of vascular endothelial cells; VIP, vasoactive intestinal polypeptide; WHO, World Health Organization.

Cristina Scavone, Simona Brusco and Michele Bertini have equally contributed.

Francesco Rossi and Annalisa Capuano are both lead authors.

[The copyright line for this article was changed on 19 September 2020 after original online publication]

ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

J. Grein, N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M.L. Green, F.-X. Lescure, E. Nicastri, R. Oda, K. Yo, E. Quiros-Roldan, A. Studemeister, J. Redinski, S. Ahmed, J. Bernett, D. Chelliah, D. Chen, S. Chihara, S.H. Cohen, J. Cunningham, A. D'Arminio Monforte, S. Ismail, H. Kato, G. Lapadula, E. L'Her, T. Maeno, S. Majumder, M. Massari, M. Mora-Rillo, Y. Mutoh, D. Nguyen, E. Verweij, A. Zoufaly, A.O. Osinusi, A. DeZure, Y. Zhao, L. Zhong, A. Chokkalingam, E. Elboudwarej, L. Telep, L. Timbs, I. Henne, S. Sellers, H. Cao, S.K. Tan, L. Winterbourne, P. Desai, R. Mera, A. Gaggar, R.P. Myers, D.M. Brainard, R. Childs, and T. Flanigan

ABSTRACT

BACKGROUND

Remdesivir, a nucleoside analogue prodrug that inhibits viral RNA polymerases, has shown in vitro activity against SARS-CoV-2.

METHODS

We provided remdesivir on a compassionate-use basis to patients hospitalized with Covid-19, the illness caused by infection with SARS-CoV-2. Patients were those with confirmed SARS-CoV-2 infection who had an oxygen saturation of 94% or less while they were breathing ambient air or who were receiving oxygen support. Patients received a 10-day course of remdesivir, consisting of 200 mg administered intravenously on day 1, followed by 100 mg daily for the remaining 9 days of treatment. This report is based on data from patients who received remdesivir during the period from January 25, 2020, through March 7, 2020, and have clinical data for at least 1 subsequent day.

RESULTS

Of the 61 patients who received at least one dose of remdesivir, data from 8 could not be analyzed (including 7 patients with no post-treatment data and 1 with a dosing error). Of the 53 patients whose data were analyzed, 22 were in the United States, 22 in Europe or Canada, and 9 in Japan. At baseline, 30 patients (57%) were receiving mechanical ventilation and 4 (8%) were receiving extracorporeal membrane oxygenation. During a median follow-up of 18 days, 36 patients (68%) had an improvement in oxygen-support class, including 17 of 30 patients (57%) receiving mechanical ventilation who were extubated. A total of 25 patients (47%) were discharged, and 7 patients (13%) died; mortality was 18% (6 of 34) among patients receiving invasive ventilation and 5% (1 of 19) among those not receiving invasive ventilation.

CONCLUSIONS

In this cohort of patients hospitalized for severe Covid-19 who were treated with compassionate-use remdesivir, clinical improvement was observed in 36 of 53 patients (68%). Measurement of efficacy will require ongoing randomized, placebo-controlled trials of remdesivir therapy. (Funded by Gilead Sciences.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Brainard at Gilead Sciences, 333 Lakeside Dr., Foster City, CA 94404, or at diana.brainard@gilead.com.

This article was published on April 10, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2007016

EDITORIAL

Aerosol reduction urgency in post-COVID-19 dental practice

Aerosols are essentially suspensions of liquid droplets or fine solid particles in air. The three potential sources of aerosols in dental settings are dental instruments, saliva and respiratory sources, and the operative site.[1] Although attempts have been made in the past to compare the different types of aerosol reduction mechanisms produced during dental procedures, especially when using ultrasonic scaling,[2] aerosol management in dentistry is currently in the limelight during this COVID-19 pandemic. Most of the aerosol production in clinical dental practice is via air-driven handpieces, ultrasonic devices, air polishers, and airborne-particle abrasion units. Aerosols are also possible in certain periodontal and oral surgical procures.[1] A high volume evacuator (HVE), with its large diameter (> 8 mm) helps in removing large volumes of air/splatter/droplets in a short amount of time, which reduces the amount of bio-aerosols up to 90%.[1]

Aerosols can be differentiated based on particle size. When the particle size is less than 50 µm, it is called splatter; in excess of 50 µm, it is termed droplet. If the particle size is less than 10 µm, the term droplet nuclei is used. In dental settings, 90% of aerosols produced are smaller than 5µm.[1,3] SARS-CoV-2 particle sizes vary from 0.06 to 0.14µm.[4] In one dry-field in vitro study conducted in 2012, it was shown that using rubber dam with HVE or a commercially available system reduced aerosol splatter significantly more than when using HVE alone.[5] Most studies prior to 2020 were focused on oral bacterial colonization; however, in the present situation, high transmissibility of SARS-CoV-2 must be taken into account. The spread is thought to be amplified via aerosols. Therefore, aerosol containment and complete reduction in the splatter must be a top priority as the world begins to heal and dental practices get back to normalcy.

Several adapters are commercially available that have combined illumination with an HVE adapter. They can be steam-autoclaved at temperatures up to 138°C/280°F. The existing guidelines from CDC refer to cleaning and heat-sterilizing aerosol-producing handpieces between patients and following standard disinfection procedures for overall infection control in the dental office.[3] For post-COVID-19 dental practice, there is an urgent need to address the aerosol reduction because SARS-CoV-2 can be spread via droplets and splatter. Detection of SARS-CoV-2 in the saliva of infected patients may indicate a salivary gland infection, but this could also be due to contamination from lung secretions via the nasopharynx.[6] Use of appropriate personal protective equipment (PPE), along with reduced splatter and use of high efficiency particulate arrestor (HEPA) filters (to arrest the most penetrating particle sizes – 0.3 µm) might be a winning combination for dental practitioners and patients. Although negative pressure operatories were initially mandated for dentists who treated emergency patients during the pandemic, state health authorities in the United States have removed this restriction if all other history and physical examination findings point to an asymptomatic patient. The dental profession should look at this important aspect urgently and come up with isolation and splatter reduction techniques that can be universally adapted.

In the Occupational Safety and Health Administration (OSHA) occupational risk pyramid for COVID-19, dentists fall under "very high exposure risk."[7] Aerosol reduction or mitigation should remain a top priority for the dental profession in the post-COVID-19 dental practice.

Mel Mupparapu, DMD
Scientific Associate Editor

References

1. Harrel SK, Molinari J. Aerosols and splatter in dentistry: a brief review of the literature and infection control implications. J Am Dent Assoc 2004;135:429–437.

2. Holloman JL, Mauriello SM, Pimenta L, Arnold RR. Comparison of suction device with saliva ejector for aerosol and spatter reduction during ultrasonic scaling. J Am Dent Assoc 2015;146:27–33.

3. Kohn WG, Collins AS, Cleveland JL, et al. Guidelines for infection control in dental health-care settings – 2003. MMWR Recomm Rep 2003;52(RR-17). https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5217a1.htm. Accessed 22 May 2020.

4. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–733.

5. Dahlke WO, Cottam MR, Herring MC, et al. J Am Dent Assoc 2012;143:1199–1204.

6. To KK, Tsang OT, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva (epub ahead of print, 12 Feb 2020). Clin Infect Dis doi: 10.1093/cid/ciaa149.

7. Guidance on preparing workplaces for COVID-19. US Department of Labor. Occupational Safety and Health Administration. 2020. https://www.osha.gov/Publications/OSHA3990.pdf. Accessed 22 May 2020.

Mel Mupparapu

REV PORT ESTOMATOL MED DENT CIR MAXILOFAC. 2013;**54(1)**:2–7

ELSEVIER DOYMA

Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial

www.elsevier.pt/spemd

Research

Air quality assessment during dental practice: Aerosols bacterial counts in an universitary clinic

Patrícia Manarte-Monteiro[a], *Alexandrine Carvalho*[a], *Cristina Pina*[b], *Hélder Oliveira*[a], *Maria Conceição Manso*[c,d,*]

[a] *Department of Medical Sciences, Faculty of Health Sciences, University Fernando Pessoa, Portugal*

[b] *CEBIMED, Department of Microbiology, Faculty of Health Sciences, University Fernando Pessoa, Porto, Portugal*

[c] *Faculty of Health Sciences, University Fernando Pessoa, Porto, Portugal*

[d] *REQUIMTE, University of Porto, Portugal*

ARTICLE INFO

Article history:
Received 24 March 2012
Accepted 1 October 2012
Available online 21 February 2013

Keywords:
Aerosols
Microbiology
Dental cavity preparation/instrumentation
Infection control, dental/instrumentation

ABSTRACT

Objective: The main aim of this study was to assess the clinic atmosphere quality regarding the Index of Air Microbial contamination (IMA), according to dental aerosols bacterial counts, when different dentistry procedures are performed.

Material and methods: The aerosols generated by dentistry and endodontic procedures were analyzed in 26 dental units of the dental clinic. Blood agar plates ($n = 244$) were incubated at 37 °C/48 h and the colony forming units (CFU) were calculated.

All statistical analysis methods were conducted using the SPSS® vs.17.0 software (SPSS Inc., IL, Chicago, USA), using $\alpha = 0.05$ for the comparison tests used (non parametric tests of Mann–Whitney and Wilcoxon).

Results: The IMA median value in the dental clinic was of 10.4 CFU/dm^2/h. Aerosols' CFU counts were significantly higher at 0.5 m and during endodontic treatments. Longer treatment times were associated with higher CFU counts both in dentistry and endodontic procedures. The use and time of turbine use did not significantly affect the CFU counts. *Micrococcus* sp., *Staphylococcus* sp. and *Streptococcus* sp. were identified with presumptive tests after isolation of representative colonies.

Conclusion: Considering the IMA, the dental clinic atmosphere quality was found to be good.

Avaliação da qualidade do ar na prática clínica: contagens bacterianas em aerossóis numa clínica universitária

Palavras-chave:
Aerossóis

RESUMO

Objetivo: O objetivo principal deste trabalho foi determinar a qualidade do ar da clínica utilizando o *Index of Air Microbial contamination* (IMA), mediante utilização de contagens

* *Corresponding author.*
E-mail address: cmanso@ufp.edu.pt (M.C. Manso).

1646-2890/$ – see front matter © 2012 Sociedade Portuguesa de Estomatologia e Medicina Dentária. Published by Elsevier España, S.L. All rights reserved.
http://dx.doi.org/10.1016/j.rpemd.2012.10.002

Int. J. Odontostomat.,
14(4):519-522, 2020.

Los Aerosoles Dentales a Propósito de la Pandemia por COVID-19

Dental Aerosols in the Context of COVID-19 Pandemic

César Rivera

RIVERA, C. Los aerosoles dentales a propósito de la pandemia por COVID-19. *Int. J. Odontostomat., 14(4)*:519-522, 2020.

RESUMEN: La pandemia por COVID-19 ha hecho que la atención odontológica de rutina se suspenda. La causa principal es el pobre control del aerosol en la consulta dental. Los aerosoles liberados por el instrumental odontológico son esenciales para la remoción de los tejidos bucales enfermos. Sin embargo, al mezclarse con saliva o sangre contaminada, los aerosoles pueden diseminar microorganismos infectivos fuera de la boca del paciente. Existe evidencia de que el SARS-CoV-2 se encuentra en la saliva del 91,7 % de los sujetos enfermos. Este artículo presenta evidencias y reflexiones para el control del aerosol odontológico, las que podrían permitir aumentar la seguridad del ejercicio de la odontología durante la pandemia y pospandemia.

PALABRAS CLAVE: COVID-19, SARS-CoV-2, odontología, aerosoles.

INTRODUCCIÓN

A finales de 2019, se identificó un nuevo coronavirus como la causa de un grupo de casos de neumonía en Wuhan, una ciudad de China. Se extendió rápidamente, dando como resultado una pandemia. En febrero de 2020, la Organización Mundial de la Salud designó la enfermedad COVID-19, que significa enfermedad por coronavirus 2019 (World Health Organization, 2020). El virus que causa COVID-19 se denomina coronavirus tipo 2 del síndrome respiratorio agudo severo (SARS-CoV-2). La pandemia generada llevó a múltiples agrupaciones dentales, entre ellas a la Asociación Dental Americana, a hacer un llamado a suspender los procedimientos odontológicos electivos (American Dental Association, 2020a). Este texto aporta evidencias para profundizar la reflexión de la comunidad odontológica respecto al control de los aerosoles dentales.

El SARS-CoV-2 es un patógeno de alto riesgo individual y comunitario

El SARS-CoV-2 es un virus de alto riesgo individual y comunitario, que se propaga muy fácilmente y de manera continua entre las personas. La diseminación puede ocurrir por gotitas respiratorias que se producen cuando una persona (sintomática o asintomática) infectada tose, estornuda o habla. Las gotas liberadas recorren más de 2 metros, llegando incluso a los 8 metros (Bahl *et al*., 2020). Las partículas virales son muy pequeñas, con un tamaño de entre 0,06 y 0,14 micrones (Zhu *et al*., 2020). La proteína Spyke (S) del SARS-CoV-2 se une a la enzima convertidora de angiotensina 2 (ACE2), y en concierto con proteasas del hospedero, principalmente la serina proteasa transmembrana de tipo 2 (TMPRSS2), promueve la entrada celular. Este evento ocurriría en las células caliciformes nasales, los neumocitos tipo II pulmonares y en los enterocitos absorbentes ileales (Ziegler *et al*., 2020). El tamaño del virus es suficiente para ingresar a los alvéolos, torrente sanguíneo y llegar hasta órganos diana, como el corazón y el cerebro (Froum, 2020). Por eso se hace necesario que para la protección clínica contra el SARS-CoV-2 los profesionales de la salud requieran mascarillas o respiradores eficientes. Clínicamente, los respiradores N100 y FFP3 tienen la mejor performance (sobre un 99,9 % de filtrado de partículas de 0,3 micrones) seguido de los respiradores N95 y FFP2 (con un filtrado de 95 % y 94 % respectivamente) (Fathizadeh *et al.,* 2020). Sin embargo, estos implementos podrían no ser totalmente capaces de filtrar las partículas más pequeñas de

Magíster en Patología Oral y Doctor en Estomatopatología. Grupo de Medicina Oral, Departamento de Estomatología, Facultad de Ciencias de la Salud, Universidad de Talca, Chile.

CORRESPONDENCE

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1

TO THE EDITOR: A novel human coronavirus that is now named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly called HCoV-19) emerged in Wuhan, China, in late 2019 and is now causing a pandemic.[1] We analyzed the aerosol and surface stability of SARS-CoV-2 and compared it with SARS-CoV-1, the most closely related human coronavirus.[2]

We evaluated the stability of SARS-CoV-2 and SARS-CoV-1 in aerosols and on various surfaces and estimated their decay rates using a Bayesian regression model (see the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org). SARS-CoV-2 nCoV-WA1-2020 (MN985325.1) and SARS-CoV-1 Tor2 (AY274119.3) were the strains used. Aerosols (<5 μm) containing SARS-CoV-2 ($10^{5.25}$ 50% tissue-culture infectious dose [$TCID_{50}$] per milliliter) or SARS-CoV-1 ($10^{6.75-7.00}$ $TCID_{50}$ per milliliter) were generated with the use of a three-jet Collison nebulizer and fed into a Goldberg drum to create an aerosolized environment. The inoculum resulted in cycle-threshold values between 20 and 22, similar to those observed in samples obtained from the upper and lower respiratory tract in humans.

Our data consisted of 10 experimental conditions involving two viruses (SARS-CoV-2 and SARS-CoV-1) in five environmental conditions (aerosols, plastic, stainless steel, copper, and cardboard). All experimental measurements are reported as means across three replicates.

SARS-CoV-2 remained viable in aerosols throughout the duration of our experiment (3 hours), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per liter of air. This reduction was similar to that observed with SARS-CoV-1, from $10^{4.3}$ to $10^{3.5}$ $TCID_{50}$ per milliliter (Fig. 1A).

SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces (Fig. 1A), although the virus titer was greatly reduced (from $10^{3.7}$ to $10^{0.6}$ $TCID_{50}$ per milliliter of medium after 72 hours on plastic and from $10^{3.7}$ to $10^{0.6}$ $TCID_{50}$ per milliliter after 48 hours on stainless steel). The stability kinetics of SARS-CoV-1 were similar (from $10^{3.4}$ to $10^{0.7}$ $TCID_{50}$ per milliliter after 72 hours on plastic and from $10^{3.6}$ to $10^{0.6}$ $TCID_{50}$ per milliliter after 48 hours on stainless steel). On copper, no viable SARS-CoV-2 was measured after 4 hours and no viable SARS-CoV-1 was measured after 8 hours. On cardboard, no viable SARS-CoV-2 was measured after 24 hours and no viable SARS-CoV-1 was measured after 8 hours (Fig. 1A).

THIS WEEK'S LETTERS

News Releases
2021 Archive
2020 Archive
2019 Archive
Press Room Home

American Dental Association Responds to World Health Organization Recommendation: Dentistry is Essential Health Care

August 12, 2020

Contact Information:
mediarelations@ada.org

CHICAGO, August 12, 2020 —The American Dental Association (ADA) respectfully yet strongly disagrees with the World Health Organization's (WHO) recommendation to delay "routine" dental care in certain situations due to COVID-19.

"Oral health is integral to overall health. Dentistry is essential health care," states ADA President Chad P. Gehani, D.D.S. "Dentistry is essential health care because of its role in evaluating, diagnosing, preventing or treating oral diseases, which can affect

Int. J. Odontostomat.,
14(4):555-560, 2020.

Manifestaciones Orales de la Infección por COVID-19

Oral Manifestations of COVID-19

María Eugenia Nemeth Kohanszky[1]; Carolina Paz Matus Abásolo[2] & Rolando Rafael Carrasco Soto[3,4]

NEMETH, K. M. E.; MATUS, A. C. P. & CARRASCO, S. R. R. Manifestaciones orales de la infección por COVID-19. *Int. J. Odontostomat., 14(4)*:555-560, 2020.

RESUMEN: El 8 de enero de 2020, el Centro Chino para el Control y Prevención de Enfermedades anunció oficialmente la identificación de una nueva cepa de coronavirus (SARS-CoV-2) como el patógeno causante de la pandemia mundial de COVID-19. Las principales manifestaciones clínicas producidas por SARS-CoV-2 se encuentran ampliamente descritas en la literatura, sin embargo, la información acerca de las alteraciones que podrían producirse a nivel oral, es escasa. Se ha sugerido que la cavidad oral es un perfecto hábitat para la invasión por SARS-CoV-2 debido a la especial afinidad que tiene el virus por células con los receptores para la enzima convertidora de angiotensina (ECA2) como son las del tracto respiratorio, mucosa oral, lengua y glándulas salivales, pudiendo afectar, de este modo, el funcionamiento de las glándulas salivales, las sensaciones del gusto, olfato y la integridad de la mucosa oral. El nuevo coronavirus tendría la capacidad de alterar el equilibrio de la microbiota oral, lo que sumado a un sistema inmune deprimido permitiría la colonización por infecciones oportunista. Se ha establecido que un correcto higiene oral podría disminuir la incidencia y gravedad de las principales complicaciones del COVID-19. El objetivo de este estudio es realizar una revisión y análisis de la evidencia disponible en relación a las manifestaciones orales a nivel de las mucosas, trastornos de las glándulas salivales y alteraciones en el sistema olfatorio y gustativo en el contexto de la infección por SARS-CoV-2.

PALABRAS CLAVE: COVID-19, SARS-CoV-2, manifestaciones orales

INTRODUCCIÓN

El 8 de enero de 2020, el Centro Chino para el Control y Prevención de Enfermedades anunció oficialmente la identificación de una nueva cepa de coronavirus (SARS-CoV-2) como el patógeno causante de la pandemia mundial de COVID-19 (Li *et al*. 2020). En comparación con otras pandemias recientes el COVID-19 tiene, en general, una presentación clínica menos severa, sin embargo, se propaga con mayor facilidad, lo que ha generado aproximadamente 16,7 millones de contagios y más de 650.000 muertes a nivel mundial, al 29 de julio del 2020 (World Health Organization, 2020).

La información disponible acerca de las principales manifestaciones clínicas producidas por SARS-CoV-2 tales como fiebre, tos seca, diarrea y dificultad respiratoria es amplia y detallada, sin embargo, aquella sobre los síntomas reportados más recientemente, presentes en su mayoría en una etapa más temprana de la infección, tales como lesiones cutáneas, alteraciones del olfato y repercusiones a nivel oral, es escasa.

El impacto del COVID-19 en la salud oral está principalmente determinado por el sistema inmunológico del paciente, la farmacoterapia que recibe y por la patogenia del virus. Se ha sugerido que la cavidad oral es un perfecto hábitat para la invasión por SARS-CoV-2 debido a la especial afinidad que tiene el virus por células con los receptores para la enzima convertidora de angiotensina (ECA2) como son las del tracto respiratorio, mucosa oral, lengua y glándulas salivales (Xu *et al*., 2020; Peng *et al*., 2020).

Se ha demostrado que el SARS-CoV-2 es un virus neurotrópico y mucotrópico, pudiendo afectar el funcionamiento de las glándulas salivales, las sensa-

[1] Cirujana Dentista, Facultad de Odontología, Universidad del Desarrollo, Concepción.
[2] Cirujana Dentista, Facultad de Odontología, Universidad de Chile.
[3] Especialista en Cirugía y traumatología Maxilofacial, Hospital San Juan de Dios, Santiago, Chile
[4] Especialista en Cirugía y traumatología Maxilofacial, Clínica Las Condes, Santiago, Chile.

The Laryngoscope

Anosmia and Ageusia: Common Findings in COVID-19 Patients

Luigi A. Vaira, MD; Giovanni Salzano, MD; Giovanna Deiana, MD; Giacomo De Riu, MD, FEBOMFS

In a not negligible number of patients affected by COVID-19 (coronavirus disease 2019), especially if paucisymptomatic, anosmia and ageusia can represent the first or only symptomatology present.

***Laryngoscope*, 00:1, 2020**

RAPID COMMUNICATION

Europe and America currently represent the new front where the battle against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is being fought. In the management of the health crisis, the identification of paucisymptomatic patients is emerging as a crucial factor in order to interrupt the transmission chain of the virus. In the centers that are facing this emergency, a significant number of patients presenting anosmia and ageusia associated with fever (> 37.5°C) as onset symptoms are being detected. This minor and nonspecific symptomatology can represent the only manifestation of the disease.

Mao et al.[1] analyzed the frequency of neurological manifestations in 214 patients with coronavirus disease 2019 (COVID-19), identifying anosmia in 11 (5.1%) patients and ageusia in 12 (5.6%) patients. There are no other studies in the literature regarding neurological symptoms in patients with COVID-19.

Unfortunately, the actual emergency situation does not allow us to provide a precise incidence of the manifestation, but our estimates from history and physical examination of the first 320 patients for whom we have data indicate that chemosensory dysfunction is present in 19.4%. This incidence can be underestimated because the gustatory and olfactory function is not always investigated.

Anosmia has already been reported in the course of SARS[2] and other coronavirus[3,4] infections; however, it represents a rare occurrence. Interestingly, in COVID-19 patients ageusia and anosmia are not accompanied by nasal obstruction or other rhinitis symptoms. Therefore, this is probably due to the direct damage of the virus on the olfactory and gustatory receptors.[5] Currently, it is not possible to determine whether there will be a full recovery of the olfactory and gustatory functions or how long it will take.

However, on the basis of the experience that is being acquired in Italy, we believe it is important to inform otolaryngologists colleagues to pay attention to these possible manifestations of SARS-CoV-2 infection. In a non-negligible number of patients, especially if paucisymptomatic, ageusia and anosmia can represent the first or the only symptomatology manifestation. It will be important, when feasible, to obtain olfactory and gustatory testing data on patients with confirmed COVID-19 testing to provide quantitative data on the incidence and severity of these sensory losses. Finally, understanding mechanisms of sensorineural olfactory loss with coronavirus infections might provide novel insights into aspects of viral pathogenesis.

ACKNOWLEDGMENT

The authors would like to thank all Italian health workers for the efforts and sacrifices they are making during this serious health crisis.

BIBLIOGRAPHY

1. Mao L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. *MedR* 2020;xiv. https://doi.org/10.1101/2020.02.22.20026500.
2. Hwang CS. Olfactory neuropathy in severe acute respiratory syndrome: report of a case. *Acta Neurol Taiwan* 2006;15:26–28.
3. De Haro-Licer J, Roura-Moreno J, Vizitiu A, Gonzàlez-Fernàndez A, Gonzàlez-Ares JA. Long term serious olfactory loss in cold and/or flu. *Acta Otorrinolaringol Esp* 2013;64:331–338.
4. Suzuki M, Saito K, Min WP, et al. Identification of viruses in patients with postviral olfactory dysfunction. *Laryngoscope* 2007;117:272–277.
5. Yamagishi M, Fujiwara M, Nakamura H. Olfactory mucosal findings and clinical course in patients with olfactory disorders following upper respiratory viral infection. *Rhinology* 1994;32:118–133.

From the Maxillofacial Surgery Unit (L.A.V., G.D.R.), University Hospital of Sassari, Sassari, Italy; Department of Medical, Surgical and Experimental Sciences (G.D.), University of Sassari, Sassari, Italy; and the Maxillofacial Surgery Unit (G.S.), University Hospital of Naples “Federico II”, Naples, Italy.

Editor's Note: This Manuscript was accepted for publication on March 31, 2020.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Send correspondence to Luigi A. Vaira, Viale San Pietro 43/B, 07100 Sassari, Italy. E-mail: luigi.vaira@gmail.com

DOI: 10.1002/lary.28692

J Oral Med Oral Surg 2020;26:18

https://doi.org/10.1051/mbcb/2020011

https://www.jomos.org

JOMOS
Journal of Oral Medicine and Oral Surgery

Letter to the Editor

Oral manifestation of Covid-19 as an inaugural symptom?

Anne-Gaëlle Chaux-Bodard[1,2,*], Sophie Deneuve[2], Aline Desoutter[2]

[1] Département de Chirurgie Orale, Faculté d'Odontologie, Université Claude Bernard Lyon I, Lyon, France
[2] Unité de chirurgie cervico-faciale, Centre Régional de Lutte contre le Cancer Léon Bérard, Lyon, France

(Received: 11 April 2020, accepted: 12 April 2020)

Covid-19 has a huge range of clinical manifestations and, due to the high number of patients involved, the diagnosis is mostly based on clinical findings or suspicions [1].

A 45-years-old female patient presented with an irregular ulcer on the dorsal side of the tongue (Fig. 1a). History of the lesion revealed 24 h painful inflammation of a tongue papilla, followed by 24 h of erythematous macula, which evolved into irregular and asymptomatic ulcer. After 10 days, the ulcer completely healed without scar.

At Day 3, after occurrence of the oral lesion, an erythematous plane lesion appeared on the big toe (Fig. 1b). It was also painful during 48 h and then became asymptomatic. General symptoms were mild asthenia. Considering the general aspects of the lesions, and despite a lack of general status alterations and symptoms, a nasopharyngeal Covid-19 test was performed at Day 8. The test was positive.

Cutaneous lesions related to Covid-19 have been described [2] and reported by dermatologists, but to our knowledge, oral lesions have not been yet described with a proven Covid-19 infection. The irregular ulcer observed occurred after a short time of macular erythematous lesion, which could be explained by vasculitis. Coronavirus disease 2019 is associated with a variable inflammatory reaction that can induce vascular inflammation [3]. Erythematous rash has been described [2] and could also be explained by an inflammatory reaction.

Thus, this irregular oral ulcer could be an inaugural symptom of Covid-19 which needs to be proven in larger cohorts of patients.

Fig. 1. a: Irregular oral ulcer of the tongue at Day 4. b: Erythematous plane lesion of the toe.

Conflict of interest

The authors have no conflict of interest to declare.
Patient's consent has been obtained for publication.

References

1. Jin YH, Cai L, Cheng ZS, *et al*. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res 2020;7:4.
2. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol 2020 Mar 26 [Online ahead of print].
3. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of Coronaviruses on the cardiovascular system: a review. JAMA Cardiol 2020 Mar 27 [Online ahead of print].

* Correspondence: anne-gaelle.bodard@lyon.unicancer.fr

DOI: 10.1002/jmv.26221

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

Oral erosions and petechiae during SARS-CoV-2 infection

To the Editor,

An increasing number of reports have been written regarding cutaneous manifestations during the coronavirus disease-2019 (COVID-19),[1-3] though knowledge of the possible oral manifestations is still poor. This may be due to a lack of intraoral examinations, which may be caused by limited availability of the recommended protective measures and the use of telemedical consultations for SARS-CoV-2 infections. We describe a patient presenting with cutaneous and oral lesions associated with a SARS-CoV-2 infection.

A previously healthy 19-year-old woman presented to the Emergency Department with a seven-day history of intermittent fever and sore throat. She had started taking oral cefixime (400 mg per day) 3 days earlier. She also reported a sudden onset of fatigue, hyposmia, and asymptomatic cutaneous and oropharyngeal lesions that started 2 days before admission. On admission, she was afebrile and her vital signs (blood pressure, beats/minute, oxygen saturation) were normal. Physical examination revealed erythematous macules, papules and petechiae on the lower extremities (Figure 1A); erosions, ulcerations, and blood crusts on the inner surface of the lips (Figure 1B) and palatal and gingival petechiae. Chest radiograph and pulmonary ultrasound were normal. A complete blood cell count revealed increased white cells (12 000/mm^3, 60% of lymphocytes), aspartate aminotransferase (200 U/L), alanine aminotransferase (140 U/L), lactic dehydrogenase (LDH) (300 mU/mL) and severe thrombocytopenia (platelet count 2000/mm^3). Hemoglobin and C-reactive protein levels were normal. Real-time reverse transcriptase–polymerase chain reaction (PCR) from a nasopharyngeal swab was positive for SARS-CoV-2. Antibiotic therapy was discontinued and intravenous immune globulins (400 mg/kg) and methylprednisolone (1 mg/kg) was administered for 5 days.

On day 5, the systemic symptoms regressed, though some maculopapular lesions were still present on the legs; the platelet count had increased to 98 000/mm^{3,} and aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase returned to normal ranges. On day 10, the complete blood count was normal (white cells 9000/mm^3 with 40% of lymphocytes; platelet count 152,000/mm^3) and skin and mucosal lesions disappeared.

In the literature, the prevalence of cutaneous findings in SARS-CoV-2 patients ranges from 0,2%[1] to 20,4%.[2] Skin lesions are heterogeneous and divided into acral erythematous-edematous chilblain-like lesions, maculopapular, vesicular and urticarial eruptions.[3] Petechial eruptions are sporadically reported,[4] while oropharyngeal lesions have been described in only seven patients to date (Table 1).[5-8] They were all adult patients (mean age 57 years), often affected by diabetes and hypertension, presenting with painful oropharyngeal lesions in the form of ulcers (5 cases),[5,6,8] blisters and gingivitis (1 case),[5] palatal petechiae, erythema and pustules (1 case).[7] Histological analysis, performed in three cases revealed inflammatory infiltrates and focal necrosis-hemorrhages in the lamina propria, and in one case, small vessel obliteration with thrombi. In these three cases, infections with herpes simplex virus (HSV)1/2 were excluded through in-situ hybridization and PCR on the lesion tissue.[6,8]

Compared to the previously reported cases,[5-8] our patient was younger and without comorbidities. Notably, the oral lesions in our patient were painless, heterogeneous in morphology, and associated

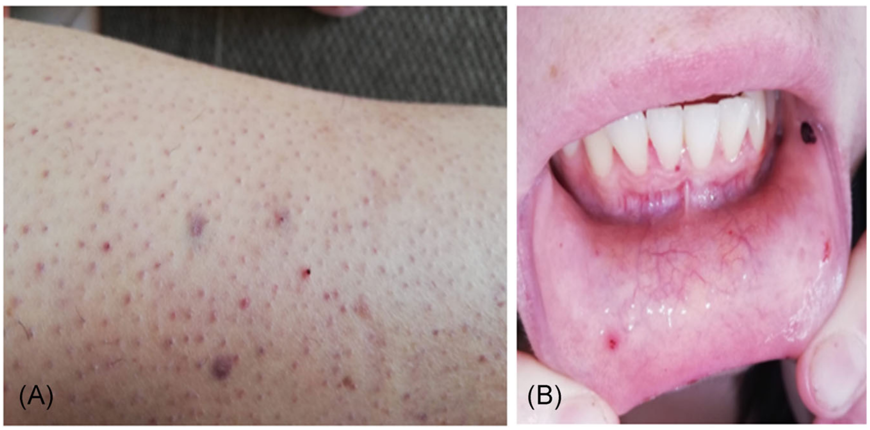


FIGURE 1 A, Erythematous macules, papules, and petechiae on the lower extremities. B, erosions and blood crust on the inner surface of the lower lip and gingival petechiae

Received: 20 April 2020 | Revised: 24 April 2020 | Accepted: 28 April 2020
DOI: 10.1111/odi.13382

SHORT COMMUNICATION

ORAL DISEASES WILEY

Oral vesiculobullous lesions associated with SARS-CoV-2 infection

Carmen Martín Carreras-Presas[1] | Juan Amaro Sánchez[2] | Antonio Francisco López-Sánchez[3] | Enric Jané-Salas[4] | Maria Luisa Somacarrera Pérez[1]

[1]Adult's Dentistry Department, Oral Medicine, Universidad Europea de Madrid, Madrid, Spain
[2]Master in Periodontics, Universidad Rey Juan Carlos, Madrid, Spain
[3]Head of Master in Periodontics, Universidad Rey Juan Carlos, Madrid, Spain
[4]Dentistry Department, Universidad de Barcelona, Barcelona, España

Correspondence: Carmen Martín Carreras-Presas, Adult's Dentistry Department, Oral Medicine, Universidad Europea de Madrid, Urb. El Bosque, Tajo Street, 28670 Villaviciosa de Odón, Madrid, Spain.
Email: carmen.martin2@universidadeuropea.es

1 | INTRODUCTION

Humans infected with SARS-CoV-2 are at risk of developing serious and life-threatening conditions, such as severe acute respiratory syndrome.

Recent data suggest the more common signs and symptoms of SARS-CoV-2 infection to be headache, sore throat, hyposmia, hypogeusia, diarrhea, dyspnea, and in severe cases pneumonia. (Wang et al., 2020).

Some authors in Italy reported cases of dermatologic implication in patients affected by SARS-CoV-2 infection (Recalcati, 2020). Since then, we have seen more reports describing dermatologic involvement, including lesions that range from affectation of hands and feet in teenagers to vasculitis, rash, urticaria, and varicella-like lesions. (Estebanez et al., 2020).

Spain has been severely affected by the COVID-19 outbreak (Bonanad et al., 2020). The majority of dental clinics and university clinics are closed, only treating emergencies if the entity has the protective measures necessary. There is a nationwide lack of serological tests available, both for patients and for healthcare providers.

We here present three cases associated with this virus: two where there is a suspicion of COVID-19 and one case of confirmed infection. All cases presented ulcers or blisters in the oral cavity, appearing and developing during the isolation period between the last week of March and the first week of April 2020. We were not able to examine them in our clinic due to the state of alarm declared from the 14th of March, but offered the possibility of video consultations.

2 | PATIENT 1

A 56-year-old healthy male patient without any relevant medical history was isolated with suspected infection of SARS-CoV-2. He presented asthenia and fever for 2 days, reporting hyposmia, dysgeusia, and enlargement of lymph nodes in the neck. Testing for COVID-19 was not performed in the hospital due to the non-severity of his case. He was sent home by his general practitioner. He complained of pain in his palate and sore throat. We asked him to send us a photograph (Figure 1). The lesions resembled a herpetic recurrent

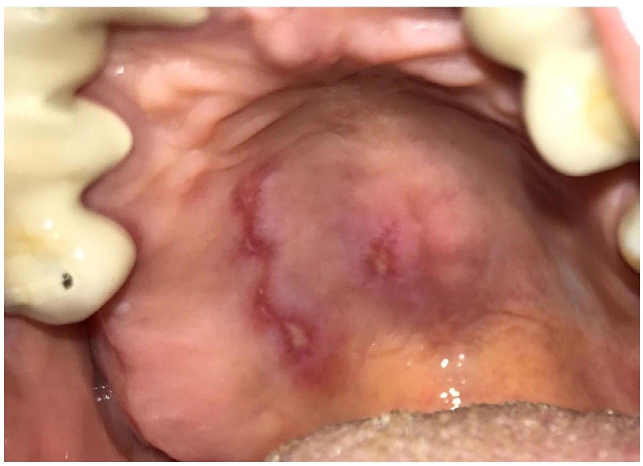


FIGURE 1 Multiple orange-colored ulcers with an erythematous halo and symmetric distribution on the right hard palate of the patient

Journal section: Oral Medicine and Pathology
Publication Types: Letter

doi:10.4317/medoral.24044

Letter to Editor: Oral lesions in a patient with Covid-19

Ciro Dantas Soares [1,4], Rejane Andrade de Carvalho [2], Kalline Andrade de Carvalho [3], Maria Goretti Freire de Carvalho [4], Oslei Paes de Almeida [1]

[1] DDS, Ph.D. Department of Oral Diagnosis, Piracicaba Dental School, University of Campinas, Piracicaba, SP, Brazil
[2] DDS, Ph.D. Department of Endodontics, Federal University of Rio Grande do Norte (UFRN), Natal, RN, Brasil
[3] M.D. Brazilian Dermatology Society member. Department of Dermatology, Federal University of São Paulo (UNIFESP), São Paulo, SP, Brazil
[4] M.D., Ph.D. Laboratório de Citopatologia, Private Service, Natal, RN, Brazil

Correspondence:
Department of Oral Diagnosis
Piracicaba Dental School, University of Campinas
Piracicaba, SP, Brazil
ciro.dss@gmail.com

Received: 02/06/2020
Accepted: 04/06/2020

Soares CD, Carvalho RAd, Carvalho KAd, Carvalho MGFd, Almeida OPd. Oral lesions in a patient with Covid-19. Med Oral Patol Oral Cir Bucal. 2020 Jul 1;25 (4):e563-4.

Article Number: 24044 http://www.medicinaoral.com/

eMail: medicina@medicinaoral.com
Indexed in:
Science Citation Index Expanded
Journal Citation Reports
Index Medicus, MEDLINE, PubMed
Scopus, Embase and Emcare
Indice Médico Español

Dear Editor:

The coronavirus disease 2019 (COVID-19) is a global pandemic burden caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection with variable clinical outcome. The symptoms of this disease include headache, sore throat, fever, and dyspnoea. About 10% of the patients develop severe acute respiratory syndrome and 1-2 %, particularly elderly, die (1,2). Possible oral-related symptoms include hypogeusia, xerostomia and chemosensory alterations (3).

We report here the clinical and microscopical characteristics of oral reddish lesions and ulceration that occurred in a 42-year-old male patient positive for SARS-Cov-2 confirmed by polymerase chain reaction (PCR). The patient also had a history of diabetes and hypertension, and when admitted to the hospital presented fever (temperature of up to 39.3°C), cough and shortness of breath. On the skin it was observed some petechia-like and small vesicobullous lesions of unknown aetiology. A treatment with dexamethasone and dipyrone was established for 1 week.

The patient also complained of a painful ulceration in the buccal mucosa that was biopsied. Oral examination showed besides the ulcerated lesion, multiple reddish macules of different sizes scattered along the hard palate, tongue, and lips (Fig. 1). After 3 weeks of follow up the lesions presented complete remission.

Microscopically the biopsied lesion, presented the epithelium with severe vacuolization and occasional exocytosis (Fig. 1). In the lamina propria, a diffuse chronic inflammatory infiltrate was associated with focal areas of necrosis and haemorrhage. Conspicuous superficial and deep small vessels were obliterated by evident thrombi (Fig. 1). Small thrombi seemed to be composed mainly by endothelial cells, while the larger ones were composed by fibrin and endothelial cells, and in either cases CD34 was positive for cells in the luminal component (Fig. 1). Adjacent minor salivary glands exhibited an intense lymphocytic infiltration, mostly positive for CD3 (Fig. 1) and CD8 (Fig.

Mucosal involvement in a COVID-19-positive patient: a case report

Filiz Cebeci Kahraman MD,[1] Hülya Çaşkurlu MD[2]

[1]Department of Dermatology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

[2]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

Corresponding author: Filiz Cebeci Kahraman

Address: İstanbul Medeniyet Üniversitesi, Dermatoloji Anabilim Dalı,

Eğitim Mah., Dr. Erkin Cad. 34722 Kadıkoy/ Istanbul, Turkey

Telephone: +902165664000-extension: 9126 Fax: +902165666614

E-mail: cebecifiliz@yahoo.com

Conflict of Interest: Authors have no conflict of interest to declare.

Funding Sources: None

Informed Consent Form: Consent form that signed by patient can be found in documents.

Key Words: Corona virüs infection, COVID-19, Mucosal involvement, Oral lesions

Received: 9 July 2020 | Revised: 4 August 2020 | Accepted: 19 August 2020

DOI: 10.1111/scd.12520

WILEY

CASE HISTORY REPORT

Oral mucosal lesions in patients with SARS-CoV-2 infection. Report of four cases. Are they a true sign of COVID-19 disease?

Roberto Onner Cruz Tapia[1] | **Alberto Jose Peraza Labrador**[2] | **Douglas Magno Guimaraes**[3] | **Luciano Hermios Matos Valdez**[4]

[1] Department of Oral and Maxillofacial Pathology, Postgraduate and Research Division, Universidad Nacional Autónoma de México, Mexico City, Mexico

[2] Department of Oral and Maxillofacial Pathology, Universidad El Bosque, Bogota, Colombia

[3] School of Dentistry, Centro Universitario do Estado do Para, Belem, Brazil

[4] Faculty of Dentistry, Postgraduate Unit, Universidad Nacional Mayor de San Marcos, Lima, Peru

Correspondence
Luciano Hermios Matos Valdez, Faculty of Dentistry, Postgraduate Unit, Universidad Nacional Mayor de San Marcos, Lima 01, Peru.
Email: lmatosv@unmsm.edu.pe; diagnocentrobucal@gmail.com

Abstract

Background: Vesiculobullous and macular lesions in the oral mucosa have been reported in patients positive for SARS-CoV-2 infection. Nonetheless, the significance and physiopathology of oral manifestations have not been clearly established in the clinical progression or outcome of the infection.

Aim: To describe the clinico-pathological oral mucosal lesions in four patients with confirmed SARS-CoV-2 infection.

Methods and Results: Four patients with COVID-19 disease and confirmed by polymerase chain reaction (PCR) presented angina bullosa hemorragica-like lesion, vascular disorder, and nonspecific stomatitis, one patient with histological analysis demonstrated perivascular reactive lymphocitic infliltrate, focal capillary thrombosis, and hemorrhage. According to the discrimination of other local and systemic conditions and the synchronous onset of oral and systemic symptoms, the diagnosis of oral lesions probably associated with COVID-19 was established.

Conclusion: Infection with SARS-CoV-2 may result in oral manifestations with various clinical presentations, which presumably support the hypothesis of thrombi formation and vasculitis; nevertheless, these findings need more evidence and a long-term follow up of patients to accurately establish the significance of the oral mucosa affection in the COVID-19 disease.

KEYWORDS
case reports, COVID-19, oral manifestations, SARS-CoV-2

1 | INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), etiology for the new Coronavirus disease 2019 (COVID-19), has reached a high infectivity rate with approximately worldwide projections of 23 000 000 million cases and 900 000 deaths by September 2020.[1] Elderly patients (> 70 years) and vulnerable patients with comorbidities, such as hypertension, diabetes, cardiovascular disease, lung disease, chronic kidney disease, and immunosuppressed conditions, predispose to develop severe acute respiratory, heart, and kidney failure and poor prognosis.[2] The clinical course of COVID-19 depends on the host immune response, and frequent symptoms include fever,

DR JUAN JIMENEZ-CAUHE (Orcid ID : 0000-0002-6190-0147)
DR DANIEL ORTEGA-QUIJANO (Orcid ID : 0000-0002-4990-1075)
DR DAVID SACEDA-CORRALO (Orcid ID : 0000-0001-6315-5462)
DR DIEGO FERNANDEZ-NIETO (Orcid ID : 0000-0003-4461-1770)

Article type : Correspondence

Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings.

J. Jimenez-Cauhe,[1] D. Ortega-Quijano,[1] I. Carretero-Barrio,[2] A. Suarez-Valle,[1] D. Saceda-Corralo,[1] C. Moreno-Garcia del Real[2] and D. Fernandez-Nieto[1]

[1]Dermatology Department; [2] Pathology Department, Hospital Universitario Ramon y Cajal, IRYCIS, Madrid, Spain.

Corresponding author: Juan Jimenez-Cauhe
Email: jjimenezc92@gmail.com

This article has no funding source.

The authors have no conflict of interest to declare.

To the Editor,

Cutaneous manifestations in patients with COVID-19 infection are being increasingly reported. Several patterns have been described since the initial report by Recalcati,[1] including erythematous maculo-papular,[1] urticarial,[1,2] chickenpox-like,[1,3] purpuric peri-flexural,[4] transient livedo reticularis,[5] and acro-ischemic or chilblain-like lesions.[6,7] Herein we report the observation a new pattern with erythema multiforme-like lesions in 4 hospitalized patients with COVID-19 infection. All of them were women, and

Pesquisa Brasileira em Odontopediatria e Clínica Integrada 2020; 20(supp1):e0104
https://doi.org/10.1590/pboci.2020.112
ISSN 1519-0501 / eISSN 1983-4632

CRITICAL REVIEW

Salivary Glands, Saliva and Oral Findings in COVID-19 Infection

Marlus da Silva Pedrosa[1], Carla Renata Sipert[2], Fernando Neves Nogueira[1]

[1]Departament of Biomaterials and Oral Biology, School of Dentistry, University of São Paulo, SP, Brazil.
[2]Departament of Restorative Dentistry, School of Dentistry, University of São Paulo, SP, Brazil.

Author to whom correspondence should be addressed: Fernando Neves Nogueira, Departamento de Biomateriais e Biologia Oral, Faculdade de Odontologia, Universidade de São Paulo, Av. Prof. Lineu Prestes, 2227, Cidade Universitária, São Paulo, SP, Brazil. 05508-900. Phone: +55 1130917849. E-mail: fnn@usp.br.

Academic Editor: Yuri Wanderley Cavalcanti

Received: 25 May 2020 / Accepted: 03 June 2020 / Published: 19 June 2020

How to cite this article: Pedrosa MS, Sipert CR, Nogueira FN. Salivary glands, saliva and oral findings in COVID-19 infection. Pesqui Bras Odontopediatria Clín Integr. 2020; 20(supp1):e0104. https://doi.org/10.1590/pboci.2020.112

Abstract
The world is under the threat of the novel coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Despite several efforts to contain the disease spread, it still constitutes a public health emergency of international concern. Several published reports in the scientific literature called attention of the oral cavity as the potential route of infection, the implications for dental practice and the use of saliva in the diagnose of the COVID-19. The aim of this article is to provide an overview of the literature on the salivary glands and saliva in the context of SARS-CoV-2 infection. A brief discussion of taste disturbances and oral findings in COVID-19 patients is also presented. The literature shows that SARS-CoV-2 could infect the salivary glands. It is not possible, however, to make speculations regarding them as reservoirs for the SARS-CoV-2. In addition, patients with COVID-19 presented several oral repercussions, including hyposalivation and taste disturbances. A few reports showed oral ulcers and blisters associated with SARS-CoV-2 infection. However, it remains not fully understood and might lead to erroneous assumptions. Overall, further studies are necessary to understand the real role of salivary glands and saliva in the context of SARS-CoV-2 infection.

Keywords: Infections; Severe Acute Respiratory Syndrome; Salivary Glands; Saliva; Oral Manifestations.

Received: 27 May 2020 | Revised: 25 June 2020 | Accepted: 26 June 2020

DOI: 10.1111/myc.13137

ORIGINAL ARTICLE

mycoses Diagnosis, Therapy and Prophylaxis of Fungal Diseases

WILEY

Oropharyngeal candidiasis in hospitalised COVID-19 patients from Iran: Species identification and antifungal susceptibility pattern

Mohammadreza Salehi[1] | Kazem Ahmadikia[2] | Shahram Mahmoudi[3] | Saeed Kalantari[4] | Saeidreza Jamalimoghadamsiahkali[5] | Alireza Izadi[2] | Mohammad Kord[2] | Seyed Ali Dehghan Manshadi[1] | Arash Seifi[1] | Fereshteh Ghiasvand[1] | Nasim Khajavirad[6] | Saeedeh Ebrahimi[4] | Amirhossein Koohfar[1] | Teun Boekhout[7,8] | Sadegh Khodavaisy[2]

[1]Department of Infectious Diseases and Tropical Medicine, Imam Khomeini Hospital complex, Tehran University of Medical Sciences, Tehran, Iran

[2]Department of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

[3]Department of Medical Parasitology and Mycology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

[4]Antimicrobial Resistance Research Center, Iran University of Medical Sciences, Tehran, Iran

[5]Department of Infectious Diseases and Tropical Medicine, Ziaeian Hospital, Tehran University of Medical Sciences, Tehran, Iran

[6]Department of Internal Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

[7]Westerdijk Fungal Biodiversity Institute, Utrecht, The Netherlands

[8]Institute of Biodiversity and Ecosystem Dynamics (IBED), University of Amsterdam, Amsterdam, The Netherlands

Correspondence
Sadegh Khodavaisy, Department of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
Email: sadegh_7392008@yahoo.com

Funding information
Tehran University of Medical Sciences and Health Services, Grant/Award Number: 99-1-99-47198

Abstract

Background: Emergence of coronavirus disease 2019 (COVID-19) is a major health-care threat. Apparently, the novel coronavirus (SARS-CoV-2) is armed by special abilities to spread and dysregulate the immune mechanisms. The likelihood of oropharyngeal candidiasis (OPC) development in COVID-19 patients with a list of attributable risk factors for oral infections has not yet been investigated.

Objectives: We here aim to investigate the prevalence, causative agents and antifungal susceptibility pattern of OPC in Iranian COVID-19 patients.

Patients and Methods: A total of 53 hospitalised COVID-19 patients with OPC were studied. Relevant clinical data were mined. Strain identification was performed by 21-plex PCR and sequencing of the internal transcribed spacer region (ITS1-5.8S-ITS2). Antifungal susceptibility testing to fluconazole, itraconazole, voriconazole, amphotericin B, caspofungin, micafungin and anidulafungin was performed according to the CLSI broth dilution method.

Results: In 53 COVID-19 patients with OPC, cardiovascular diseases (52.83%) and diabetes (37.7%) were the principal underlying conditions. The most common risk factor was lymphopaenia (71%). In total, 65 *Candida* isolates causing OPC were recovered. *C albicans* (70.7%) was the most common, followed by *C glabrata* (10.7%), *C dubliniensis* (9.2%), *C parapsilosis* sensu stricto (4.6%), *C tropicalis* (3%) and *Pichia kudriavzevii* (=*C krusei*, 1.5%). Majority of the *Candida* isolates were susceptible to all three classes of antifungal drugs.

Conclusion: Our data clarified some concerns regarding the occurrence of OPC in Iranian COVID-19 patients. Further studies should be conducted to design an appropriate prophylaxis programme and improve management of OPC in critically ill COVID-19 patients.

KEYWORDS

coinfection, COVID-19, oral candidiasis, oropharyngeal candidiasis

Received: 26 May 2020 | Accepted: 31 May 2020

DOI: 10.1111/odi.13462

LETTER TO THE EDITOR

ORAL DISEASES WILEY

Necrotizing periodontal disease: Oral manifestation of COVID-19

We read with interest the series of cases reported by Martín Carreras-Presas, Amaro Sánchez, López-Sánchez, Jané-Salas, and Somacarrera Pérez (2020). We believe that the described oral vesiculobullous manifestations were suggestive of coronavirus disease 2019 (COVID-19) co-infections, which, at present, are overlooked and poorly understood (Cox, Loman, Bogaert, & O'Grady, 2020). Increased disease severity and mortality among individuals with respiratory viral infections are often attributed to subsequent bacterial co-infections, accounting for approximately 95% of deaths during the 1918 Spanish flu pandemic (Morens, Taubenberger, & Fauci, 2008).

We predict a spontaneous rise in the prevalence of acute periodontal lesions, particularly necrotizing periodontal disease (NPD), in accordance with the increase in COVID-19 confirmed cases. The etiology of NPD lesions may be associated with bacterial co-infections occurring intra-orally in COVID-19 patients. Metagenomic analyses of those infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) frequently detect abnormally high bacterial reads of *Prevotella intermedia* in addition to common pathogenic genera implicated in the onset and progression of oral diseases such as *Streptococci*, *Fusobacterium*, *Treponema*, and *Veillonella* (Chakraborty, 2020). *P. intermedia* is considered a major etiological bacterial species for several acute periodontal lesions, which, alongside *Fusobacterium* and *Treponema* species, constitute a large proportion of the microbiota present in NPD lesions (Herrera, Retamal-Valdes, Alonso, & Feres, 2018). NPDs are more prevalent in patients with HIV (Herrera et al., 2008). In a mechanistically similar way, SARS-CoV-2 infection may predispose individuals to NPDs through bacterial co-infection propagated by *P. intermedia* (Patel & Sampson, 2020). We present a case of a patient attending the King's College Hospital with NPD and suspected COVID-19:

A 35-year-old female patient without any relevant medical history attended the acute dental emergency setting reporting fever, halitosis, intense gingival pain, and bleeding. The fever presented 3 days prior to any oral symptoms. Examination revealed that she was apyrexic. She presented bilateral submandibular lymphadenopathy, and an intra-oral examination confirmed severe halitosis, generalized erythematous and edematous gingivae, and necrotic interdental papillae in both the maxillary and mandibular labial sextants. Bleeding was evident from the gingival sulcus without provocation, and there was no detectable attachment loss. A clinical diagnosis of necrotizing gingivitis was made. Although COVID-19 was suspected, it was not possible to provide testing at the time. The patient was prescribed 400mg metronidazole three times daily for 5 days and 0.12% chlorhexidine mouthwash twice daily for 10 days. Following national guidance on COVID-19, the patient was advised to return home immediately to self-isolate for 7 days. The patient was called 5 days later and described complete resolution of her oral symptoms and fever. Notably, this patient's oral and COVID-19 suspected symptoms had resolved following the antibiotic regimen, strengthening the role of bacterial co-infections in COVID-19 severity.

There is an urgent need to study co-infections in COVID-19 patients and encourage clinicians to diagnose these conditions early, owing to their contribution to mortality and heightened disease severity in historic pandemics of respiratory viral infections. Routine intra-oral examinations for COVID-19 patients should be provided across healthcare disciplines.

KEYWORDS

bacterial co-infection, coronavirus disease 2019, COVID-19, necrotizing periodontal disease

ACKNOWLEDGEMENTS

We thank Dr Thuy Do (University of Leeds) for her suggestions and feedback.

CONFLICT OF INTEREST

None to declare.

AUTHOR CONTRIBUTION

Jay Patel: Conceptualization; Data curation; Writing-original draft; Writing-review & editing. **Julian Woolley:** Writing-original draft; Writing-review & editing.

Jay Patel[1]

Julian Woolley[2]

The copyright line for this article was changed on 10 July 2020 after original online publication.

DR. WENJI CAI (Orcid ID : 0000-0002-5548-1396)

PROF. MARIANO SANZ (Orcid ID : 0000-0002-6293-5755)

Article type : Original Article Clinical Periodontology

Association between periodontitis and severity of COVID-19 infection: a case-control study

Nadya Marouf, BDS, MSc [1], Wenji Cai BDS, MSc [2], Khalid N. Said, BDS[1], Hanin Daas, MSc [3], Hanan Diab, BDS, MSc[1], Venkateswara Rao Chinta[4], Ali Ait Hssain, MD[4], Belinda Nicolau, DDS, PhD[2], Mariano Sanz, MD, PhD [5], Faleh Tamimi, BDS, PhD [3]

[1]Department of Dentistry, Oral Health Institute, Hamad Medical Corporation, Doha, Qatar

[2]Faculty of Dentistry, McGill University, Montreal, Canada

[3]College of Dental Medicine, QU Health, Qatar University, Doha, Qatar

[4]Hamad Medical Corporation, Doha, Qatar

[5]ETEP Research Group, Faculty of Odontology, University Complutense of Madrid, Madrid, Spain

Contact information of corresponding author:

Dr Faleh Tamimi, PhD, BDS, College of Dental Medicine, Building H12 annex, Qatar University, P.O. Box 2713, Doha, Qatar.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/JCPE.13435

Int. J. Odontostomat.,
14(4):538-539, 2020.

Carta al Editor

COVID-19 y manifestaciones orales

COVID-19 and Oral Manifestations

Marco Cornejo Ovalle[1,2] & Iris Espinoza Santander[3]

Sr. Editor,

El coronavirus SARS-CoV-2 causa la enfermedad por coronavirus 2019 (COVID-19), una infección que produce un síndrome respiratorio agudo severo, que se ha caracterizado por fiebre, síntomas respiratorios y gastrointestinales, así como otras manifestaciones sistémicas (Guan *et al*., 2020).

Dado que este virus se informó oficialmente en diciembre de 2019 y se asoció con COVID-19, ha surgido literatura científica con informes de casos y manifestaciones menos frecuentes, que han esbozado mejor la historia natural y la semiología de la enfermedad de COVID-19. Sin embargo, hasta la fecha todavía hay preguntas importantes relacionadas con el enfoque clínico de la pandemia de COVID-19 y todavía hay aspectos que deben estudiarse.

En este contexto, se han ido reportado manifestaciones clínicas, que han ido enriqueciendo el conocimiento sobre las características del cuadro clínico. Uno de los aspectos escasamente documentados es la semiología a nivel de la cavidad oral. Lo que, desde nuestro punto de vista, puede deberse a que los odontólogos, a nivel mundial, se han visto separados de la actividad clínica rutinaria por los riesgos de la potencial transmisión derivados, principalmente, de la presencia de aerosoles de saliva en algunas de las prestaciones odontológicas (Pan *et al*., 2020). Tras la declaración de la pandemia por COVID-19 muchas de las atenciones dentales se han suspendido. Entre otras razones, porque las autoridades sanitarias han recomendado limitarlas solo a las atenciones de urgencias/emergencias odontológicas. Por ejemplo, en Chile en las Orientaciones para la Atención odontológica en Fase IV COVID-19 del Ministerio de Salud (Ministerio de Salud, 2020). Dichas atenciones también se han visto limitadas debido a la escasez de los elementos de protección personal (EPP) en distintos países durante los primeros meses de la pandemia (Pecchia *et al*., 2020). Por otro lado, las personas han dejado de asistir al dentista, ya sea por el temor que se ha generado, o como secuencia de la situación de confinamiento, recomendado u obligatorio, en la que gran parte de la población mundial ha sido expuesta.

Desde nuestro punto de vista, y como hemos señalado, estas razones podrían explicar el escaso reporte de lesiones de la mucosa oral en pacientes COVID-19 u otras manifestaciones orales. Especialmente, si consideramos que, en muchos entornos, son los odontólogos los profesionales más idóneos para evaluar clínicamente la salud oral de las personas.

Entre los síntomas orales que se han descrito en los pacientes COVID-19, están la ageusia (Vaira *et al*., 2020), la hipogeusia y la disgeusia (Vinayachandran & Balasubramanian, 2020), Esto es de particular importancia porque, el receptor de la enzima convertidora de angiotensina 2, al que se une el SARS-CoV-2 para poder entrar en la célula huésped, se expresa altamente en las células epiteliales, especialmente en la lengua, en comparación con los tejidos orales o gingivales de la cavidad oral (Xu *et al*., 2020). Por otro lado, hasta mediados de junio de 2020 se han publicado solo cuatro reportes (Chaux-Bodard *et al*., 2020; Galván *et al*., 2020; Jimenez-Cauhe *et al*., 2020; Carreras-Presas *et al*., 2020) y además otro, que es el único que incluye el estudio histopatológico y que menciona un posible mecanismo etipatologénico (Soares *et al*., 2020). Todos esos reportes abordan una escasa casuística, lo que sugiere, por un lado, que algunas lesiones orales pudieran ser expresión clínica de la infección por SARS-CoV-2, y por otro, que los pacientes deban ser evaluados con un examen oral completo para diagnosticar adecuadamente la presencia posible de estas lesiones y relacionarlas con la COVID-19.

[1] Área de Salud Pública del Instituto de Investigación en Ciencias Odontológicas, Facultad de Odontología, Universidad de Chile, Chile.
[2] Becario Postdoctoral en Unidad de Control de Tabaco, Instituto Catalán de Oncología, Barcelona, España.
[3] Departamento de Patología y Medicina Oral, Facultad de Odontología, Universidad de Chile, Chile.

World Health Organization

Considerations for the provision of essential oral health services in the context of COVID-19

3 August 2020 | COVID-19: Essential health services


Considerations for the provision of essential oral health services in the context of COVID-19
Interim guidance
3 August 2020

Overview

The purpose of this document is to address specific needs and considerations for essential oral health services in the context of COVID-19 in accordance with WHO operational guidance on maintaining essential health services.

CORRINGENDUM

WHO TEAM

WHO Headquarters (HQ)

NUMBER OF PAGES

5

REFERENCE NUMBERS

WHO REFERENCE NUMBER:

WHO/2019-nCoV/Oral_health/2020.1

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 26, 2020 VOL. 382 NO. 13

Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia

Qun Li, M.Med., Xuhua Guan, Ph.D., Peng Wu, Ph.D., Xiaoye Wang, M.P.H., Lei Zhou, M.Med., Yeqing Tong, Ph.D., Ruiqi Ren, M.Med., Kathy S.M. Leung, Ph.D., Eric H.Y. Lau, Ph.D., Jessica Y. Wong, Ph.D., Xuesen Xing, Ph.D., Nijuan Xiang, M.Med., Yang Wu, M.Sc., Chao Li, M.P.H., Qi Chen, M.Sc., Dan Li, M.P.H., Tian Liu, B.Med., Jing Zhao, M.Sc., Man Liu, M.Sc., Wenxiao Tu, M.Med., Chuding Chen, M.Sc., Lianmei Jin, M.Med., Rui Yang, M.Med., Qi Wang, M.P.H., Suhua Zhou, M.Med., Rui Wang, M.D., Hui Liu, M.Med., Yinbo Luo, M.Sc., Yuan Liu, M.Med., Ge Shao, B.Med., Huan Li, M.P.H., Zhongfa Tao, M.P.H., Yang Yang, M.Med., Zhiqiang Deng, M.Med., Boxi Liu, M.P.H., Zhitao Ma, M.Med., Yanping Zhang, M.Med., Guoqing Shi, M.P.H., Tommy T.Y. Lam, Ph.D., Joseph T. Wu, Ph.D., George F. Gao, D.Phil., Benjamin J. Cowling, Ph.D., Bo Yang, M.Sc., Gabriel M. Leung, M.D., and Zijian Feng, M.Med.

ABSTRACT

BACKGROUND

The initial cases of novel coronavirus (2019-nCoV)–infected pneumonia (NCIP) occurred in Wuhan, Hubei Province, China, in December 2019 and January 2020. We analyzed data on the first 425 confirmed cases in Wuhan to determine the epidemiologic characteristics of NCIP.

METHODS

We collected information on demographic characteristics, exposure history, and illness timelines of laboratory-confirmed cases of NCIP that had been reported by January 22, 2020. We described characteristics of the cases and estimated the key epidemiologic time-delay distributions. In the early period of exponential growth, we estimated the epidemic doubling time and the basic reproductive number.

RESULTS

Among the first 425 patients with confirmed NCIP, the median age was 59 years and 56% were male. The majority of cases (55%) with onset before January 1, 2020, were linked to the Huanan Seafood Wholesale Market, as compared with 8.6% of the subsequent cases. The mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days. In its early stages, the epidemic doubled in size every 7.4 days. With a mean serial interval of 7.5 days (95% CI, 5.3 to 19), the basic reproductive number was estimated to be 2.2 (95% CI, 1.4 to 3.9).

CONCLUSIONS

On the basis of this information, there is evidence that human-to-human transmission has occurred among close contacts since the middle of December 2019. Considerable efforts to reduce transmission will be required to control outbreaks if similar dynamics apply elsewhere. Measures to prevent or reduce transmission should be implemented in populations at risk. (Funded by the Ministry of Science and Technology of China and others.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Feng at the Chinese Center for Disease Control and Prevention, No. 155 Changbai Rd., Changping District, Beijing, China, or at fengzj@chinacdc.cn; to Dr. G.M. Leung or Dr. Cowling at the School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, 21 Sassoon Rd., Pokfulam, Hong Kong, China, or at gmleung@hku.hk or bcowling@hku.hk, respectively; or to Dr. B. Yang at the Hubei Center for Disease Control and Prevention, No. 35 Zhuodaoquan North Rd., Hongshan District, Wuhan, Hubei, China, or at 49205957@qq.com.

Drs. Q. Li, X. Guan, P. Wu, and X. Wang and Drs. B. Cowling, B. Yang, M. Leung, and Z. Feng contributed equally to this article.

This article was published on January 29, 2020, and last updated on January 31, 2020, at NEJM.org.

N Engl J Med 2020;382:1199-207.
DOI: 10.1056/NEJMoa2001316

Guidance for Dental Settings

Interim Infection Prevention and Control Guidance for Dental Settings During the Coronavirus Disease 2019 (COVID-19) Pandemic

Updated Dec. 4, 2020   Print

Key Points

- Recognize dental settings have unique characteristics that warrant specific infection control considerations.
- Prioritize the most critical dental services and provide care in a way that minimizes harm to patients from delaying care and harm to personnel and patients from potential exposure to SARS-CoV-2 infection.
- Proactively communicate to both personnel and patients the need for them to stay at

News Releases

2021 Archive

2020 Archive

2019 Archive

Press Room Home

CDC Guidance for Dental Settings Echoes ADA Guidance

Organizations Recommend How to Move Forward With Dental Care During Pandemic

May 29, 2020

Contact Information:
mediarelations@ada.org

CHICAGO, May 29, 2020 — The American Dental Association (ADA) welcomes the release of the U.S. Centers for Disease Control and Prevention (CDC)'s recently updated Guidance for Dental Settings, noting it is very similar to science-based

Int. J. Odontostomat.,
14(4):468-473, 2020.

Medidas para Prevenir el COVID-19 en el Consultorio Dental

Measures to Prevent COVID-19 in the Dental Office

Britto E. Falcón-Guerrero[1] & Guido S. Falcón-Pasapera[2]

FALCÓN-GUERRERO, B. E. & FALCÓN-PASAPERA, G. S. Medidas para prevenir el COVID-19 en el consultorio dental. *Int. J. Odontostomat., 14(4)*:468-473, 2020.

RESUMEN: El 11 de marzo del 2020, la OMS reconoció al COVID-19 como pandemia mundial. El coronavirus (COVID-19) ha desafiado a los sistemas de salud y demanda una rápida reacción de respuesta, ante el aumento de infectados. El ámbito del trabajo odontológico, está sujeto a un riesgo significativo de contaminación cruzada y difusión de esta enfermedad, siendo muy importante las estrictas medidas de protección. El objetivo de esta revisión es informar sobre las medidas que se deben realizar durante los tratamientos dentro del consultorio dental para prevenir la propagación del COVID-19.

PALABRAS CLAVE: Coronavirus, COVID-19, prevención, infección, odontología.

INTRODUCCIÓN

El COVID-19, es una enfermedad causada por un nuevo coronavirus, que tiene una morbilidad alta, específicamente en los ancianos y en las poblaciones comórbidas (Basile *et al*., 2020). Este es un b-coronavirus, que está envuelto en un virus de ARN de sentido positivo no segmentado (sarbecovirus subgénero, subfamilia de Orthocoronavirinae); según la secuenciación del genoma del virus y el análisis evolutivo, se sospecha que el murciélago es el huésped natural del origen del virus, y podría transmitirse del murciélago a través de huéspedes intermedios desconocidos hasta llegar a infectar a los humanos (Chen *et al*., 2020a; Guo *et al*., 2020; Feng He *et al*., 2020).

El COVID-19, causada por el síndrome respiratorio agudo severo coronavirus-2 (SARS-CoV-2) surgió en diciembre de 2019 en Wuhan, China, se ha extendido a más de 113 países; y con 118,326 infectados y 4,292 fallecidos al 11 de marzo 2020, este mismo día, la Organización Mundial de la Salud (OMS) anunció al COVID-19 como una pandemia mundial. (Wan *et al*., 2020a; Sun *et al*., 2020; Ye *et al*., 2020; Smith *et al*., 2020).

Dentro de la sintomatología, la fiebre es el síntoma más común, luego la tos, disnea y fatiga/mialgia; y síntomas menos comunes, donde destacan el dolor de cabeza y confusión, náuseas o vómitos, hemoptisis y diarrea. Se observó rinorrea y esputo en solo el 4 %, dolor de garganta en el 5 % y faringoalgia en el 7,4 % de los pacientes con información clínica relevante (Lai *et al*., 2020a; Guan *et al*., 2020; Hui *et al*., 2019; Chen *et al*., 2020b; Huang *et al*., 2020; Ding *et al*., 2020).

La estimación actual del período de incubación medio para el COVID-19 es de 6,4 días, que oscila entre 2,1 y 14,1 días, y podría ser de 0 hasta 24 días en casos excepcionales, con posible transmisión asintomática.(Guan *et al*; Repici *et al*., 2020) y, Backer *et al*. (2020); mencionaron un período de incubación promedio de COVID-19 de 6,4 días que varía de 2,1 a 11,1 días.

Inicialmente, se pensó que la transmisión era de animal a humano. Pero el aumento de casos ha demostrado que la transmisión principal es de humano a humano, a través de aspirados respiratorios, de

[1] Facultad de odontología, Universidad Latinoamericana CIMA, Tacna, Perú.
[2] Facultad de odontología, Universidad Peruana Cayetano Heredia, Lima, Perú.

PERSPECTIVE

COVID-19 Considerations in Pediatric Dentistry

H. Bahramian[1], B. Gharib[2], and A. Baghalian[3]

Abstract: *One of the most important current medical concerns across the globe is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, which has been designated by the World Health Organization as a novel viral pneumonia named coronavirus disease 2019 (COVID-19). COVID-19 has substantially affected all aspects of human lives and forced most people to self-quarantine themselves and stay home in order to remain safe. As pediatric dentists as a part of the health care system deferring elective procedures, we are obliged to manage emergency situations such as cellulitis, severe tooth pain, and dental trauma. Therefore, we need to beware of the symptoms and risks of the emerging disease and, accordingly, change the policies in our offices to minimize the risk of transmission while checking up and treating our patients in the safest possible way.*

Knowledge Transfer Statement: *This article aims to acquaint clinicians treating pediatric patients with COVID-19 hazards and delineate the steps required for minimizing cross-infection in case of providing emergency treatment to children in dental offices.*

Keywords: coronavirus, virology, dental care for children, infection control, transmission, dental practice management

Coronavirus disease 2019 (COVID-19), designated as a pandemic disease, has globally affected many countries (World Health Organization 2020). Yet, no one can precisely predict when a definitive drug therapy and/or vaccine will be available. Pediatric dentists play pivotal roles in the health care system by continuing to manage emergency dental situations while taking special measures to practice universal infection control. The common transmission routes of this novel virus include direct transmission through coughing, sneezing, and droplet inhalation as well as contact transmission via oral, nasal, and eye mucous membranes (National Center for Immunization and Respiratory Diseases 2020). Eye (conjunctival) exposure has also been declared as another way through which the virus enters the body (Lu et al. 2020). Airborne transmission of COVID-19 through aerosols produced in medical procedures is another probable route of transmission that could be very urgent in dental procedures (Wax and Christian 2020). The incubation period has been reported to be 1 to 14 d, although there are some reports showing that even those without symptoms during the incubation period can spread the virus (Guan et al. 2020; Huang et al. 2020).

Latif Panahi et al., in a systemic review study of 14 full-text articles regarding clinical features of COVID-19 infection in newborns and pediatrics, showed that children with this infection can be completely asymptomatic or have mild and moderate symptoms. Ogimi et al. (2019) showed that young age, especially younger than school age; underlying disease; and immunosuppression are predictors of disease severity. Clinical manifestation of COVID-19 infection in children include fever, dry cough, fatigue, symptoms of upper respiratory tract infection (runny nose), and gastrointestinal symptoms (anorexia, diarrhea, nausea, and vomiting) (Panahi et al. 2020). The most common symptoms are fever and dry cough, and unlike adults, inferior respiratory tract (portion of the larynx below the vocal folds, trachea, bronchi and bronchioles) infection rarely occurs in children (Wu and McGoogan 2020; Zhou et al. 2020). According to the report on 10 children affected by COVID-19 in China, symptoms in children were nonspecific,

DOI: 10.1177/2380084420941503. [1]Community Oral Health Department, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran; [2]Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran; [3]Pediatric Dentistry Department, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.
Corresponding author: A. Baghalian, Pediatric Dentistry Department, School of Dentistry, Tehran University of Medical Sciences, North Kargar St., Tehran, 1439955991, Iran.
Email: abaghalian@sina.tums.ac.ir

Interim Mask and Face Shield Guidance

ADA

These recommendations align with existing CDC recommendations for patients without signs/symptoms of COVID-19.

It's always a good idea to conduct a hazard assessment before seeing patients. It can help identify and mitigate potential risks that may exist. Based on the results of the hazard assessment, using the level of PPE indicated in the chart is one way to reduce the risk of exposure. Of course, it's important to recognize that some risk is inherent in all scenarios. If masks with either goggles or face shields are not available, please understand there is a higher risk for infection.

It should be assumed that all patients may transmit COVID-19, given that individuals who are asymptomatic can still be infectious.

Mask Type – With Goggles or Face Shield (Understanding Mask Types)	Infection Risk***
N95	Minimized
N95 EQUIVALENT MASK* KN/KP95, PFF2, P2, DS/DL2, KOREAN SPECIAL 1ST	Minimized
SURGICAL (LEVEL 3) MASK**	May be elevated depending on hazard assessment

**The FDA has authorized the use of masks equivalent to the N95 during the pandemic period. Manufacturers approved can be found here: https://www.fda.gov/media/136663/download*

***ASTM has established performance levels for surgical masks based on fluid resistance, bacterial filtration efficiency, particulate filtration efficiency, breathing resistance and flame spread.*

- *Level 1 masks have the least fluid resistance, bacterial filtration efficiency, particulate filtration efficiency, and breathing resistance.*
- *Level 2 masks provide a moderate barrier for fluid resistance, bacterial and particulate filtration efficiencies and breathing resistance.*
- *Level 3 masks provide the maximum level of fluid resistance recognized by ASTM and are designed for procedures with moderate or heavy amounts of blood, fluid spray or aerosol exposure.*

****The level of risk to DHCP depends in part on the generalized infection level in the community.*

Professional judgment should be exercised when considering the use of gowns, foot covers and head covers.

These guidelines are intended to help dental practices lower (but not eliminate) the risk of coronavirus transmission. Dentists should also be aware of any relevant laws, regulations, or rules.

Int. J. Odontostomat.,
14(4):544-547, 2020.

Uso de Peróxido de Hidrógeno como Enjuague Bucal Previo a la Consulta Dental para Disminuir la Carga Viral de COVID-19. Revisión de la Literatura

Use of Hydrogen Peroxide as a Dental Pre-consultation Mouthwash to Decrease the Viral Load of COVID-19. Literature Review

Méndez, J.[1,2] & Villasanti, U.[3]

MÉNDEZ, J. & VILLASANTI, U. Uso de peróxido de hidrógeno como enjuague bucal previo a la consulta dental para disminuir la carga viral de Covid-19. Revisión de la Literatura. *Int. J. Odontostomat., 14(4)*:544-547, 2020.

RESUMEN: La utilización de enjuagues antisépticos previo a la atención odontológica favorecería la disminución del virus en la cavidad oral. Se ha planteado el uso de peróxido de hidrógeno preconsulta dental. Se revisaron las bases de datos PubMed, Cochrane y Elsevier publicados desde Enero 2019 a junio 2020. Los estudios que cumplieron los criterios de inclusión fueron revisados por 2 autores individualmente. Se realizó una revisión cualitativa de los datos. No existen ensayos controlados aleatorios o estudios de observación clínica sobre el efecto curativo o preventivo del peróxido de hidrógeno contra el COVID-19, pero si protocolos de ensayos clínicos que están en proceso de reclutamiento. El enjuague bucal con peróxido de hidrógeno podría ser una solución viable pre consulta dental que debe ser estudiada para reducir la carga viral del COVID-19.

PALABRAS CLAVE: peróxido de hidrógeno, COVID-19, enjuague bucal.

INTRODUCCIÓN

La utilización de enjuagues antisépticos previo a la atención odontológica favorecería la disminución del virus en la cavidad oral. Se ha planteado el uso de peróxido de hidrogeno preconsulta dental (Meng *et al*., 2020). Esto es importante debido a la cantidad de aerosoles que se generan durante una consulta dental.

Diversos agentes biocidas pueden inactivar al SARS-CoV y MERS-CoV de forma efectiva, estos son el etanol (alcohol etílico) 78 % - 95 % durante 30 segundos, 2-propanol (alcohol isopropílico) 70 % - 100 % durante 30 segundos, formaldehido 0,7 % - 1 % durante 2 minutos, povidona yodada 0,23 % - 7,5 % durante 1 minuto. El glutaraldehído 2,5 % durante 5 minutos o 0,5 % durante 2 minutos inactiva al SARS-CoV, pero sin estudios para MERS-CoV. El hipoclorito de sodio requiere una concentración mínima de 0,21 % durante 30 segundos para ser efectivo y el peróxido de hidrogeno una concentración de 0,5 % durante un minuto, aunque estos resultados fueron con otros coronavirus y no MERS-CoV o SARS-CoV. La OMS recomienda utilizar hipoclorito de sodio 0,5 % o alcohol etílico 70 % durante, al menos, 1 minuto (Guiñez, 2020). También se ha recomendado estudiar los efectos preventivos de los enjuagues de biofilm orales terapéuticos con bCD-Citrox para reducir la carga viral de la infección y posiblemente la progresión de la enfermedad (Carrouel *et al*., 2020).

El uso de un enjuague bucal contra el covid-19 debe ser con elementos oxidativos, como la yodo povidona al 0,23 % o peróxido de hidrógeno al 1 %. Se debe tener en cuenta que los enjuagues con clorhexidina, parecen no ser eficaces para matar al virus (González-Quintanilla & Santos-López, 2020; Peng *et al*., 2020).

[1] Instituto Regional de Investigación en Salud, Universidad Nacional de Caaguazú, Paraguay.
[2] Facultad de Ciencias Médicas, Universidad de la Frontera, Temuco, Chile.
[3] Facultad de Odontología, Universidad Nacional de Caaguazú, Paraguay.

Int. J. Odontostomat.,
14(4):513-518, 2020.

Mouthwashes and Nasal Sprays as a Way to Prevent the Spread of SARS-CoV-2

Enjuagues Bucales y Aerosoles Nasales como un Método de Prevenir la Propagación de SARS-CoV-2

Matías Santos-López[1]; Diego Jaque[1]; Edgardo Fuentes[2] & David González-Quintanilla[2]

SANTOS-LÓPEZ, M.; JAQUE, D.; FUENTES, E. & GONZÁLEZ-QUINTANILLA, D. Mouthwashes and nasal sprays as a way to prevent the spread of SARS-CoV-2. *Int. J. Odontostomat., 14(4)*:513-518, 2020.

ABSTRACT: COVID-19 pandemic has infected millions of people around the world. Due to its large accumulation in the nasopharyngeal region and transmission through respiratory fluids, its spread among people is extremely high. Considering the needed time for treatments and vaccine development, the research of preventive methods, such as the use of mouthwash and nasal spray, that could decrease the viral load in the nasopharyngeal region, and thus the spread of SARS-CoV-2, becomes fundamental. The evidence has shown that there are compounds with antiviral capacity that could be used for this purpose, among which are povidone-iodine, hydrogen peroxide, cyclodextrins, and the synthetic drug PUL-042. Currently, there is no clinical evidence that proves the effectiveness of these substances against SARS-CoV-2. Nevertheless, there are ongoing clinical trials to prove it and generate methods that could help to prevent or, at least, decrease its spread among the population and stop this pandemic.

KEYWORDS: SARS-CoV-2, COVID-19, Mouthwashes, Nasal sprays, prevention.

INTRODUCTION

In December 2019, medical centers in Huanan, China, reported multiple cases of atypical pneumonia, with an etiologic agent unknown until then. The outbreak was linked to the Huanan Seafood Wholesale Market, warning of a possible zoonotic origin of the disease (Lake, 2020; Zhu *et al*., 2020). In January 2020, the China Center for Disease Control and Prevention (China CDC) announced the discovery of a new coronavirus type, named COVID-19, to which the outbreak in December was attributed (Meng *et al*., 2020). On January 31st, 2020, after the exponential increase in cases around the world, the World Health Organization (WHO) declared the Severe Acute Respiratory Syndrome virus (officially named as SARS-CoV-2) and its disease COVID-19 as a pandemic (Mahase, 2020).

Until June 06, 2020, SARS-CoV-2 had infected 6,855,858 people in 187 countries, killing 398,321 of them (Johns Hopkins University & Medicine, 2020).

SARS-CoV-2. SARS-CoV-2 is a positive-sense single-stranded RNA virus, part of the beta coronaviruses family (Cheng & Shan, 2020). Phylogenetically is 97 % related to bats coronavirus, 79 % to the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), and 50 % to the Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Lu *et al*., 2020; Zhou *et al*., 2020; Perlman, 2020).

A zoonotic origin is considered, transmitted by consumption of wild animals that host it (Perlman), and then, between humans by close contact or through respiratory secretions (Rothan & Byrareddy, 2020; Chan *et al*., 2020; Phelan *et al*., 2020; Jin *et al*., 2020). The median incubation period varies between 4 and 5.2 days, with a range between 0 and 24 days (Rothan & Byrareddy; Guan *et al*., 2020; Li *et al*., 2020; Wang *et al*., 2020a).

SARS-CoV-2 infects host cells, through the spike protein, which binds to cellular ACE2 receptors

[1] Faculty of Dentistry, Universidad Finis Terrae, Chile.
[2] Faculty of Health Sciences, Universidad Autónoma de Chile, Chile.

DOI: 10.1111/ipd.12653

EDITORIAL

Coronavirus disease (COVID-19): Characteristics in children and considerations for dentists providing their care

Abstract

The emergence of the novel virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic called coronavirus disease (COVID-19) and has become one of the most significant challenges to the healthcare profession. Dental practices are focal points for cross-infection, and care must be taken to minimise the risk of infection to, from, or between dental care professionals and patients. The COVID-19 epidemiological and clinical characteristics are still being collated but children's symptoms seem to be milder than those that adults experience. It is unknown whether certain groups, for example children with comorbidities, might be at a higher risk of more severe illness. Emerging data on disease spread in children, affected by COVID-19, have not been presented in detail. The purpose of this article was to report current data on the paediatric population affected with COVID-19 and highlight considerations for dentists providing care for children during this pandemic. All members of the dental team have a professional responsibility to keep themselves informed of current guidance and be vigilant in updating themselves as recommendations are changing so quickly.

1 | INTRODUCTION

At the beginning of 2020, the novel virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appeared, causing the coronavirus disease (COVID-19). The emerging virus has resulted in a global pandemic declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) Director-General on the recommendation of the International Health Regulations (2005) Emergency Committee.[1] The case detection rate is changing daily and can be tracked in almost real time.[2] As of 31 March 2020, 19:50 hours (Central Standard Time), the number of confirmed cases was 857 487 and reported deaths were 42 106 with 169 418 recovered patients.[2] The first case of a dentist being tested positive for COVID-19 was reported on 23 January 2020 at the Department of Preventive Dentistry in the Wuhan University Dental Hospital. Eventually, the transmission of disease to eight other oral healthcare professionals was identified.[3] The characteristics of epidemiological spread and clinical manifestations of COVID-19 in children have not yet been thoroughly elucidated. This article reports current data on the paediatric population affected with COVID-19 and emphasises the importance of following locally, regionally, and nationally relevant safety measures to protect dental care professionals as well as the child patient, whilst providing clinical care for the obviously affected children and those potential carriers of the infection. We emphasise that, in a rapidly changing pandemic landscape, practitioners must actively, regularly seek and use reputable and reliable sources of information on managing child patients that are appropriate for their own region and circumstances.

2 | COVID-19

2.1 | Clinical characteristics of COVID-19 in children

The clinical symptoms of COVID-19 are still being documented and collated, although the majority of affected patients exhibit symptoms including a dry cough which is usually accompanied by fever.[4] Difficulty in breathing, fatigue, and other less typical symptoms can also occur.[5,6] Signs and symptoms include different stages as asymptomatic, mild, moderate, severe, and critical.[7] Children tend to present with similar but milder symptoms to adults. To date, 3092 paediatric cases have been reported to have tested positive, and 1412 children were suspected of having been infected with COVID-19. A survey of 1391 children in China found 171 (12.3%) cases tested positive for SARS-CoV-2.[8] An analysis of more than 2000 child patients with suspected or confirmed COVID-19 in Hubei, China, found that over 90% presented as asymptomatic or with mild to moderate symptoms.[9] A summary of paediatric cases reported

Epidemiology and Transmission of COVID-19 in Shenzhen China: Analysis of 391 cases and 1,286 of their close contacts

Qifang Bi [1,#], Yongsheng Wu [2,#], Shujiang Mei [2,#], Chenfei Ye [3,4,#], Xuan Zou [2], Zhen Zhang [2], Xiaojian Liu [2], Lan Wei [2], Shaun A. Truelove [1], Tong Zhang [4], Wei Gao [2], Cong Cheng [2], Xiujuan Tang [2], Xiaoliang Wu [2], Yu Wu[2], Binbin Sun [3,4], Suli Huang [2], Yu Sun [4], Juncen Zhang [4], Ting Ma [3,4,*], Justin Lessler [1,*], Tiejian Feng [2,*]

1. Johns Hopkins Bloomberg School of Public Health, Baltimore, United States
2. Shenzhen Center for Disease Control and Prevention, Shenzhen, China
3. Harbin Institute of Technology at Shenzhen, Shenzhen, China
4. Peng Cheng Laboratory, Shenzhen, China

[#] Contributed equally
* Contributed equally

Received: 23 March 2020 | Revised: 5 April 2020 | Accepted: 10 April 2020
DOI: 10.1002/jdd.12163

ADEA THE VOICE OF DENTAL EDUCATION WILEY

REVIEW ARTICLE

Impact of COVID-19 on dental education in the United States

Parvati Iyer BDS, DDS | **Kalid Aziz DDS, MS** | **David M. Ojcius PhD**

Arthur A. Dugoni School of Dentistry, University of the Pacific, San Francisco, California, USA

Correspondence
Parvati Iyer, BDS, DDS, Arthur Dugoni School of Dentistry, University of the Pacific, 155 Fifth Street, San Francisco, CA 94103, USA.
Email: piyer@pacific.edu

Abstract
Dental institutions in the United States are reeling from the consequences of the novel SARS-CoV2 coronavirus, the causative agent of CODIV-19. As oral health care providers, we have been trained on prevention of aerosol transmissible diseases, but we are still grappling with many unknown factors regarding COVID-19. While the Centers for Disease Control and Prevention (CDC), American Dental Association (ADA), and local state agencies are releasing updates on guidelines for dentists and patients, no official information exists for dental institutions on how to effectively follow the recommended guidelines including "shelter in place" with social distancing to protect students, faculty, staff, and patients, and still ensure continuity of dental education. This article discusses the challenges that we face currently and offers some simple strategies to bridge the gaps in dental education to overcome this emergency.

KEYWORDS
coronavirus, COVID-19, dental education, education technology, e-learning, online learning, oral health, pandemic

During the current pandemic, the Occupational Safety and Health Administration (OSHA.gov) classified dentists in the very-high-risk category because of the potential of exposure to coronavirus through aerosol-generating procedures.[1,2] What are dental schools doing during this pandemic to prevent transmission to dental students? How are dental schools managing students and their general anxiety about redesigned classes, patient care, inability to fulfill clinical requirements for graduation, and concerns for safety? Being in an environment that is changing by the minute, it is imperative that dental schools make appropriate and timely modifications to their teaching and learning methods to ensure continuity of education, and implement interim policies and protocols to protect our staff, students, faculty, and patients. This paper makes simple recommendations to dental educators and administrators that could be easily adopted to tide over the COVID-19 emergency and be better prepared for similar disruptions in the future.

1 | BACKGROUND

Though there have been 2 outbreaks with coronaviruses in the recent past—causing severe acute respiratory syndrome (SARS), which emerged in late 2002 and disappeared by 2004; and Middle East respiratory syndrome (MERS), which was transmitted from camels and camel products to humans[3-6]—there is not much research on the impact of the pandemic caused by the novel coronavirus on dental education. Patil et al.[7] wrote about SARS and its effect on medical education. Park et al.[8] discussed the measures taken by a dental school in South Korea to prevent infection with MERS. Kharma et al.[9] measured the awareness of dental students regarding the MERS outbreak. The most recent article, by Meng et al.[10], discussed the impact of COVID-19 on dental and oral medicine in China. However, a comprehensive description of the impact of COVID-19 on dental education in the United States has not been reported yet.

Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK

Merryn Voysey, Sue Ann Costa Clemens*, Shabir A Madhi*, Lily Y Weckx*, Pedro M Folegatti*, Parvinder K Aley, Brian Angus, Vicky L Baillie, Shaun L Barnabas, Qasim E Bhorat, Sagida Bibi, Carmen Briner, Paola Cicconi, Andrea M Collins, Rachel Colin-Jones, Clare L Cutland, Thomas C Darton, Keertan Dheda, Christopher J A Duncan, Katherine R W Emary, Katie J Ewer, Lee Fairlie, Saul N Faust, Shuo Feng, Daniela M Ferreira, Adam Finn, Anna L Goodman, Catherine M Green, Christopher A Green, Paul T Heath, Catherine Hill, Helen Hill, Ian Hirsch, Susanne H C Hodgson, Alane Izu, Susan Jackson, Daniel Jenkin, Carina C D Joe, Simon Kerridge, Anthonet Koen, Gaurav Kwatra, Rajeka Lazarus, Alison M Lawrie, Alice Lelliott, Vincenzo Libri, Patrick J Lillie, Raburn Mallory, Ana V A Mendes, Eveline P Milan, Angela M Minassian, Alastair McGregor, Hazel Morrison, Yama F Mujadidi, Anusha Nana, Peter J O'Reilly, Sherman D Padayachee, Ana Pittella, Emma Plested, Katrina M Pollock, Maheshi N Ramasamy, Sarah Rhead, Alexandre V Schwarzbold, Nisha Singh, Andrew Smith, Rinn Song, Matthew D Snape, Eduardo Sprinz, Rebecca K Sutherland, Richard Tarrant, Emma C Thomson, M Estée Török, Mark Toshner, David P J Turner, Johan Vekemans, Tonya L Villafana, Marion E E Watson, Christopher J Williams, Alexander D Douglas*, Adrian V S Hill*, Teresa Lambe*, Sarah C Gilbert*, Andrew J Pollard* on behalf of the Oxford COVID Vaccine Trial Group†*

Summary

Background A safe and efficacious vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), if deployed with high coverage, could contribute to the control of the COVID-19 pandemic. We evaluated the safety and efficacy of the ChAdOx1 nCoV-19 vaccine in a pooled interim analysis of four trials.

Methods This analysis includes data from four ongoing blinded, randomised, controlled trials done across the UK, Brazil, and South Africa. Participants aged 18 years and older were randomly assigned (1:1) to ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugate vaccine or saline). Participants in the ChAdOx1 nCoV-19 group received two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort); a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort). The primary efficacy analysis included symptomatic COVID-19 in seronegative participants with a nucleic acid amplification test-positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to treatment received, with data cutoff on Nov 4, 2020. Vaccine efficacy was calculated as 1 – relative risk derived from a robust Poisson regression model adjusted for age. Studies are registered at ISRCTN89951424 and ClinicalTrials.gov, NCT04324606, NCT04400838, and NCT04444674.

Findings Between April 23 and Nov 4, 2020, 23 848 participants were enrolled and 11 636 participants (7548 in the UK, 4088 in Brazil) were included in the interim primary efficacy analysis. In participants who received two standard doses, vaccine efficacy was 62·1% (95% CI 41·0–75·7; 27 [0·6%] of 4440 in the ChAdOx1 nCoV-19 group *vs* 71 [1·6%] of 4455 in the control group) and in participants who received a low dose followed by a standard dose, efficacy was 90·0% (67·4–97·0; three [0·2%] of 1367 *vs* 30 [2·2%] of 1374; $p_{interaction}$=0·010). Overall vaccine efficacy across both groups was 70·4% (95·8% CI 54·8–80·6; 30 [0·5%] of 5807 *vs* 101 [1·7%] of 5829). From 21 days after the first dose, there were ten cases hospitalised for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death. There were 74 341 person-months of safety follow-up (median 3·4 months, IQR 1·3–4·8): 175 severe adverse events occurred in 168 participants, 84 events in the ChAdOx1 nCoV-19 group and 91 in the control group. Three events were classified as possibly related to a vaccine: one in the ChAdOx1 nCoV-19 group, one in the control group, and one in a participant who remains masked to group allocation.

Interpretation ChAdOx1 nCoV-19 has an acceptable safety profile and has been found to be efficacious against symptomatic COVID-19 in this interim analysis of ongoing clinical trials.

Funding UK Research and Innovation, National Institutes for Health Research (NIHR), Coalition for Epidemic Preparedness Innovations, Bill & Melinda Gates Foundation, Lemann Foundation, Rede D'Or, Brava and Telles Foundation, NIHR Oxford Biomedical Research Centre, Thames Valley and South Midland's NIHR Clinical Research Network, and AstraZeneca.

Published Online December 8, 2020 https://doi.org/10.1016/S0140-6736(20)32661-1

See Online/Comment https://doi.org/10.1016/S0140-6736(20)32623-4

*Contributed equally

†Members are listed in appendix 1 (pp 21–44)

Oxford Vaccine Group, Department of Paediatrics, University of Oxford, Oxford, UK (M Voysey DPhil, P K Aley PhD, S Bibi PhD, R Colin-Jones MSc, K R W Emary BM BCh, S Feng PhD, S Kerridge MSc, A Lelliott BMBS, Y F Mujadidi MSc, P J O'Reilly MBChBAO, E Plested, M N Ramasamy DPhil, S Rhead MBChB, N Singh DPhil, R Song MD, M D Snape MD, A J Pollard FMedSci); **Jenner Institute, Nuffield Department of Medicine, University of Oxford, UK** (P M Folegatti MD, B Angus MD, P Cicconi PhD, K J Ewer PhD, S H C Hodgson DPhil, S Jackson MRCP, D Jenkin MRCP, C C D Joe PhD, A M Lawrie PhD, A M Minassian DPhil, H Morrison MRCP, M E E Watson PhD, A D Douglas DPhil, A V S Hill FMedSci, T Lambe PhD, S C Gilbert PhD); **Institute of Global Health, University of Siena, Siena, Brazil;** (S A C Clemens PhD); **Department of Paediatrics** (S A C Clemens) **and Clinical**

Int. J. Inter. Dent Vol. 13(2); 57-58, 2020

DOI: 10.4067/S2452-55882020000200057

CARTA AL EDITOR

El odontopediatra del futuro para tiempos post COVID-19.

The pediatric dentist of the future for post COVID-19 times.

Vidal Pérez[1*], Jaime Díaz[2], Sandra Rojas[3], Juan Eduardo Onetto[4]

1. Departamento de Pediatría Estomatológica, Facultad de Ciencias de la Salud, Universidad de Talca. Chile.
2. Departamento de Odontopediatría y Ortodoncia, Facultad de Odontología, Universidad de La Frontera. Chile.
3. Departamento del Niño y Ortopedia Dentomaxilar, Facultad de Odontología, Universidad de Chile. Chile.
4. Cátedra de Odontopediatría, Facultad de Odontología, Universidad de Valparaíso. Chile.

**Correspondencia a: Vidal Pérez. | Universidad de Talca. Av. Lircay s/n, Talca, Chile. | Teléfono: +56 71 2203026 (extensión 3026) | E-mail: vperez@utalca.cl*
Trabajo recibido 03/06/2020
Aprobado para su publicación 08/06/2020

Desde la llegada del coronavirus SARS-CoV-2 a nuestro país en marzo 2020, la enfermedad COVID-19 se ha diseminado entre nuestra población provocando, como en todo el mundo, cambios significativos en nuestros estilos de vida[1,2]. Esta pandemia ha golpeado a la odontología y la odontopediatría en particular en sus ámbitos profesionales y formativos[3,4]. A pesar de nuestros esfuerzos, el retorno a la actividad clínica requerirá la adquisición de nuevas competencias transversales importantes en la formación del odontopediatra que requerirá nuestra sociedad en los tiempos post COVID-19[5,6].

Luego del arribo de este virus, las universidades chilenas comenzaron a utilizar masivamente plataformas virtuales y recursos digitales, no exento de dificultades[7]. Las escuelas y facultades de odontología siguieron esos lineamientos con un ajustado plan de trabajo para enfrentar los desafíos que involucra la enseñanza de la odontología y particularmente de la odontopediatría en tiempos de COVID-19. Durante este primer semestre, los programas curriculares de pre y postgrado han sido adaptados para una docencia teórica online, al igual que en todo el ámbito de la educación superior[8]. Por otro lado, las actividades clínicas han sido suspendidas en forma temporal, a la espera de la resolución sanitaria del Ministerio de Salud que permita volver con las normas de bioseguridad adecuadas a las actividades académicas en los diferentes campos clínicos. Aunque todas las instancias universitarias promueven una búsqueda de medidas que protejan a profesores, estudiantes (residentes), personal administrativo y pacientes, se ve incierto el retorno a la actividad clínica en el segundo semestre.

Los académicos hemos aplicado una variedad de estrategias metodológicas para entregar los contenidos teóricos, de manera de lograr los objetivos de aprendizaje planificados. Entre éstas se destacan: clases asincrónicas y sincrónicas, talleres de resolución de problemas, foros para resolver dudas y canales de YouTube para almacenar las creaciones docentes de libre acceso para los estudiantes[5,7,8]. Paralelamente, se han diseñado una serie de evaluaciones formativas que refuerzan los contenidos presentados en clases y talleres. Todo lo anterior, tratando de respetar los tiempos de trabajo autónomo y brindando la contención emocional que promueva la resiliencia necesaria (que amerita el contexto social que estamos viviendo), ya que, tanto estudiantes como académicos estamos en un proceso de aprendizaje digital continuo[9,10]. Sin embargo, estamos ciertos que la enfermedad COVID-19 impactará significativamente la forma de enseñar odontología y especialmente odontopediatría en el futuro inmediato[11-13]. Al respecto, la restricción de la atención clínica que ha establecido la Autoridad Sanitaria en Chile, que autoriza solo atenciones de urgencias, nos obligan a analizar profundamente la forma en que regresaremos a la atención clínica de pacientes, tanto en el contexto público, privado y en la academia.

Posiblemente y de acuerdo a lo observado en múltiples publicaciones e informes de diferentes instancias rectoras de salud en el mundo, realizar un diagnóstico a distancia de las condiciones de salud general y bucal del paciente a través de tele-odontología, control de temperatura, desinfección de calzado y lavado frecuente de manos, entre otras, serán procedimientos habituales en nuestra práctica clínica futura[14-16]. Una adecuada desinfección de hall de ingresos, salas de espera y box clínicos junto con el uso y recambio de los equipos de protección personal, serán procedimientos de rutina que extenderán los tiempos en el tratamiento de pacientes, reduciendo el número de atenciones[17,18]. En este escenario complejo el desarrollo de nuevas tecnologías (como sistemas de aspiración, nuevos agentes de irrigación, entre otros) que reduzcan la carga vírica de los ambientes de trabajo serán necesarias[19,20]. Sin embargo, estos aspectos son solo una parte de los cambios que requerirá nuestra profesión y particularmente nuestra especialidad.

Es probable que esta pandemia despierte en la odontología en general y odontopediatría en particular, la necesidad de métodos alternativos de entrenamiento que permitan a nuestros especialistas el desarrollo de competencias acordes a los tiempos post COVID-19 que viviremos[5,11]. Entonces, es de la mayor importancia que las instituciones de educación superior, sus escuelas y facultades de odontología actúen en forma rápida y proactiva reevaluando el perfil de egreso de sus estudiantes pre y postgrado. Por lo anterior, se hace necesario entonces repensar las competencias que requiere este “nuevo odontopediatra”.

El odontopediatra del futuro debería ser hábil en el uso de las Tecnologías de la Información y Comunicación (TIC) a distancia existentes y emergentes, por lo que las habilidades telemáticas (propias de la ingeniería) son saberes a incorporar en su plan de estudio[21,22]. Tan importante como lo anterior, las habilidades comunicativas de nuestro especialista serán altamente requeridas para transmitir los conceptos de promoción y prevención en salud bucal tanto a nivel comunitario como individual[23-25]. En este contexto, la educación de los pacientes y sus familias requerirá un dentista hábil en observar la “realidad del paciente y su entorno biopsicosocial” y utilizar esa información como un instrumento que facilite la educación en salud bucal. Por lo anterior, se hace necesario considerar decididamente el uso de estrategias educativas basadas en los conceptos de la entrevista motivacional u otras similares, siendo alternativas a implementar

Healthcare Workers
Testing
Vaccination
Clinical Care
Infection Control
First Responders
Exposure in Healthcare Settings

Using Telehealth to Expand Access to Essential Health Services during the COVID-19 Pandemic

Updated June 10, 2020 Español Print

Purpose of this Guidance

To describe the landscape of telehealth services and provide considerations for healthcare systems, practices, and providers using telehealth services to provide virtual care during and beyond the COVID-19 pandemic.

On This Page