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COVID-19 – A COMPREHENSIVE INSIGHT INTO THE PANDEMIC AND THE DENTAL PRACTITIONER'S DEFENSE

Dental Science

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ABSTRACT

'Coronavirus' became a household name worldwide when the World Health Organization (WHO) declared Coronavirus disease (COVID-19) as a global health emergency on 30th January 2020. With millions of active cases and thousands of deaths, the pandemic is still active and poses a serious public health concern internationally.

The aim of the article is to provide a bird's eye view of our current understanding of the Coronavirus disease (COVID-19), the SARS COV-2 virus, its pathogenesis, modes of transmission and clinical presentation. Additionally, screening and diagnostic tests, recent developments in the antiviral drugs along with other experimental treatment modalities have also been discussed. The article also provides a brief set of recommendations to be followed by a dental practitioner while handling any emergency case during these times to prevent the risk of spread of the disease.

The article was last updated on 25th May 2020.

KEYWORDS

COVID-19 Testing, Treatment, Dental Management

INTRODUCTION

The city of Wuhan in Central China, in December 2019, became the epicenter of an outbreak of several atypical pneumonia cases of unknown etiology, with a common link to Wuhan's Huanan Seafood Wholesale fish and live animal Market.[1] Cases showed symptoms such as fever, dry cough, dyspnoea; radiological findings showed bilateral lung infiltrates[2]. A few days later, Chinese authorities identified a novel coronavirus (2019-nCoV) as the causative agent of the outbreak[3].

The virus has formally been named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease as "coronavirus disease 2019" (COVID-19) [4]**On 30 January 2020**, the World Health Organization (WHO)declared this first outbreak of novel coronavirus a 'public health emergency of international concern. [5]

WHAT IS COVID-19?

COVID-19 is an acronym for Coronavirus disease 2019. It is a viral disease caused by a novel coronavirus now called *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2; formerly called 2019-nCoV)

Coronaviruses (CoVs) are a large family of positive-sense single-stranded RNA viruses (+ss RNA) with a crown-like appearance under the electron microscope (Latin, coronum= crown) due to the presence of spike glycoproteins on the envelope.[6] [7] Discovered in the 1960s, Coronaviruses were classified under family *Coronaviridae*. Subfamily *Orthocoronavirinae* of this family includes four genera: α, β, γ, and δ based on their genomic structure. α and β coronaviruses infect only mammals, including bats. γ, and δ coronaviruses mostly infect birds and mammals. [8, 9, 10]

The first human coronavirus outbreak was recorded in 1965 - HCoV-229E, followed by two outbreaks of similar capacity - SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV) in 2003 and 2012, respectively.

VIROLOGY

The SARS-CoV-2 is a beta-coronavirus mostly affecting human beings through zoonotic transmission[11]. The life cycle of the virus within the host has the following steps:

- **Attachment** of viruses to host receptors.
- Their **penetration** into the host cells.
- **Biosynthesis** of viral proteins when viral RNA enters the nucleus for replication.
- **Maturation** of new viral particles and their **release**.

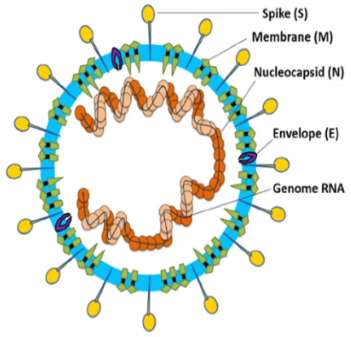

Figure 1 CORONAVIRUS PARTICLE

Image citation: Li G, Fan Y, Lai Y, et al. Coronavirus infections and immune responses. Journal of Medical Virology 2020; 92: 424-432.

SARS-CoV-2 possesses the structure of a typical coronavirus which consists of four structural proteins; Spike (S), membrane (M), envelop (E), and nucleocapsid (N). The S protein can bind to the receptors of the host to facilitate viral entry into target cells.

Spike (S) protein determines the diversity of coronaviruses and host tropism. It has two functional subunits; the S_1 subunit is responsible for binding to the host cell receptor and the S_2 subunit is for the fusion of the viral and cellular membranes. [12, 13]

PATHOPHYSIOLOGY

SARS-CoV-2 binds to human *angiotensin-converting enzyme 2* (**ACE2**), found in the lower respiratory tract of humans. ACE2, a known cell receptor for SARS-CoV-2 regulates both cross-species and human-to-human transmission.[14, 15] Isolated from the bronchoalveolar lavage fluid (BALF) of a COVID-19 patient, Zhou et al. [16] have confirmed that the SARS-CoV-2 uses the same cellular entry receptor, ACE2, as SARS-CoV.

ACE2 expression is high in lung, heart, ileum, kidney, and bladder. In the lungs, ACE2 is highly expressed on the apical side of epithelial cells in the alveolar space, this virus can likely enter and

destroy them. This matches with the fact that the early lung injury was often seen in the distal airway. ACE2 is also expressed in the endothelial cells which represent one-third of lung cells. Microvascular permeability as a result of the endothelial injury can facilitate viral invasion. [9, 10] Whether or not SARS-CoV-2 binds to an additional target needs further investigation.

MODES OF TRANSMISSION

According to current evidence, SARS-CoV-2, the virus that causes COVID-19, is thought to be spread **primarily through respiratory droplets** when an infected person coughs, sneezes, or talks.

The transmission of virus between people can occur primarily by **direct contact** with infected people and **indirect contact** with surfaces in the immediate environment or with objects used on the infected person (e.g., thermometer or stethoscope). [17]

Airborne transmission (due to the presence of microbes in the air for long periods) from person-to-person over long distances is unlikely but may be possible in circumstances and settings which generate aerosols. The virus has been shown to survive in aerosols for hours and on some surfaces for days. There are also indications that patients may be able to spread the virus while pre-symptomatic or asymptomatic.

However, the detection of RNA in environmental samples based on PCR-based assays is not indicative of a viable virus that could be transmissible. Further studies are needed in this regard. [17,18]

Environmental Stability Of The Virus
SARS-CoV-2 can stay viable for up to 3 hours in the air post aerosolization, up to 4 hours on copper, up to 24 hours on cardboard, and up to 2–3 days on plastic and stainless steel, albeit with significantly decreased titres.

A recent study showed that the virus was more stable on smooth surfaces, with the detection of the infective virus on surgical mask material for up to 7 days. In vitro tests showed that in the transport medium, the virus is stable at 4 degrees C for up to 14 days but inactivated after 5minutes at 70 degrees C. However, these results from experimental studies do not directly translate to fomite infectivity in the real world. [18]

CLINICAL PRESENTATION[19]

A wide range of symptoms has been reported in people with COVID19– ranging from mild symptoms to severe illness.

After exposure to the virus, symptoms may take 2-14 days to appear. Presence of these symptoms or combinations of symptoms may suggest COVID-19:

- Cough
- Shortness of breath or difficulty breathing

Or at least two of these symptoms:

- Fever
- Chills
- Repeated shaking with chills
- Muscle pain
- Headache
- Sore throat
- New loss of taste or smell[19]

The clinical spectrum varies from asymptomatic forms to clinical conditions like severe acute respiratory illness which includes severe pneumonia to respiratory failure that necessitates ventilation and support, to serious complications, such as acute respiratory distress syndrome,arrhythmia, shock, and multi-organ dysfunction syndrome (MODS). [7,19]

Mostchestcomputed tomography (CT) showed bilateral pneumonia, with ground-glass opacity and bilateral patchy shadows being the most common patterns (Guan et al. 2020 [20]; Wang et al. 2020 [21]).

The incubation period is two days to 14 days.

The fatality rate of COVID-19, as per current data, is 2.3%, which is lower than that of SARS (severe acute respiratory syndrome; ≈10%) and MERS (Middle East respiratory syndrome; ≈34%) [22]

Any age group can be affected, most of the cases being in the 30 - 69 years age group. Individuals with pre-existing hypertension, diabetes, cardiovascular, cancer, and chronic respiratory illness are at a higher risk of complications. [23,24]

COVID-19 TESTING

Tests may use two methods to detect the SARS-CoV-2 virus-
I. Immunoglobulin detection-based test (serology)
II. Genomic detection based (molecular) test

I. Immunoglobulin detection test [25](Diagnostic test)
This test is based on the qualitative detection of IgM and IgG that are specifically generated by the body in response to SARS-CoV-2 infection. In order to fight the infection, IgM and IgG target specific antigens on the surface of the SARS-nCoV-2 virus.

- 2-3 drops of fresh blood/serum or plasma are placed in a sample container(cassette) and 2-3 drops of the provided buffer are added in it.
- The diluted sample moves through the cassette by capillary action.
- The cassette has labelled SARS-CoV-2 antigen that may bind chemically with either IgM or IgG to form antigen/antibody complexes of antigen/IgG and/or antigen/IgM
- Then antigen/antibody product passes over anti-IgM and anti-IgG antibodies that are immobilized in a line within the cassette.
- The anti-IgM and/or anti-IgG then captures the specific complex and signal a result (a red line) if either complex is bound to the immobile anti-IgM or anti-IgG.
- The results are read after 10-15 minutes.
- A third line is a control line which indicates that the test is working properly.

Immunoglobulin tests can only tell whether a person has been exposed to SARS-CoV-2 in the past or not. It cannot confirm the presence of the virus in your system. Therefore, it should only be used alone as a screening test and should be used in tandem with a genetic-based test to determine a complete status. [25]

II.Genomic Detection Based (molecular) Test
Currently, a real-time reverse transcription-polymerase chain reaction (rRT-PCR) based technique is used to confirm the cases. Upper respiratory specimen (nasopharyngeal) is also used to detect SARS-CoV-2. The respiratory specimen preferably from the lower respiratory tract (sputum, bronchoalveolar lavage, bronchial aspirate) is used for higher yield. [26]

PCR Test for COVID 19 infection [27]

- A swab is collected from the back of the nose or mouth.
- The sample is processed to convert the viral RNA to complementary DNA for testing.
- Amplification of DNA with specific primers to create millions of copies.
- Fluorescent markers bound to the copies during PCR are released and detected when amplification occurs.
- Presence of viral genetic material, fluorescence detected POSITIVE RESULT
- Absence of viral genetic material, no fluorescence NEGATIVE RESULT

TREATMENT

- Currently, no specific antiviral agents are approved for novel coronavirus disease 2019 (COVID-19). Mainly supportive care is given to the patients to help alleviate symptoms. In severe cases, vital organ function also needs support. [28]
- Among the *pharmacotherapeutic* agents being evaluated, high-dose Vitamin C, favipiravir, adalimumab, dihydro-artemisinin piperaquine, leflunomide, dipyridamole, chloroquine or hydroxychloroquine, suramin sodium, lopinavir/ritonavir and arbidol (umifenovir), and IFN-alpha 2b are some of the highlighted ones.[29]
- A current paper reported by Zhonghua Jie He He Hu Xi Za Zhi depicts an inhibitor effect of **remdesivir** (a new antiviral drug) and chloroquine (an old antimalarial drug) on the growth of SARS-CoV-2 in vitro.[30] Remdesivir was developed to treat several other severe viral diseases, including the disease caused by the Ebola virus (not a coronavirus). It works by inhibiting the ability of the coronavirus to replicate. [31]

- **Hydroxychloroquine** (an analogue of chloroquine) has a clinical safety profile superior to that of chloroquine (during long-term use) and requires higher regular doses and has fewer complaints about drug-drug interactions. (Gautret et al. (2020)
- **Azithromycin** is not an anti-viral drug but does have some anti-inflammatory action. Initial findings suggest the synergistic effect of the mixture of hydroxychloroquine with azithromycin. It is active in vitro against Zika and Ebola viruses and to prevent severe respiratory tract infections when administrated to patients suffering from viral infections. [32]
- Another drug undergoing major clinical trials is **Favipiravir.** It is a new breed of RNA-dependent polymerase (RdRp) inhibitor which can prevent the replication of the virus. It became authorized for the treatment of novel influenza in China from 15 February 2020.[33]
- **IFN-α** (Alpha interferon) is a broad-spectrum antiviral that is usually used to treat hepatitis. Based on the preliminary outcomes of clinical studies it is reported to inhibit SARS-CoV reproduction in vitro.[34]

Convalescent Plasma As A Potential Therapy For COVID 19 [31,35,36]

- Another investigational treatment being explored for COVID-19 is the use of **convalescent plasma (plasma from recovered patients)**.
- Previously, the use of convalescent plasma has also been studied during the 2003 SARS-CoV-1 epidemic and the 2012 MERS-CoV epidemic.
- This therapy is based on the premise that plasma collected from individuals who have recovered from COVID-19 contains antibodies to SARS-CoV-2 (the virus that causes COVID-19). This plasma from a recovered patient is given by transfusion to a patient who is suffering from COVID-19 to help the patient fight the illness, possibly shortening the length or reducing the severity of the disease.
- Although still experimental, on March 24th, the FDA allowed convalescent plasma to be used in patients with serious or immediately life-threatening COVID-19 infections.

Extracorporeal membrane oxygenation therapy in the COVID-19 pandemic

- ECMO is a form of mechanical cardiopulmonary support that can provide prolonged extracorporeal life support in patients who are unresponsive to conventional management. There are two forms of ECMO: venovenous (VV) typically used in cases of severe respiratory failure, and veno-arterial (VA) or venovenous-arterial (VVA) for patients with cardiogenic shock.[37]
- Although providing complex therapies such as ECMO during outbreaks of emerging infectious diseases has unique challenges, ECMO has developed from being used as a 'rescue therapy' to become an accepted treatment option for patients with severe ARDS.[38]
- Currently, many other potential treatment modalities for COVID-19 are under investigation including drugs that have been used to treat malaria and autoimmune diseases; several antiviral drugs that were developed for other viruses, and antibodies from recovered patients.

VACCINE FOR COVID-19

- According to the WHO's global database of research into the novel coronavirus, currently seven vaccine candidates have entered human trials across the world. [39]
- Typically, vaccines go through various stages of research, which involve testing on animals and at least three phases of human clinical trials. All this can take several years, sometimes up to a decade.
- The severity of the pandemic and rapid spread globally has forced scientists to skip or combine various phases of trials to accelerate the process. Although the approach is risky, it may deliver a suitable vaccine in record time.

RECOMMENDATIONS FOR DENTAL PRACTITIONERS

Dental practitioners are at tremendous risk of COVID 19 infection as the procedures involve face-to-face communication with patients, and frequent exposure to saliva, blood, and other body fluids, and the handling of sharp instruments. Droplet and aerosol transmission of the virus are the most important concerns in dental clinics and hospitals as the virus can stay viable in the aerosol for up to 3 hours. [18,40]

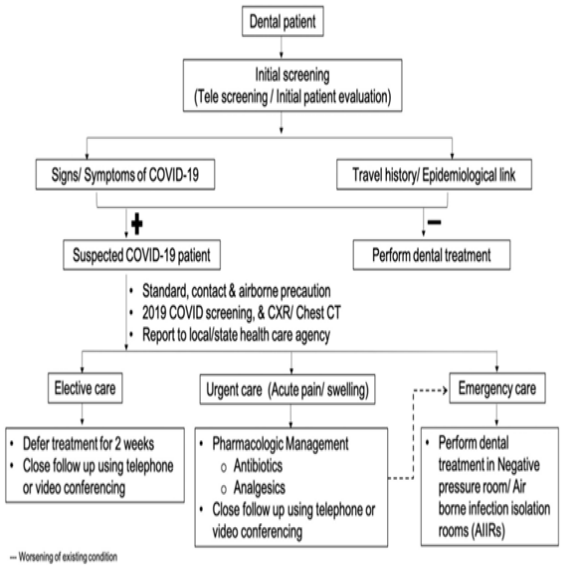

Figure 2 Patient screening for COVID-19 and Dental Management

Citation: Ather A et al. COVID-19: Implications for Clinical Dental Care. JOE 2020.

Emergency care to patients WITHOUT COVID-19 during the pandemic

Assess the patient at the time of check-in. Take proper history, ask about the presence of symptoms of any respiratory illness, recent travel history to sensitive areas, any contact with an infected individual. Measure his/her temperature with a contact-free infrared thermal temperature sensor. If the temperature is less than 100.4˚F and the patient is without symptoms consistent with COVID-19, emergency care may be provided.

Prioritize minimally invasive/atraumatic restorative techniques (hand instruments only).

Emergency dental care can be given to people with COVID-19 who have ended home isolation. This is decided in two ways:

1)Non-test based

At least 3 days have passed since recovery and at least 7 days have passed since symptoms first appeared.

2)Test-based

o People with COVID-19 with symptoms-: Resolution of fever without the use of anti-pyretic **and** improvement in respiratory symptoms **and** negative results of a molecular assay for COVID-19 from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart[4]

oPeople with lab-confirmed COVID-19 without any symptoms: At least 7 days have passed since the date of the first positive COVID-19 diagnostic test and have had no subsequent illness. [41]

Patients WITH COVID-19(suspected or confirmed) infection

- Such cases should not be treated in a routine dental setting. Instead, they should be treated in negative-pressure rooms or airborne infection isolation rooms (AIIRS) [28]
- Preprocedural mouth rinse with 0.2% povidone-iodine might reduce a load of coronaviruses in saliva. Alternatively, use 0.5-1% hydrogen peroxide mouth rinse, as it has nonspecific oxidative viricidal activity against coronaviruses [42-44]
- To prevent cross-contamination use of disposable items is encouraged.
- Use a rubber dam to minimize splatter generation.
- Extraoral imaging techniques should be preferred to intraoral imaging to avoid gag or cough reflex. Also, sensors should be covered in double barrier whenever intraoral imaging is mandated.
- Minimize the use of high-speed handpieces, ultrasonic scalers, and three-way syringes to reduce the risk of aerosol generation.
- Anti-retraction dental handpiece with specially designed anti-

retractive valves or other anti-reflux designs should be used as an extra preventive measure for cross-infection. The high-speed dental handpiece without anti-retraction valves may aspirate and expel the debris and fluids during the procedure and may further contaminate the air and water tubes within the dental unit, and thus can potentially cause cross-infection.

- The use of barrier-protection equipment, including protective eyewear, surgical masks or N95 respirator, gloves, caps, face shields, and protective outwear, is strongly recommended for all clinicians. The clinician must also know how to properly don, use, and doff the personal protective equipment (PPE) in a manner to prevent self-contamination.
- Strict adherence to meticulous hand hygiene and following the infection control guidelines along with proper disinfection and sterilization measures is crucial.
- The medical waste generated by the treatment of patients with suspected or confirmed 2019-nCoV infection are regarded as infectious medical waste. Double-layer yellow color medical waste package bags and "gooseneck" ligation should be used. The surface of the package bags should be marked and disposed of according to the requirement for the management of medical waste.[28,45]

CONCLUSION

Epidemics and pandemics are not new to the human race, but with increased globalization and population growth, outbreaks of infectious disease can move from a remote village to a major city in the other part of the world in no time. We need to be adequately prepared to respond to these emerging and re-emerging infectious threats.

As of 25thMay 2020, the outbreak of COVID-19 has reached a total of 5,304,772 confirmed cases and **3**42,029 fatalities worldwide (as per WHO reports). Understanding of the disease and related factors is a key tool in this battle against COVID-19.

The role of dental professionals in preventing the transmission of COVID-19 is also critically important due to the mode of transmission of SARS-CoV-2 and increased risk of cross-contamination in a dental clinic. The practitioners can contribute to the global and individual battle against this disease by using the available knowledge to educate themselves and their patients to prevent the transmission of COVID-19.

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