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Review Article

To study the pathophysiology, clinical features, diagnosis and management of coronovirus: A review study

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ABSTRACT:
In the current scenario, amongst the various other diseases, covid-19 is one of the deadliest one. Its outbreak began in China but soon the disease spread worldwide. It's a highly contagious disease, being airborne therefore, dentists and other health professionals must be well informed about the symptoms of this disease and the precautionary methods to protect themselves and the general population from it. The objective of this paper is to raise awareness of the above review of PPE, its findings and their relevance to dentistry.In this article, we have tried to mention few of the precautionary methods that can be followed by the dental and other medical professionals to protect themselves from this disease.
Key words: Covid-19, PPE, Dentistry, Masks, Infection, Dental practice, Risk management

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INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease that is caused by severe acute respiratory syndrome coronavirus 2 (SARSCoV-2).[1]This virus was named as the severe acute respiratory syndrome coronavirus-2 because of its high homology to SARS-CoV, which caused acute respiratory distress syndrome (ARDS). Its outbreak of was assumed to have initially started via a zoonotic transmission associated with the seafood market in Wuhan, China. Later on it was found that human to human transmission was a major factor in its outbreak.[2]Other novel pathogenic human coronaviruses that were emerged from animal reservoirsare Middle East respiratory syndrome-related coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), and, most recently, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[3]The viral RNA infects both animals and humans mayproduce respiratory, gastrointestinal and nervous symptoms.[4]The respiratory symptoms of COVID-19 are extremely variable, ranging from minimal symptoms to intense hypoxia with ARDS. Themedian incubation period is5 days (ranging from 2 to 14 days), people develop symptoms within 12 days of infection (ranging from 8 to 16 days).Time period between onset of symptoms and the development of ARDS can be as short as 9 days and studies show that mortalities rates are higher in elder population and the incidence of this disease is much lower in children.[2]If the infection is mild it may recover in 2 weeks' time period, however, if the infection is severe patients may take 6 weeks to recover. Therefore, large-scale diagnostic testing has been suggested in areas containing outbreaks such as COVID-19 to control the spread.[5]One key discovery in understanding the mechanism of SARS-CoV-2 infection the role of the transmembrane serine protease 2 (TMPRSS2), a cell-surface protein that is expressed by epithelial cells of specific tissues including those in the aerodigestive tract.[6]

ROUTES OF TRANSMISSION

The virus is mainly transmitted by direct transmission (i.e., cough, sneeze, and droplet inhalation), contact transmission (i.e. contact with oral, nasal, and eye mucous membranes), and fomites (i.e. inanimate objects that, when contaminated with or exposed to infectious pathogens, can transfer disease to a new

host. at room temperature the viral particles of SARSCoV-2 without the host remain infectious from 2 hours up to 9 days and persist better at higher (50%) compared to lower (30%) humidity. Contaminated blood samples are often used to perform laboratory diagnostic tests and should also be considered possible routes of transmission for SARS-CoV-2.[7] Dental procedures such as using a high speed handpiece or ultrasonic instruments which release aerosols into the air (which means almost all dental procedures) may heighten the possibility of contamination. The professionals can act as transmitters as well as they could become infected during human-to human transmission, through non-invasive salivary secretions like a patient's cough or sneeze or treatment procedures.[8] Some suggest that salivary glands might act as a reservoir for COVID-19 asymptomatic infection. In fact, the expression of Angiotensin-converting enzyme 2 (ACE2), a key receptor for COVID-19, is higher in minor salivary glands than in the lungs.[9] Transmission via droplets occurs only in cases of close contact (within 1 metre) with those who have respiratory symptoms because there is a risk of oral/nasal mucosa or conjunctiva getting exposed to potentially infected respiratory droplets when the person sneezes, coughs, or talks loudly.[10] According to results some studies, the COVID-19 outbreak began with a single transmission from animal to human and was then followed by ongoing human-to-human spread [11]

It is transmitted through both Flugge (microdroplets due to direct proximity) and core droplets that remain suspended in aerosol through coughing or sneezing by an infected person and possible transmission through fomites.[12] virus viability in the aerosol was to exceed 3 h and surface stability of the virus exceeded 72 h.[13][14]

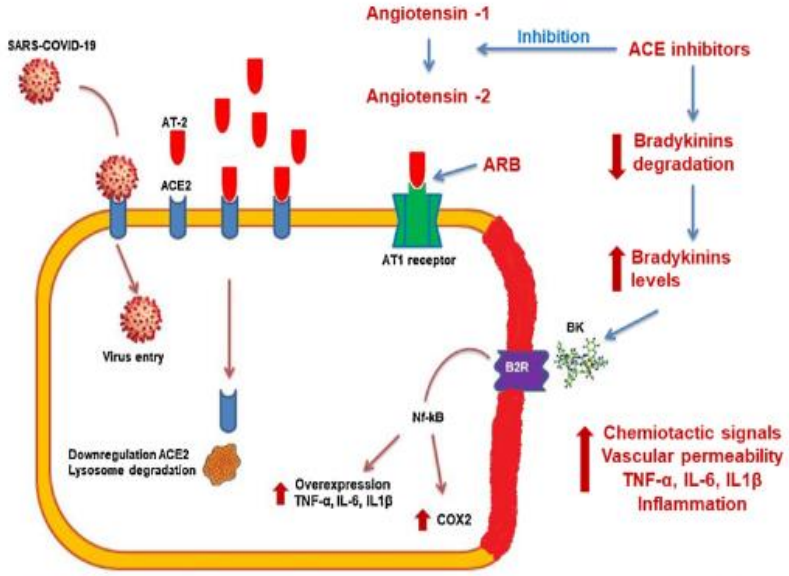

Fig. 1. Schematic diagram of the potential mechanisms linking the ACE system and COVID-19 infection. The virus could enter directly inside the epithelial cell of the respiratory system via the ACE2 receptor or induce an inflammatory cascade by bradykinin escape related to ACEI therapy. The subsequent increase in prostaglandins and cyclooxygenases leads to interleukin production, which causes cell membrane inflammation potentially leading to apoptosis. Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; AT, angiotensin; B2R, bradykinin 2 receptor; BK, bradykinin; COX, cyclooxygenase.

R0 (the basic reproductive number/ infectious agent's epidemic potential) for SARS-CoV-2 ranges between 1.4 and 6.5, with an average of 3.[12] Patients were shown to be contagious prior to the onset of clinical symptoms. The contagiousness could persist up to three weeks after recovery.[14] Results from some studies have shown that aerosols from highly virulent pathogens like severe acute respiratory syndrome-coronavirus can travel more than six feet.Hand contact with contaminated surfaces may lead to pathogen acquisition and transfer to the eyes, nose, or mouth, resulting in a new case of infection. A review conducted by Zemouri et al. (2017) showed that 38 types of microorganisms could be found in the air of the dental clinic, including Legionella pneumophila, the causative agent of severe pneumonia.[15]

In clinical settings, as in dental clinics, where a large volume of aerosol is produced, airborne infection transmission is likely, and hence dentists and allied dental staff need to consider extra airborne and droplet precautions during the pandemic (World Health Organization, 2020).

Moreover, it has been reported that stools of infected individuals are also contaminated with SARS-CoV-2 findings, together with the fact that ACE2 is expressed in the gastrointestinal tract and reports of infected individuals presenting with diarrhoea, tend

to imply that faecal–oral transmission route of SARS-CoV-2 is plausible.[16]

SYMPTOMS

COVID-19 demonstrates a wide spectrum of clinical manifestations and may range from asymptomatic or paucisymptomatic forms, to severe viral pneumonia with respiratory failure, multiorgan and systemic dysfunctions in terms of sepsis and septic shock, and eventually may result in death. In symptomatic patients, the clinical manifestations of the disease usually start after less than a week and consists of fever, cough, nasal congestion, fatigue and other signs of upper respiratory tract infections. Sometimes, gastrointestinal symptoms and asymptomatic infections are also seen. The infection can progress to severe disease with dyspnoea and severe chest symptoms corresponding to pneumonia in approximately 75% of patients, as seen by CT scan on admission.Some may exhibit mild to moderate symptoms, but 15% of the cases progress to severe pneumonia and 5% eventually develop acute respiratory distress syndrome (ARDS).Most patients present with influenza-like illness (ILI) or mild pneumonia. Neurologic symptoms associated with covid-19 include headache, altered mental status, and anosmia seen in plenty of patients. Asymptomatic patients may act as reservoirs for the disease and are active carriers to the community, and it has been revealed that virulence increases with the severity of symptoms of the carrier. During the incubation period of the virus, infected individuals can also serve as carriers for COVID-19. A lot of studies have confirmed that asymptomatic patients can transmit the disease to others.[17]

DIAGNOSIS OF COVID-19

Diagnosing the disease is the most important step in preventing its spread. Current diagnostic tests for coronavirus include reverse-transcription polymerase chain reaction (RT-PCR), real-time RT-PCR (rRT-PCR), and reverse transcription loop-mediated isothermal amplification (RT-LAMP) and if done rapidly, these diagnostic tests can limit the covid-19 outbreak.[18]

A. SALIVARY METHODS: The collection of upper respiratory samples via nasopharyngeal and oropharyngeal swabs is the primary and preferred method. Alternatively, tracheal aspiration and nonbronchoscopicsamples can also be used to collect respiratory specimens in intubated patients.[19] The COVID-19 can also be identified in saliva of infected patients. 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.[20]Saliva can be obtained with minimal discomfort and adequate safety. Presence of covid-19 in the saliva may be due to:

1) from the upper respiratory tract fluids moving back into the oral cavity
2) from blood
3) from infection of the major and minor salivary glands.

The clearance time of the virus varies per body specimen. For instance, viral RNA was still detectable in urine or stool specimen, while matched saliva throat swabs from the same patient were already negative.[21]Salivary diagnostic tests are economical, noninvasive, healthier to apply than serum sampling, produces results well in time, does not require specialized healthcare workers, multiple samples can be obtained effortlessly,testing is doable at home, minimum risk of cross-infection, better shipping and storage than serum sampling, lesser agitation during the diagnostic process, screening assays are commercially available, and saliva doesn't clot and can be handled easily.[22] Studies showed that the positive rate of SARS-CoV2 was 91.7% in the patients' self-collected saliva by using RTqPCR, therefore, it can be concluded that saliva is a promising non-invasive specimen for the diagnosis, monitoring, and infection control of patients with SARS-CoV-2 infection.[23]

B. RT-PCR: Most patients of the patients are RT-PCR positive at the first time of testing of either throat swab or sputum samples and its results become positive after several days (2-8 days). Patients having symptoms of covid-19 coupled with recent exposure to COVID-19 infection should be diagnosed with typical chest computerized tomography (CT), despite negative RT-PCR-results.[18] RT-qPCR tests may create certain biological safety hazards because of the retention and operation of patient samples, cumbersome nucleic acid detection operations, and long waiting time for results.

C. CT IMAGING: CT findings show bilateral pulmonary parenchymal ground-glass along with consolidative pulmonary opacities, sometimes with a rounded morphology and peripheral lung distribution in patients with covid-19.[8]Consolidationdefined as highdensity patchy opacities, inside which air bronchogram(s) could be observed. Lymphadenopathy defined as a lymph node >1.0 cm in short-axis diameter was observed.[24]When a suspicious patient is negative for RT-qPCR tests, a combination of repeated RT-qPCR tests and chest CT can be done, high-resolution CT (HRCT) for the chest is essential for early diagnosis and evaluation of disease severity of patients with SARS-CoV-2.CT scans, however, are unable to distinguish from other viral pneumonia.[23]

D. LAB TEST: A decrease in peripheral T cell subsets is a unique feature in patients affected by covid-19 and in patients who have recovered, a rapid restoration of peripheral T cell subsets can

be seen, thus, peripheral T cell number can serve as an accurate diagnostic tool for SARS.[1]

E. UPPER RESPIRATORY TRACT SECRETIONS: In intubated patients with negative upper respiratory tract samples, bronchoscopy can be performed. SARS-CoV-2 RNA has been extracted from both upper and lower respiratory tract specimens.

In one study it was found that the levels of SARS-CoV-2 RNA were higher in samples collected from the upper respiratory tract and in the first 3 days after symptom onset, and high levels of SARS-CoV-2 RNA were also found in samples of asymptomatic patient. The specificity of the RT-PCR test seems to be very high, but sometimes, due to swab contamination, there can be seen false positive results. A single negative test can't state that the person is free of covid-19 infection, especially if there exposure to the virus is high.And in such cases, it may be advisable to repeat the test or collect a deeper respiratory tract sample, such as BAL.[19]

F. CRP LEVELS: CRP level of 1.1 mg/dL can be seen in patients with normal percentage of oxygen saturation (SatO2) and of 6.6 mg/dL in hypoxaemic patients.[19]

G. IgM and IgG: The use of IgM and IgG over nucleic acid detection is highly recommended. Likewise, the decrease in WBC and lymphocyte count can also seen in covid-19 affected patients. To identify the infection, a comprehensive diagnosis must be made using distribution pattern, quantity and range, density, shape, interface, internal features of the lesion and adjacent structural changes, CT staging, quantitative CT, and artificial intelligence (AI).Analyzing the CT images by AI using deep learning helps reduce the uncertainty in the confirmation of the positive new cases. Another reliable method is deep learning which was proposed based on the CT diagnosis system to detect patients with COVID-19 with the use of radiograph imaging.[25] Artificial intelligence, including deep learning, is an emerging computer technology that can automatically recognize images withaccuracy. It may have the potential to help interpret medical images and enable such examinations. [26]

PROTECTION AGAINST COVID-19

Dentists must be aware of the methods that can be used for prevention of covd-19 and must reduce the number of patients in the out patient department by providing more telephone consultations. Since COVID-19 stays contagious from 2 hours to as long as 9 days at room temperature and continues well at 50% correlating with the 30% relative humidity. So, the perseverance of COVID-19 could be decreased in the dental setup by maintaining a dry and clean environment. Effective contamination control approaches are required to avoid the spread of COVID-19 via these contact practices.[26] Patients must be asked for any symptoms of covid-19 before giving them appointment at the clinic this can be done via phone calls. Once the patient is confirmed to be free of covid-19, the treatment should then be started and hand hygiene must also be practiced by the dentists, ie:washing hands before and after patient treatment to avoid cross-infection.[34] After the completion of the treatment proper waste disposal must be followed in waste bags, coded in a double-layer yellow-colored waste bag.[17] Some of the suggested methods of protection are as follows:

1. **PREOPERATIVE MOUTHWASHES:** All the patients must be offered rinses with preoperative mouthwash containing oxidative agents, such as 1–1.5% hydrogen peroxide or 0.2% povidione iodine, and antiseptic mouth rinses, e.g., Chlorhexidine (0.2%) and Listerineexhibit viricide properties. Flavonoids and β-Cyclodextrin-Citrox compounds can also be effective. However, it is not yet clear how long the antiviral effect of mouthwashes may last because of the constant production of saliva in the mouth.[14] The treatment should be done using rubber dams to avoid splashing of fluids from patient's mouth.
2. **DISINFECTANT**: Disinfectants are chemical agents that are used to inactivate or destroy microorganisms and SARS-CoV-2 is susceptible to a wide variety of disinfectants like lipid solvents, including ethanol (> 75%), formaldehyde (> 0.7%), isopropanol (> 70%), povidone-iodine (> 0.23%), sodium hypochlorite (> 0.21%), or hydrogen peroxide (H2O2; > 0.5%). Disinfectants are specifically formulated to inactivate or destroy microorganisms and maybe classified as detergents, acids, oxidizing agents, alcohols, alkalis, aldehydes, biguanides, halogens, phenols, and quaternary ammonium compounds. Their mechanism of action may vary,the majority of them target the outer lipid layer of coronaviruses (CoVs) and inactivate the viral particles. Alcohol causes damage to microorganisms by denaturing proteins, leading to membrane damage and cell lysis.[27] Hand disinfection agents of limited antiviral activity are also effective. Disinfectants containing ethanol (78%–95%), iodopovidone solution (0.23%–7.5%) inactivates high-concentration coronavirus within 30 s to 1 min.[14]Coronavirus could be effectively eliminated in 1 minute when the surfaces were disinfected with 62%−71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite.[28] After the working day or lunch hours, clinical area must be disinfected through irradiation using an ultraviolet lamp for 30–60 min, and the windows must be kept open for 30 min and also the floor should be disinfected

using 500–1,000 mg/L chlorine concentration and then kept dry for every 2 hr.

3. **MASKS:**

a. **Cloth Mask:** In the general public, masks made of cloth are also used to prevent the transmission of COVID19 disease, although this material is less effective to protect against aerosol transmission. they are not recommendable for health workers, especially in high-risk situations.

b. **Surgical Mask:** has been proven to be able to stop transmission of influenza by preventing the spread of infectious droplets from an infected person to healthy people in the surrounding. Surgical masks are less effective at filtering SARSCoV-2 infection during coughing by infected patients, because the size and concentration of this virus in aerosols, that are generated during coughing is unknown. People recommended to use surgical masks include health workers, laboratory workers, people with respiratory symptoms, caregivers for COVID-19 positive patients at home and hospital cleaners.

c. **N95masks:** Health workers who provide services prone to aerosol transmission, are advised to use a respirator mask, such as an N95. This mask prevents users from inhaling small airborne particles and its design allows it to fit snugly on the face.[30]

Masks were found to be an effective measure to prevent infection. N95 respirators significantly reduced bacterial colonization in hospitals. Studies demonstrate that tightly sealed surgical mask blocks 94.5% of total virus whereas a tightly sealed respirator blocked 5 of 15 99.8%. However, a poorly fitted respirator blocks only 64.5%. Masks should be changed after the completion of treatment, before treating the next patient or when the masks become considerably wet.

4. **PPE:** Dental care providers should adhere to standard personal protective equipment (PPE) to protect their skin and mucous membrane from exposure to infectious organisms and materials.PPE kit includedisposable waterproof scrubs and bonnets, gloves, eyewear protection, face shields, disposable shoe-covers and masks. Surgical masks capture bodily fluids leaving the wearerthus protecting the patient from the risk of contamination by healthcare personnel. After every procedure, dental care providers should remove PPE in sequence according to CDC guidelines and perform hand hygiene throughout the process.

5. **FFP:** N95 respirator was proposed to be reused in case of shortage of PPE kits with multiple removals between patients. Face shields provide about 96% prevention immediately after exposure to influenza-laden cough aerosol and goggles may provide increased eye protection.

FFP masks are designed to protect the wearer and are divided into the following different categories based on their filtration efficiency towards powders ≥0.3 mm in diameter: FFP1 (80% minimal total filtration efficiency); FFP2 (94% minimal total filtration efficiency); and FFP3 (99% minimal total filtration efficiency). The most efficient masks are presumed to be FFP2/N95, FFP3/N99 and N100. In dental procedures, the mask should be considered as disposable and the mean surgical period does not exceed 2 hours; therefore, it is suggested to use a mask with the highest filtration efficacy without a valve, or a valved mask covered by a surgical mask.[28]

6. **EYEWEAR:** Eyewear with enveloping frames should be used, and should have wide lenses to cover the face as much as possible. As a general rule, patients affected by COVID-19 with a body temperature of >37.5°C (99.5°F) cannot be treated in a dental clinic, and should be confined to their home or hospitalised if they exhibit severe symptoms.

7. **VENTILATION:** COVID-19 inpatient wards are expected to have adequate ventilation strategies than general hospital wards. When patients are coughing or sneezing, the droplets containing pathogens can be sprayed as air jets with velocities greater than 11 m/s. These pathogens can spread in the air and deposit on the surface of nursing equipment or on the floor close to the entrance door, creating hazardous working environment for the working doctors and nurses. Therefore, ventilation strategy as a determinant controlling contaminant flow paths has been recommended. Compared to general hospital wards, COVID-19 inpatient wards have their special requirements of ventilation system like a negative pressure in an isolation room. The minimum air change should be over 12 per hour.It has been recommended that an hourly average ventilation rate of 160 l/s/patient for airborne precaution rooms should be there.Some suggested the use of negative pressure isolation rooms for dental emergency care for patients infected with covid-19 and aerosol-generating procedures. Coronavirus can be effectively inactivated by UVC disinfection.Minimizing the patient inflow in a dental clinic and social distancing in waiting areas should be done.

8. **ANTIRETRACTION:** High speed handpieces should be used because they can effectively reduce the return of bacteria and viruses.An adequate air change after each dental procedure by opening the windows in surgical rooms and in the waiting room is suggested.[28] Aerosols containing viral particles could be transmitted through the eyes and goggles or face shields may help decrease the risk of the infections.[19]

CONCLUSION

Looking at the current scenario where a number of outbreak of viruses is seen it can be said that a thorough understanding of the various viruses especially coronavirus is of utmost importance so that in coming future further outbreak can be stopped and it would be beneficial for the mankind. Thisarticle aims at exploring the various aspects of the coronavirus and further study needs to be done in this regard in future.

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