Review Article

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Protocols for dentist during Covid-19 Pandemic.

ABSTRACT

A novel coronavirus (COVID-19) 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 across the globe. COVID-19 declared as pandemic in Feb 2020'. COVID-19 was different from SARS-CoV, but shared the same host receptor the human angiotensin-converting enzyme 2 (ACE2). It has been documented that ACE2 is the main host cell receptor of COVID-19 virus and plays a crucial role in the entry of virus into the cell to cause the fatal infection. Interestingly, it has been found that ACE2 receptor are highly enriched in epithelial cells of tongue and saliva can act as a diagnostic marker for detecting virus. Dental personnel are expose to tremendous risk of COVID-19 infection due to face-to-face communication and the exposure to saliva, blood, and other body fluids etc. Dental professionals plays great roles in preventing the transmission of COVID-19.

Keywords: PANDEMIC, COVID-19, ACE2,SALIVA, PPE, CORONAVIRUS

Introduction:

In late December 19' increase number of patients were reported with pneumonia of unknown cause in Wuhan, Hubei province china, that has attracted attention of concern not only in China but across the globe.[1] The disease outbreak- started from the local sea food market. On December 31, 2019, the Chinese Center for Disease Control and Prevention investigated the unknown cause of disease at early stage of outbreak in Hubei Province, Wuhan City China and number of possible etiological agents were ruled out, including severe acute respiratory syndrome coronavirus (SARS-CoV), middle east respiratory syndrome coronavirus (MERS-CoV), avian influenza virus etc.[1,2] Finally a new corona virus temporally named as 2019-nCoV was identified to be the pathogen responsible for disease by WHO on 12th Jan 2020'. COVID-19 is the 7th member of the family coronavirus that is known to infect humans. On 11thFeb 2020 the new disease was named as Corona Virus Disease 19 (COVID-19) and the virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by World Health Organization (WHO).[2,3]

Since, the first human coronavirus detected in 1960'. SARS-CoV first emerged in 2002–2003 in Guangdong, China as an atypical pneumonia marked by fever, headache and subsequent onset of respiratory symptoms such as cough and pneumonia, which may later develop into life-threatening respiratory failure and acute respiratory distress syndrome.

On 11th March 2020', WHO declared Novel Coronavirus Disease (COVID-19) outbreak as a pandemic and reiterated

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the call for countries to take immediate actions and scale up response to treat, detect and reduce transmission to save people's lives.[3] Since then, from Jan 23' 2020 to April 3'2020 it counterpane across the globe with number of confirmed cases 1,056,159, death reported 57,206 in 208 countries, areas, or territories with cases with highest number of confirmed COVID-19 cases in USA, Italy and Spain.

The COVID-19 was recently identified in saliva of infected patients. Saliva can have a vital role in the human-to-human transmission. It can act as a non-invasive salivary diagnostic and a convenient cost-effective point-of-care platform for the fast and early detection of COVID-19 infection.[4,5]

History:

Coronaviridae family encompasses a broad spectrum of animal and human viruses. They all are characterized by a distinctive morphology. Virions are enveloped and spherical (coronaviruses), or disc, kidney, or rod shaped (toroviruses). Each particle is surrounded by a fringe or "corona" representing the bulbous distal ends of embedded envelope glycoproteins.[5]

Coronaviruses have the largest positive-sense RNA genome. Coronaviruses are enveloped RNA viruses that are distributed broadly among humans, mammals, and birds and can cause respiratory, enteric, hepatic, and neurologic diseases.[1,6]

Classification:

RNA virus consists of three members i.e., Nidovirales, Ateriviridae, Roniviridae. In which Nidovirales further have coronaviridae in family which consist of two subfamilies namely Corovirinae and torovirinae in which Coronavirinae further consists of:[6]

Alphacoronavirus- contains the human virus HCoV-229E, HCoV-NL63 and many animal viruses.

Betacoronavirus- It includes the prototype mouse hepatitis virus (MHV) and the three-human virus- HCoV-OC43, SARS-HCoV, and HCoV-HKU1, SARS-related coronavirus, Middle Eastern respiratory syndrome (MERS) coronavirus.

Gammacoronavirus- It contains viruses of cetaceans (whales) and birds.

Deltacoronavirus- It contains viruses isolated from pigs and birds.

SARS-CoV and MERS-CoV belong to the β-CoV. COVID-19 also belongs to the β-CoV according to the phylogenetic analysis based on the viral genome. Although the nucleotide sequence similarity is less than 80% between COVID-19 and SARS-CoV or MERS-CoV, it can also cause the fetal infection and spread more faster than the two other coronaviruses. The genome nucleotide sequence identity between a coronavirus (BatCoV RaTG13) detected in the bat Rhinolophus. 96.2%, chances are that the COVID-19 virus, natural host may be Rhinolophus affinis bat. However, the differences may also suggest that there might be more intermediate hosts between the bat and human.[7,8]

In severe cases, these four human coronaviruses (HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoV-HKU1 can cause life-threatening pneumonia and bronchiolitis especially in elderly, children and immunocompromised patients. Besides respiratory illnesses, they may also cause enteric neurological disease.[4,1,8] Coronaviruses had caused two large scale pandemics in past two decades SARS & MERS.

Pathogenicity & Symptoms:

Coronavirus enter the respiratory tract, where they replicate in the epithelial cells of the upper respiratory tract. Innate and specific immune response (e.g. cytokine dysregulation), and viral factors play a major role in the pathogenesis. Enveloped viruses retain infectivity in the presence of bile and proteolytic enzymes present in the enteric tract. During acute infection shedding of virus occurs from respiratory tract, and virus may continue to shed for some time after gastrointestinal tract recovery.[1]

Typical clinical symptoms present with fever, dry cough, dyspnea (breathing difficulties), headache, chest tightness, myalgia, pain and lymphopenia with elevated level of c-reactive protein, aspartate aminotransferase, lactic dehydrogenase and creatine kinase were observed. In addition, some patients might suffer from headache, dizziness, abdominal pain, diarrhea, nausea, and vomiting. In the first stage onset of the disease is associated with diffuse alveolar damage detected by transverse chest computerized-tomography images, with bilateral infiltrates, segmented or lobular opacities and pleural effusions. In asthmatic patient, it may worsen and even can cause death. In the second stage, organization occurs. Where further, virus replicates in enterocytes, resulting in diarrhea, and is shed in the stool, as well as urine, and possibly by other body fluids macrophage

and T-cell infiltration. In infants, the infection can be more severe, causing tracheolaryngobronchitis (croup), bronchitis and pneumonia.[9,1] We et al. 2020' reported that mostly middle aged (>30 years). Elderly get infected with symptomatic infection whereas, in children it appears to be uncommon, and when it occurs, it is usually seen to be mild with better prognosis.

Diagnostic Modality:

Firstly, SARS-CoV-2 RNA is detected by real time reverse transcriptase polymerase chain reaction (RT-PCR). Results are generally available within a few hours to 2 days. A single positive test should be confirmed by a second RT-PCR assay targeting a different SARS-CoV-2 gene. If initial testing is negative but the suspicion for COVID-19 remains, the WHO recommends re-sampling and testing from multiple respiratory tract sites.[10]

Secondly, COVID-19 rapid test qualitatively detects IgG and IgM antibodies to SARS-CoV-2 in human whole blood, serum and plasma samples. This test applies lateral flow immuno-chromatography and is a tool to assist the diagnosis of SARS-CoV-2 infections. The IgM-IgG combined assay has better utility and sensitivity compared with a single IgM or IgG test. It can be used for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic, in hospitals, clinics, and test laboratories.[10,11]

Role of Angiotensin-converting Enzyme 2

Coronavirus infection in humans present with mild severity but in 2002-2003 and in 2012 SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV) caused fatal severity. Samples were investigated from pangolins, and found that genome sequence similarity between pangolin and COVID-19 ~99% which indicates that pangolin may be the intermediate host between the disease.

Lu et al. 2020' found that 2019-nCoV was closer to bat-SL-CoVZC45 and bat-SLCoVZXC21 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).[12]

COVID-19 present with the “spike protein” like structure in the enveloped membrane, and also expresses other polyproteins, nucleoproteins, and membrane proteins i.e. RNA polymerase, 3-chymotrypsin-like protease, papain-like protease, helicase, glycoprotein, and accessory proteins. The characteristics feature of COVID-19 is still unknown. The S protein from coronavirus binds to the receptors of the host to facilitate viral entry into target cells. COVID-19 has the ability to bind with the human angiotensin converting enzyme 2 (ACE2). The ACE2 receptor from the cells are mainly found in beta coronavirus. It is known that the population with higher expression of ACE2 might be more susceptible to COVID-19 infection.[13,15,16]

Zhou et al.2020' in a study 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-NL637. He has also proved that 2019-nCoV does not use other coronavirus receptors, aminopeptidase N, and dipeptidyl peptidase 4.[14,15]

The study of Xu et al. 2020' found that the RBD domain of the 2019-nCoV S-protein supports strong interaction with human ACE2 molecules.[17]

These findings suggest that ACE2 plays a potent role in cellular entry, thus ACE2 expressing cells may act as a target cell and potential infection routes for COVID-19 infection.

As coronavirus has been identified in infected patients saliva , this pandemic is a reminder that dental and health care professionals must be diligent in protecting against the spread of infectious disease, as it provides a chance to determine a non-invasive saliva to act as a diagnostic aid for COVID-19 virus.

Transmission Routes:

Transmission routes of coronavirus include direct transmission while a person is coughing, sneezing or talking. Droplets typically travel ~ 6 feet (about two meters).Studies have shown that respiratory tract infection viruses can be transmitted direct or indirectly in the form of small droplets from one person to another. COVID-19 cases of Germany indicate that transmission of virus may occur via contact with asymptomatic individuals.[2,16]

COVID-19 virus can use ACE2 as a receptor to invade cells, which may promote human-to-human transmission. Through the developed scRNA-Seq (single-cell RNA sequencing) researchers analyzed the ACE2 RNA expression profile single-cell resolution and identified high ACE2 expression in type II alveolar cells (AT2) of lung, esophagus upper,

stratified epithelial cells, absorptive enterocytes from ileum and colon, cholangiocytes, myocardial cells, kidney proximal tubule cells, and bladder urothelial cells. The organs which are at high risk of ACE2 expression are at high risk to develop COVID-19 infection. Investigating the potential routes of COVID-19 infection in oral cavity it has been found that ACE2 can be expressed in oral cavity and is highly enriched in epithelial cells.[2] XU et al. 2020' in study reported that among different oral sites, ACE2 expression was found to be higher in tongue than in buccal and gingival tissues.

This indicates that dental patients and personnel are more likely to be exposed to pathogenic microorganism i.e. bacteria and viruses that infects the oral cavity and respiratory tract. Dental settings incessantly carry the risk of COVID-19 infection due to the specificity of its procedures.

Risk Involved in Dental Care Settings:

1. Risk for Nosocomial Infection:

As COVID-19 infection can be transmitted through contact with asymptomatic individuals. Incubation period for individuals infected with COVID-19 infection were reported to be 1-14 days. It was confirmed that those without symptoms can even spread the virus. Certain studies have revealed that live viruses were present in the saliva of infected individuals by viral culture method. This indicates diagnosis of COVID-19 can be performed using salivary diagnostic platforms. Some virus strains have been detected in saliva as long as 29 days after infection. A non-invasive platform to differentiate the biomarkers using saliva could enhance disease detection. Samples can be collected in patients who is present with oropharyngeal secretions as a symptom.[2,5,18]

Pathogenic micro-organisms can be transmitted in dental settings through inhalation of airborne particle because of aerosols or splatter produced during dental procedures of patients which remain suspended in air (particles <5µm in diameter) can remain in the air for long periods or through, direct contact with blood and oral fluids of other patients materials contact with conjunctiva, nose, or oral mucosa, indirect contact with contaminated instruments/ environmental surfaces can also be harmful to dental personnel. Therefore, it is important for dentists to amend preventive strategies to avoid the COVID-19 infection by focusing on personal protective equipment PPE, sterilization & hand hygiene. Effective infection control strategies are needed to prevent the spread of COVID-19 infection through following contact routines.[2]

The nasopharyngeal and oropharyngeal collection promotes discomfort and may promote bleeding in patients with thrombocytopenia.

There are three different pathways for COVID-19 infection to be present in saliva-

Firstly, coronavirus infection in the lower and upper respiratory tract that enters the oral cavity together with the liquid droplets frequently exchanged by these organs.

Secondly, coronavirus infection present in the blood can access the oral cavity through crevicular fluid, an oral cavity-specific exudate that contains proteins derived from extracellular matrix and serum-derived proteins.

Thirdly, coronavirus infection can occur in the oral cavity by major and minor salivary gland infection, with subsequent release of particles in saliva through salivary ducts.

Lu et in 2010' reported that the production of SARS-CoV-specific secretory immunoglobulin A (sIgA) in the saliva of intranasally immunized animal models. It is essential to point out that salivary gland epithelial cells can be infected by SARS-CoV for a short time after infection in rhesus macaques, suggesting that salivary gland cells play a pivotal role in source of this virus in saliva. Considering the similarity of both strains, it is speculated that salivary diagnosis of COVID-19 could also be performed using specific antibodies to this virus.[18]

2. Contact Spread:

As we know transmission of respiratory infection can be done through droplets: when the droplet particles are >5-10µm in diameter they are referred to as respiratory droplets, and when they are <5µm in diameter, they are referred to as droplet nuclei. According to current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and through contact route.[18,2]

Transmission may also occur through fomites in the immediate environment around the infected person. Therefore, transmission of the COVID-19 virus can occur 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., stethoscope, metal, glass, plastic, mouth mirror, probe, tweezer etc.). Therefore, contaminated

surfaces in healthcare setting are potential source for coronavirus infection. Thus, keeping a clean and dry environment in the dental office would help decrease the persistence of coronavirus infection.

3. Personal Protective Meausure for Dental Care Personnel:

Personal protective equipment i.e. gloves, mask, face shield, particulate respirator, grade N95 or higher, protective goggle ,alcohol based hand sanitizer (the CDC recommend use an alcohol based hand sanitizer (CDC recommends 60% alcohol based sanitizer), sanitize your phone (using antibacterial wipes or alcohol swabs (with 70% alcohol) and other items, including computer keyboard and mouse, house and car keys, re-usable water bottles, car keys, re-usable water bottles, car steering wheel, clothing pockets, door handles, and keep your immune system healthy.[19]

4. Infection Control Protocols:

Hand hygiene has been considered the most critical measure for reducing the risk of transmitting microorganism from one person to other (Larson et al. 2000). It has been shown that at room temperature human coronavirus infection last from 2 hour up to 9 days, and persists better at 50% compared with 30% relative humidity. This reinforces the need of good hand hygiene and thorough disinfection of all surfaces in dental care setting, use of personal protective equipment is recommended to protect skin and mucosa from (potentially) infected blood or oral fluids. A two-before and three after hand hygiene guideline is proposed by the infection control department of the West China Hospital of Stomatology, Sichuan University, to reinforce the compliance of hand washing. Hand washing technique: before touching a patient, before any clean or aseptic procedure, after body fluid exposure risk, after touching a patient, and after touching a patient's surroundings, including contaminated items or surfaces. More caution should be taken by dental professionals to avoid touching their own eyes, mouth, and nose.[19,20]

Patient Management and Prevention:

On March 16, 2020', the American Dental Association recommended that dentists postpone elective procedures for the next three weeks and instead only provide treatment for dental emergencies.[20,21]

1. Tele-counselling and Triage:

Initial screening can be done through telephone to identify the patient with suspected or possible COVID-19 infection. It can be performed at the time of scheduling appointments. The two most important questions for initial screening should include any travel history to COVID-19 affected areas and the presence of any febrile respiratory illness symptoms such as fever and cough. If patient response is positive then elective dental care should be deferred for at least two weeks. Patients should be encouraged/instructed to be in self quarantine for at least 14 days particularly if they have been to areas considered at risk for infections and inform to the infection control department at the time.

2. Patient Evaluation:

Patients should advice to complete a detailed medical history form upon arrival at dental care setting, COVID-19 screening questionnaire and assessment of a true emergency questionnaire.

The body temperature of the patient should be measured by a contact-free forehead thermometer or with cameras having infrared thermal sensors. Patients who present with fever (>100.4°F = 38°C) and/or respiratory disease symptoms, should have elective dental care deferred for at least 2-3 weeks (As per the Centers for Disease Control and Prevention (CDC) guidelines).

In an emergency cases if patients reports with severe tooth pain and/or swelling, pharmacological management in the form of antibiotics and/or analgesics should be prescribed. Patients with suspected COVID-19 infection should be seated in a separate, well-ventilated waiting area at least 6 feet from the unaffected patients seeking care.

3. Emergency Treatment Management:

In emergency condition such as dentoalveolar trauma or progressive fascial space infection uncontrolled bleeding, cellulitis or a diffuse soft tissue bacterial infection with intra-oral or extra-oral swelling, severe dental pain, pericoronitis, surgical post-operative osteitis, dry socket dressing changes, abscess, tooth fracture resulting in pain or causing soft tissue trauma, dental trauma with

avulsion/luxation, dental treatment required prior to critical medical procedures, final crown/bridge cementation if the temporary restoration is broken or causing gingival irritation, biopsy of abnormal tissue etc. In the unlikely event of providing dental care to suspected or confirmed cases of COVID-19 infection, dentists should be aware of the following recommendations:[21,22]

- Dentists should follow standard, contact, and airborne precautions including the appropriate use of personal protective equipment (PPE) and hand hygiene practices.

- Preoprocedural antimicrobial mouthrinse is believed to reduce the load of oral microbes. Chlorhexidine, is not very effective in killing COVID-19 virus infection as, COVID-19 virus are vulnerable to oxidation. So, the mouthrinse containing oxidative agents such as 1% hydrogen peroxide or 0.2% povidone is recommended.

- Single use disposable devices should be used to prevent further cross-contamination.

- Extraoral imaging such as panoramic radiograph or CBCT should be preferred over intraoral imaging to avoid the gag reflex or cough that may cause contamination.

- Dentist should use rubber dam isolation technique to minimize the production of saliva and blood-contaminated aerosol or spatter, particularly in cases when high-speed handpieces and dental ultrasonic devices are used. Samaranayake et al. 1989' reported in a study that the use of rubber dam could significantly reduce airborne particles in ~3-foot diameter of the operational field by 70%. If rubber dam isolation is not possible manual devices, such as Carisolv and hand scaler, are recommended for caries removal and for periodontal scaling, in order to minimize the generation of aerosol.

- Patients with suspected or confirmed COVID-19 infection should not be treated in routine dental practice chamber, it should be treated in negative pressure treatment room/Airborne infection isolation rooms (AIIRs).

- Hu et al. in study reported that the anti-retraction high-speed dental handpiece can significantly reduce the backflow of oral bacteria and HBV into the tubes of the handpiece and dental unit as compared with the handpiece without anti-retraction function. Therefore, the use of dental handpieces without anti-retraction function should be forbidden during the epidemic period of COVID-19.

- Dental care settings should be disinfected and cleaned in accordance with the Protocol for the Management of Surface Cleaning and Disinfection of Medical Environment (WS/T 512-2016) released by the National Health Commission of the People's Republic of China.

- Medical waste generated by the treatment of patients with suspected or confirmed COVID-19 infection are regarded as infectious medical waste. Double-layer yellow color medical waste package bags and “gooseneck” ligation should be used for discard. The surface of the package bags should be marked and disposed according to the requirement for the management of medical waste

Summary:

The newly discovered coronavirus has caused the outbreak of pneumonia across the globe. COVID-19 enters the host cells through human cell receptor ACE2, but with higher binding affinity. Bae et al in their study reported the rapidly increasing

number of cases and evidence of human-to-human transmission suggested that the virus was more contagious than SARS-CoV and MERS-CoV. According to CDC neurologist around the world noticed that small subset of patient with COVID-19 are developing serious impairment of the brain e.g. confusion, stroke, seizures (altered mental status or encephalopathy with diminished sense of smell and taste). In this outbreak, compared with adult cases, there are relatively fewer cases of children, with milder symptoms and better prognosis. Also, most infected children recover within one to two weeks after the onset of symptoms, and no deaths had been reported. So far the possible reason can be humoral and cellular immune development in children is not fully developed. This may be one of the mechanisms that lead to the absence of severe immune responses after viral infection. Vaccines for COVID-19 Altimmune's intranasal coronavirusvaccine, INO-4800 by Inovio Pharmaceuticals, mRNA-1273 vaccine by Moderna, Avian Corona virus Infectious Bronchitis Virus (IBV) vaccine by MIGAL and many more are still in developing stage.

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