Orthodontics and the COVID-19 Crisis – A Review

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Abstract

The novel coronavirus (COVID-19) pandemic started in Wuhan, China with severe acute respiratory syndrome (SARS) in December,2019. The infected people travelling from China to other countries transmitted this virus. This increased the mortality rate day by day. The transmission routes of this virus include respiratory secretions, droplet infection and direct contact with COVID-19 patients. The articles published until date regarding COVID-19 were reviewed, of which most of them were on the symptoms and progression of disease, the laboratory investigations that are followed in confirming the COVID 19 infection and the measures of safety to be followed. The COVID-19is mainly transmitted from patient to Orthodontist and Orthodontist to patient through aerosol and splatter produced by the dental procedure and saliva of an infected person. To avoid transmission of virus screening tests should be done at dental setups. The use of gloves, face shields, masks, gowns and antiseptic handwash are mandatory for the practioners. The different types of Respirator standard (masks) are studied. As an Orthodontist the emergencies should be planned properly and can use virtual assistance, WhastsApp messenger by sending photos, video call to manage the emergencies accordingly. Aerosol generating Procedures (AGPs) should be avoided by use of alternative orthodontic setting. A thorough review and analysis thus gives an impression that as health care providers, we orthodontists, should take part in this fight against dreadful virus attack, in whatever way we can and become helpful to the government authorities.

Keywords: COVID-19, Aerosol Generating Procedures (AGPs)

1. INTRODUCTION

The sudden pneumonia outbreak COVID (coronavirus disease 2019) caused by SARS-CoV-2.It is a single-stranded RNA virus from the family coronaviridae .This disease has been designated as a pandemic and by the World health Organization (WHO)[1]. This COVID -19 epicenters is meat market of Wuhan city which is in China. From here it spread to entire Wuhan province and other 24 countries.[2,3]. The world health organization declared 30th January 2020 as Public health emergency of global concern on the outbreak of COVID-19 pneumonia .

The patients who suffered from this COVID 19 showed typical symptoms such as fever, cough, fatigue with abnormal chest CT. Sputum production, head ache, hemoptysis and diarrhea[4,5,6] ·were also observed in some cases. The COVID-19 infectious agent is affecting older male patients with critical respiratory diseases[7,8] requiring special attention to older males. This coronavirus (COVID-19) clinical symptoms were different from SARS corona virus seen in 2002-2003. This human-to-human transmission of virus has developed this Coronavirus (COVID-19) outbreak[8,9.]. The new virus genome was sequenced after quick isolation in Chinese Wuhan's laboratories[10]. This infectious agent was finally identified as a novel coronavirus (COVID 19).This is the seventh member of family of corona virus which infects humans[11].The international Committee on Taxonomy of Viruses (ICTV) suggested the name "SARSCOV-2" for the new coronavirus due to the polygenetic and taxonomic analysis[12]. This novel viral pneumonia was finally named as "Corona Virus Disease (COVID 19)" by WHO on 11th February 2020.

CHARACTERISTIC OF COVID 19 VIRUS

A large, single, plus-stranded RNA is a characteristic feature of Coronaviruses family whichbelongs to the family Coronaviridae, and of order Nidovirales[13,14] .α-CoV, β-CoV, γ-CoV, and δ-CoV are the four genera of coronaviruses[15,16]:The human and vertebrates are most commonly infected by the coronavirus disease.The mammals and humans respiratory, gastrointestinal, and central nervous system are infected by α-CoV and β-CoV. While birds are mainly infected by γ-CoV and δ-CoV.

Several members of corona virus often were a cause for mild respiratory disease in humans. SAR-CoV of 2002-03, and the Middle East respiratory syndrome corona virus (MERS-CoV) of 2012 caused fatal severe respiratory diseaseswere explored[17-19]. The MERS-CoV and SARS-CoV belong to the β-CoV[20-21]. In Wuhan the COVID 19 which was studied belonged to the β-CoV. The study is as per the phylogenetic analysis relied on the viral genome[10, 11]. The nucleotide sequence similarity is less than 80% between COVID 19 and SARS-CoV or MERS-CoV. The infection caused by COVID 19 is more fatal and spreads faster than the two other corona viruses[7,9,11,22,23]. The natural host of COVID-19 could be the Rhinolophusaffins bat based on the studies which detected a corona virus (Bat CoV RaTG13) in the bat Rhinolophusaffins of Wuhan Province [11].

COVID-19 possessed typical structure. It has developed "Spike protein" membrane envelope[24]. It showed polyprotiens, nucleo proteins and membrane proteins like RNA polymerase, 3-chymotrypsin-like protese, helicase, glycoprotein, papin-like protease and accessory proteins [10,11,24]. S protein of Corona virus attaches to the receptors of host cells and attack the target cells[25,26].In between COVID 19 and SARS CoV there are four amino acid variations of S protein.COVID 19 binds to human angiotens facilitating conversion of enzyme 2(ACE2).This is also the same host receptor in SARSCoV. COVID 19 binds to ACE2 receptor from cells of human,bat,civet cat and pig.[27-29].

The serum from convalescent SARS-CoV-infected patient and recombinant ACE2-Ig antibody, a SARSCoV-specific human monoclonal antibody, which can neutralize COVID-19, confirmed ACE2 as the host receptor for COVID-19[30-33]. The high affinity between 2019-nCovS protein and ACE2 also suggested that the population that is more susceptible to COVID-19 with higher expression of ACE2[34-35]. Cellular serine protease TMPRSS2 contributes the S-protein priming of COVID-19, indicating that this serine protease might constitute a treatment option[30].

ROUTES OF TRANSMISSION OF COVID-19

In order to take preventive measures a thorough knowledge of the routes of transmission of this infectious virus is necessary. Coronavirus is commonly transmitted directly through (sneeze,droplet inhalation transmission and cough)[36]. Other means of transmission is through contact i.e. contact with nasal ,eye, mucous membranes and oral. Clinical observations of COVID-19 have shown that transmission does not occur through eye or any kind of eye symptoms. However eye exposure transmission route is also suggested from the conjunctival samples taken from confirmed cases of COVID-19. Thus the COVID-19 transmission not limited to respiratory tract, it may also be due to exposure of eye.[37]

Respiratory viruses can be transmitted from person to person either by direct or indirect contact, or through coarse or small droplets as per the detailed studies. COVID-19 is also transmitted though saliva directly or indirectly[38].Reported case in Germany shows that the viruses are transmitted through contact with asymptomatic patients[39]. COVID-19 may be airborne as per the studies revealed/suggested through aerosols produced during medical procedures[40]. The reverse transcription polymerase chain reaction is used to detect COVID-19 by taking 7th day stool sample[41]in patients. The other transmission routes such as aerosol transmission route, fecal-oral transmission route, and water transmission route are of today's public concern. The need for further study is required on these fields.

ROUTES OF TRANSMISSION OF COVID-19 IN DENTAL CLINICS

Dental doctors, staff and patients are prone to pathogenic microorganisms. Bacteria and Viruses that attack and infect the oral cavity and respiratory tract .Dental procedures involve the high risk of COVID-19 infection chances due to specificity of dental procedure .It involves close contact with patients during dental procedure and during communication. They are exposed to saliva, blood and other body fluids apart from dental sharp instruments .The infected COVID-19 dental patient may leave the pathogenic microorganisms/viruses while coughing .The airborne microorganisms/viruses that remain suspended in air for long time can be transmitted through inhalation by the dentists[42]. Transmission may be also due to direct contact with oral fluids, blood or also patient materials[43]. Non use of mask, indirect contact with contaminated instruments, and/or environmental surfaces may also lead for transmission [44,45].

Contact of conjunctival, oral mucosa, or nasal with droplets and aerosols containing microorganisms generated from an infected individual and propelled a short distance by coughing. Transmission is also due to talking without a mask[44,45], and indirect contact with contaminated instruments and/or environmental surfaces[46.] Infected individual will spread/transmit infections in above conditions. our concern is during the outbreak of COVID-19. (Fig.1).

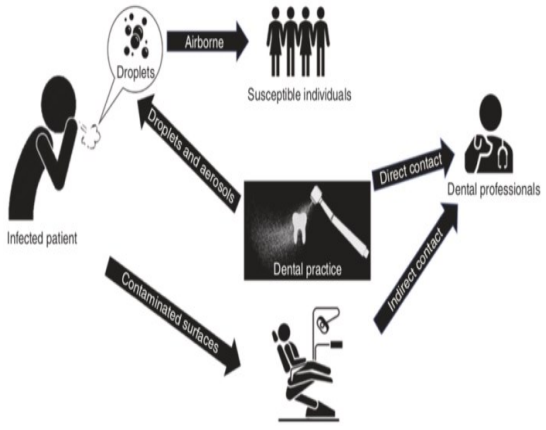

Figure 1. Illustration of routes of transmission COVID-19 in dental clinics and hospital. (Transmission routes of COVID-19 and controls in dental practice Peng et al.)

SIGNS / SYMPTOMS OF COVID-19

A person infected with COVID 19 will manifest lower respiratory tract illness, for example, dry cough (in 67-82% cases), shortness of breath that is dyspnea (in 38%), fever (in 83-99% of cases), kidney failure and eventually death.[47,48,49] Other features which are less common are headache, nausea, vomiting, diarrhea, nasal congestion and sore throat. An elevation of AST, LDH, D-dimer, and prolonged prothrombin time support the diagnosis of viral infection. Findings of pneumonia through X-rays or CT scans will be seen in all the COVID-19patients.[47]

DIAGNOSIS AND TREATMENT OF COVID-19

The nCoV-19 can be diagnosed with the help of Real-Time Polymerase Chain Reaction (RT-PCR). The suspected person has to be analyzed through RTPCR of upper respiratory (nasal and pharyngeal swabs) or lower respiratory specimens (sputum, bronchoalveolar lavage, tracheal aspirate or broncho-scopic brush biopsy).[50]The specimen of blood and feces may also be utilized for the analysis of COVID 19 through RT-PCR. RT-PCR is the available diagnostic procedure. No serological or immunochromatography technique exist for detection of COVID 19.[50] However, viral profile (Hepatitis etc.), hematological tests and creatine kinase may be performed for suspected or confirmed COVID-19 patients. Imaging techniques may also be helpful in diagnosis of COVID 19[46] Nucleic acid amplification is also utilized to diagnose SARS-CoV through saliva and sputum.[51,] The availability of salivary tests at the dental setup also helps in the diagnosis of any infectious virus[51].

The treatment of COVID 19 is mainly supportive with use of hydroxychloroquine and azithromycin, as option for these patients. However, some antiviral drugs like oseltamivir that were used for treatment of the initial cases showed no beneficial effects againstCOVID 19. In China, the drugs most commonly used to treat Human Immune Deficiency Virus, for example, ritonavirboostedlopinavir, are going to be assessed for COVID-19 infection. It is also planned to use remdisivir as a treatment option against COVID 19, as it has shown high efficacy

against MERS-CoV and SARS-CoV in the past. The WHO and CDC do not recommend the use of corticosteroids in the treatment of this COVID 19 infection. Vaccine for the control of COVID 19 is also under investigation.[46]

The algorithm followed in COVID 19 infected patients is given in the (Figure 2)

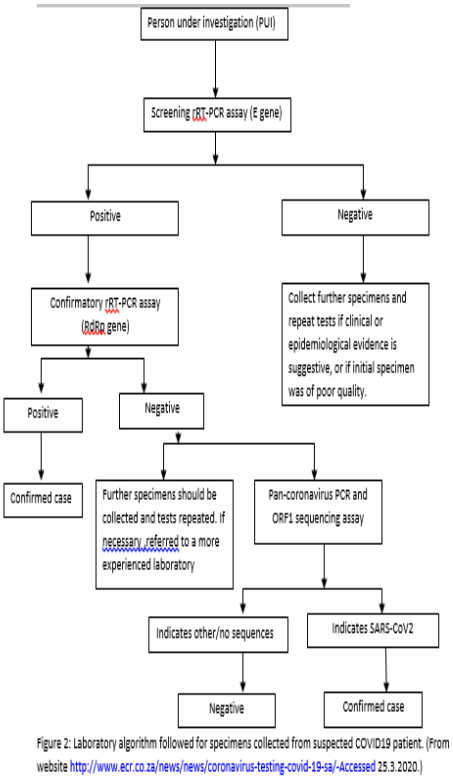

Figure 2: Laboratory algorithm followed for specimens collected from suspected COVID19 patient. (From website http://www.ecr.co.za/news/news/coronavirus-testing-covid-19-sa/-Accessed 25.3.2020.)

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AEROSOL GENERATING PROCEDURES (AGP) AND SPLATTER IN DENTISTRY

These procedures are as any patient or medical care procedure that result in production of airborne particles. The first one to use these terms were Micik and colleague, aerosol and splatter at the time when they were working on aerobiology. Aerosol is defined as those particles which have lesser than 50µm diameters. They are small enough to stay in the air before settling down or entering the respiratory tract. Diseases such as Pneumonic plague, influenza, Legionnaire's disease, and Severe Acute Respiratory Syndromes are transmitted through aerosol. The term splatter is defined as those particles that have a diameter greater than 50µm. These particles are larger in size and are unable to stay in the air. Hence there are greater chances of cross infection in dentistry are through aerosol which is airborne and can enter the respiratory tract. Also splatters are a threat to pass infection from patients to the dentist. TB is transmitted through the droplet nuclei produced during coughing or sneezing of an infected individual or from the splatter of the ongoing dental procedure. Thus splatter and droplet nuclei also transmit infectious diseases from patients to dental professionals like measles, herpes, and SARS[52]

ALTERNATIVES TO AGP IN THE ORTHODONTIC SETTING

The procedures that include for an Orthodontist include use of high speed air turbine or slow speed rotary drill, 3 in 1 air/water syringe, and enamel preparation using ultrasonic or air abrasion devices. And these procedures could lead to direct impact on adhesive removal from enamel, and the use of air/water sprays and rotary handpieces for moisture control and cleaning. Also, with the use of High-Volume Suction (HVE) and/or rubber dam to limit aerosol and the bio impact, these procedures are still considered AGP and appropriate PPE should be worn, along with appropriate decontamination protocols in the surgery. High and low volume suction themselves are NOT considered AGP.

Debond: The process of bracket removal is not considered the AGP part of debond**.** The use of a handpiece, (high speed or slow speed, with or without water coolant) ultrasonic scaler or 3 in 1 air/water spray should be avoided. The risk of continuing treatment was for the patients with poor oral hygiene, the consideration could be given to removing the brackets alone and hand trimming the adhesive carefully by the use of: i. band removing pliers, ii. Mitchell's trimmers or hand scalers, iii. adhesive removing pliers. The left over composite on the enamel surface will be lost over time with toothbrushing. There is no more enamel loss when using debanding pliers than with slow speed Tungsten Carbide bur run dry,[53] but take care not to gouge the enamel

surface. Pliers should only be used to remove the adhesive on posterior teeth, not the incisors where a Mitchell's trimmer of hand scaler should be used instead. If there are presence of large restorations on the posterior teeth, then consider placing a cotton wool roll on the occlusal surface before applying any force with the plier.

REPAIR OF BRACKETS MID TREATMENT

As above mentioned, if residual composite can be removed by hand, this may enable a new bracket to be placed (using Non AGP bonding technique - see below). The alternative options would be to place a premolar or molar band using GIC, or to bypass the debonded tooth, using dead coil or sleeve on the wire, or using sectional wires mesial to the debonded tooth.

REMOVAL OF FIXED DEVICES MID TREATMENT

The process of the removal of fixed devices such as Bands, TPA Nance arches, Quad helix and RME devices only becomes AGP if a handpiece is used to remove the residual cement. As above, consider adhesive removal using hand instruments.

BONDING

The conventional acid etch bond up protocols are AGP when using polishing/pumice prior to etching and the 3 in1 air syringe to rinse the enamel after etching. Alternative non AGP options are listed, but it should be recognised that bond strength may be compromised: Light cured resin modified GIC, can be used without the need for any pre procedural tooth preparation (i.e. pumicing/etching washing/ drying). With these materials there is no need for a dry field and indeed for successful bonding the enamel surface should remain moist during bonding. [54]

Self etch primers (SEP) can also be used without the need for etching washing and drying the enamel, but they require the pellicle to be removed prior to use, usually with a pre procedural enamel preparation such as pumice/polishing of teeth, which would be an unwanted AGP.[55]

BANDS

Avoid the use of 3 in 1 due to the AGP hazard, but suction may be used. The use of GIC or resin modified GIC doesn't not require a completely dry field on either the tooth or band prior to placement.

FITTING AND TRIMMING THE ACRYLIC ON REMOVABLE APPLIANCES

We should keep in mind that removable appliances may act as a conduit for cross infection, and laboratory protocols should be adhered to in order to minimize this risk. The new appliances cannot be assumed to be infection free[56], strict adherence to laboratory infection control procedures including processing of impressions, equipment and appliances is crucial in minimizing the risk of any cross infection. Simple fitting and adjustment of a removable appliance is not likely to be an AGP provided no acrylic trimming is required during fitting i.e. after try-in.

In the case of appliances already being worn by the patient that require repair and refitting, they should be decontaminated according to HTM01-05[57] protocol and current PHE cross infection guidance , using an appropriate disinfectant before ideally being transferred to the laboratory for repair, where superior high volume suction can be used to minimize the impact of any aerosol generated.[58]

For removable appliance acrylic trimming would be undertaken at the chairside in the clinical setting, either as part of the fitting procedure for a new appliance, or following the repair of a worn appliance. There is currently a paucity of evidence in the literature on the microbial load on a worn or tried in orthodontic appliance made from acrylic following disinfection, and no evidence that any aerosol generated during trimming is therefore not a biohazard risk. Acrylic trimming of a new but tried in appliance or currently worn appliance in the surgery should therefore be considered as an aerosol generating procedure.

REPAIR OF FIXED RETAINERS

Adhesive removal from the retainer wire can be achieved using Weingart or Birdbeak pliers, and HVE (High Volume Evacuation/Suction). Removal of adhesivel from the lingual surface of the incisors may be achieved using hand scalers or Mitchell's trimmers, or the use of adhesive removal pliers.

ALIGNER ATTACHMENTS

Placement of the aligner attachments can be considered non-AGP if placed using bonding technique as suggested above. Removal of attachments will be non-AGP if using adhesive removal tool as suggested and will only be considered AGP if a handpiece is used to remove the residual composite.

TAKING IMPRESSIONS

The process of taking impression in itself is not an AGP, but carries a risk of gag or cough reflex which is a known aerosol risk. Where accessible, an intra oral scan may be preferable (although this does not eliminate the gag/cough risk). Any impressions should be sterilized [57] in accordance with HTM01-05 protocol [57] to ensure safe transfer to the laboratory for casting and appliance production.

RETENTION PROTOCOL

Consideration should be given to changing the use of a removable retainer regime. This could be made by the remnants of a broken fixed retainer.

MANAGEMENT AND AWARENESS TO MINIMIZE THE RISK OF COVID-19

We should make sure that before going to dental setups, people should have all the related information aboutCOVID 19 . Also should be aware of the cause, signs and symptoms, and safety measures of COVID 19 infection. The necessary seminars and workshops should be arranged for the awareness of general public regarding transmission of COVID 19 and their respective preventive measures. People should be asked to avoid unnecessary visits to crowded areas and the medical health care and dental setups. If only the visit is absolutely necessary, then use of masks should be a must.

USE OF MASK

It is often said mask in our day to day life, when referring to what are technically called respirators. The N95 respirator is standard as part of the advised protective equipment in their COVID-19 FAQ and their SARS guidance (SARS being a similar type of Corona virus) according to the US Center for Disease Control (CDC). Which suggests that use of an N95 or better respirator is acceptable.

Whereas the Europe uses two different standards. The "filtering face piece" score (FFP) comes from EN standard from 149:2001. The EN 143 standard covers P1/P2/P3 ratings. CEN (European Committee for Standardization) maintains both the standards. Below is a table that illustrates the filter capacity of microns by these respirator standards. (Table1).

There have been number of questions regarding the use of respirators against biological agents. Whether or not particulate respirators can filter small particles such as fungal spores (2 to 5 µm), bacteria (0.3 to 10 µm), or viruses (0.02 to 0.3 µm) is the primary question asked.[59] An article by 3M discusses a research showing that all 6 of N95 respirator they tested can efficiently filter lower than 0.1 micron size with approximately 94% efficiency or higher.

Table 1. The comparison of different Respirator standard

Respirator Standard	Filter Capacity removers x% of all particles that are 0.3 microns in diameter or larger)
FPP1 and P1	At least 80%
FPP2 and P2	At least 94%
N95	At least 95%
N99 and FFP3	At least 99%
P3	At least 99.95%
N100	At least 99.97%

Also one should strictly avoid contact with individuals who show signs and symptoms of nCoV19 or flu and cough. After the dental procedure, the patient, as well as the dentist, should wash their hands with antiseptics. If any infected/suspected case has been transferred

from the dental office, the room where the patient was placed should not be used, the room door should remain shut, with windows opened and the air conditioning should be switched off, until it has been cleaned with detergent and disinfectant. If a suspected case spent time in waiting area or toilet facilities, then these are should also be disinfected as soon as possible. The usual PPE equipment and protocols apply when cleaning and disinfecting these areas too.

MANAGEMENT OF ORTHODONTIC EMERGENCY PROTOCOL

Professionals assess whether to stay open or to manage emergencies. One can postpone the appointments based on single Nations guidelines[60].Regarding any discomfort or problems relating to appliances should be strictly followed by the patients .Repeated breakages would prolong the treatment time and would end up in loss of confidence in appliance or operator. It would also decrease the patients' motivation. Inconvenience, distress to patient and parent can be minimized by maintaining the efficiency of appliances, providing timely management[61]. During COVID-19 pandemic guidelines issued by the Government should be strictly followed. The dentists should see such cases which cannot be postponed, such as an abscess or irreversible pulpitis. The urgent cases other than general dentistry problems should be evaluated by Orthodontists based on video call or message with photo[61]. Virtual Assistance: WhatsApp Messanger (Facebook,Inc, Mountain view, Califonia),are instant messaging applications develop from 2009. They quickly spread among users of all ages. They are used for personnel relationships, for entertainment, for study and also as virtual place of contact in group. Orthodontic emergencies should be attended step by step using new technology. Virtual assistance and whatsApp could be used in first step as good tool. Photos, videocalls, whatsApp messages/ calls are used as virtual assistance. Ways of management of different emergencies is explained in the table 2 below [61].

ORTHODONTIC EMERGENCIES

Table 2. Different scenarios of emergencies and ways to resolve them

1. Removable appliances	Functional	If the fit of the appliance is not proper or if it is broken , photo can be sent to the orthodontist and suspend the use.
	Aligners	If broken or lost can get back to previous and ask clinician.Following clinician's indication can remain on current/go with treatment.
	Retainers	If the appliance is lost or broken should ask the dentist to evaluate buying hot customable preforms on e-commerce sites.
2. Fixed appliances	The non-removable appliances. Such as (straight appliance)	-Loose Bracket: Initially send photo to dentist, remove with tweezer eventually. -Poking distal wire: Send a photo, use wax, disinfected nail clipper/hardware cuter can be used to cut. -Poking ligature: Photo can be send to dentist, wax to be used or use eraser of pencil to push it back. -If molar band is surrounded by periodontal abscess: Send photo, symptomatic therapy with FANS/ paracetamol, eventually prescription of antibiotic.

	The non-removable appliances that can be activated by patient. Such as. (Face mask, headgear or lip bumpers, palatal expanders) The non-removable appliances that can be Pre-activated. Such as (Pendulum, Forsus, Distal Jet appliance, transpalatal bar)	- To avoid future emergencies must be suspended a priori. -Picture should be taken every 3-6 weeks, if the patient feels pain or swelling, see as an emergency in dental office and remove the appliance eventually.

CONCLUSION

The COVID-19is transmitted directly by person to person contact and respiratory droplet infection. Dental staffs are at a higher risk for COVID 19 infection as they are exposed to the aerosol and splatter produced during a dental procedure. Hence the use of alternative procedures are to be practiced to avoid risk. And proper management of the Orthodontic emergencies only should be followed by the proper use of virtual assisstance.

The risk of transmission can be reduced by taking some precautions which include the use of antiseptic hand wash, rubber dam isolation, and mouth rinse for patient before dental procedure, gloves, protective eye wears, gowns, and masks and PPE. It is necessary to arrange seminars and awareness programs for the dentist regarding dental practice during this outbreak. Appropriate precautionary measures are important in reducing transmission and further spread of COVID-19 infection.

REFERENCES

1. Zhu. N. Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R. and Niu, P., 2020. A Novel Coronavirus from Patients with Pneumonia in China,2019. New Englandjournal of Medicine.
2. Wang C, Horby P.W, Hayden, F.G. and Gao, G.F.,2020. A Novel Coronavirus Outbreak of Global Health Concern. The Lancet, 395(10223), pp.470-473.
3. Liu, T., Hu, J., Kang, M., Lin, L., Zhong, H., Xiao, J., He, G, Song, T., Huang, Q., Rong, Z. and Deng, A., 2020. Transmission Dynamics of 2019 Novel Coronavirus (2019-nCov).
4. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X. and Cheng, Z., 2020.Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China. The Lancet, 395(10223), pp. 497-506.
5. Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W.H., Ou, C.Q., He, J.X., Liu, L., Shan, H., Lei, C.L., Hui, D.S. and Du, B., 2020. Clinical Characteristics of 2019 Novel Coronavirus Infection in China. MedRxiv.
6. Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z., Xiong, Y. and Zhao, Y., 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. Jama, 323(11), pp.1061-1069.
7. Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y. and Yu, T., 2020. Epidemiological and Clinical Characteristics of 99 Cases of 2019 Novel Coronavirus Pneumonia in Wuhan, China:

a Descriptive Study. The Lancet, 395(10223), pp.507-513.
8. Chan, J.F.W., Yuan, S., Kok, K.H., To, K.K.W., Chu, H., Yang, J., Xing, F., Liu, J., Yip, C.C.Y., Poon, R.W.S. and Tsoi, H.W., 2020. A Familial Cluster of Pneumonia Associated with the 2019 Novel Coronavirus Indicating Person-to-person transmission: A Study of a Family Cluster. The Lancet, 395(10223), pp.514-523.
9. Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., Ren, R., Leung, K.S., Lau, E.H., Wong, J.Y. and Xing, X., 2020. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. New England Journal of Medicine.
10. Wu, F., Zhao, S., Yu, B., Chen, Y.M., Wang, W., Song, Z.G., Hu, Y., Tao, Z.W., Tian, J.H., Pei, Y.Y. and Yuan, M.L., 2020. A New Coronavirus Associated with Human Respiratory Disease in China. Nature, 579(7798), pp.265-269.
11. 11.Zhou, P., Yang, X.L., Wang, X.G., Hu, B., Zhang, L., Zhang, W., Si, H.R., Zhu, Y., Li, B., Huang, C.L. and Chen, H.D., 2020. A Pneumonia Outbreak Associated with a New Coronavirus of Probable Bat Origin. Nature, 579(7798), pp.270-273.
12. Gorbalenya, A.E., 2020. Severe Acute Respiratory Syndrome-Related Coronavirus –The Species and its Viruses, a Statement of the Coronavirus Study Group. BioRxiv.
13. Fehr, A.R. and Perlman, S., 2015. Coronaviruses: An Overview of their Replication and Pathogenesis. In Coronaviruses (pp. 1-23). Humana Press, New York, NY.
14. Gorbalenya, A.E., Enjuanes, L., Ziebuhr, J. and Snijder, E.J., 2006. Nidovirales: Evolving the Largest RNA Virus Genome. Virus Research, 117(1), pp.17-37.
15. Nakagawa, K., Lokugamage, K. G. & Makino, S., 2016. in Advances in Virus Research (ed John Ziebuhr) vol. 96, 165–192 (Academic Press).
16. Fan, Y., Zhao, K., Shi, Z.L. and Zhou, P., 2019. Bat Coronaviruses in China. Viruses, 11(3), p.210.
17. Holmes, K.V., 2003. SARS-Associated Coronavirus. New England Journal of Medicine, 348(20), pp.1948-1951.
18. Falsey, A.R. and Walsh, E.E., 2003. Novel Coronavirus and Severe Acute Respiratory Syndrome. Lancet (London, England), 361(9366), p.1312.
19. Lancet, T., 2013. MERS-CoV: A Global Challenge. Lancet (London, England), 381(9882), p.1960.
20. Al-Tawfiq, J.A., Zumla, A. and Memish, Z.A., 2014. Coronaviruses: Severe Acute Respiratory Syndrome Coronavirus and Middle East Respiratory Syndrome Coronavirus in Travelers. Current Opinion in Infectious Diseases, 27(5), pp.411-417.
21. Song, Z., Xu, Y., Bao, L., Zhang, L., Yu, P., Qu, Y., Zhu, H., Zhao, W., Han, Y. and Qin, C., 2019. From SARS to MERS, Thrusting Coronaviruses into the Spotlight. Viruses, 11(1), p.59.
22. Al-Tawfiq, J.A., Zumla, A. and Memish, Z.A., 2014. Coronaviruses: Severe Acute Respiratory Syndrome Coronavirus and Middle East Respiratory Syndrome Coronavirus in Travelers. Current Opinion in Infectious Diseases, 27(5), pp.411-417.
23. Bai, Y., Nie, X. and Wen, C., 2020. Epidemic Prediction of 2019-nCoV in Hubei Province and Comparison with SARS in Guangdong Province. Available at SSRN 3531427.
24. Li, F., 2016. Structure, Function, and Evolution of Coronavirus Spike Proteins. Annual Review of Virology, 3, pp.237-261.
25. Hantak, M.P., Qing, E., Earnest, J.T. and Gallagher, T., 2019. Tetraspanins: Architects of Viral Entry and Exit Platforms. Journal of Virology, 93(6), pp.e01429-17.
26. Belouzard, S., Millet, J.K., Licitra, B.N. and Whittaker, G.R., 2012. Mechanisms of Coronavirus Cell Entry Mediated by the Viral Spike Protein. Viruses, 4(6), pp.1011-1033.
27. Wan, Y., Shang, J., Graham, R., Baric, R.S. and Li, F., 2020. Receptor Recognition by the Novel Coronavirus from Wuhan: An Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. Journal of virology, 94(7).
28. Chai, X., Hu, L., Zhang, Y., Han, W., Lu, Z., Ke, A., Zhou, J., Shi, G., Fang, N., Fan, J. and Cai, J., 2020. Specific ACE2

Expression in Cholangiocytes may Cause Liver Damage after 2019-nCoV Infection. BioRxiv.
29. Fan, C., Li, K., Ding, Y., Lu, W.L. and Wang, J., 2020. ACE2 Expression in Kidney and Testis may Cause Kidney and Testis Damage after 2019-nCoV Infection. MedRxiv.
30. Hoffmann, M., Kleine-Weber, H., Krüger, N., Mueller, M.A., Drosten, C. and Pöhlmann, S., 2020. The Novel Coronavirus 2019 (2019-nCoV) Uses the SARS-Coronavirus Receptor ACE2 and the Cellular Protease TMPRSS2 for Entry into Target Cells. BioRxiv
31. Huang, Q. and Herrmann, A., 2020. Fast Assessment of Human Receptor-Binding Capability of 2019 Novel Coronavirus (2019-nCoV). BioRxiv.
32. Lei, C., Fu, W., Qian, K., Li, T., Zhang, S., Ding, M. and Hu, S., 2020. Potent Neutralization of 2019 Novel Coronavirus by Recombinant ACE2-Ig. Biorxi.
33. Tian, X., Li, C., Huang, A., Xia, S., Lu, S., Shi, Z., Lu, L., Jiang, S., Yang, Z., Wu, Y. and Ying, T., 2020. Potent Binding of 2019 Novel Coronavirus Spike Protein by a SARS Coronavirus-Specific Human Monoclonal Antibody. Emerging Microbes & Infections, 9(1), pp.382-385.
34. Xu, H., Zhong, L., Deng, J., Peng, J., Dan, H., Zeng, X., Li, T. and Chen, Q., 2020. High Expression of ACE2 Receptor of 2019-nCoV on the Epithelial Cells of Oral Mucosa. International Journal of Oral Science, 12(1), pp.1-5.
35. Guy, J.L., Lambert, D.W., Warner, F.J., Hooper, N.M. and Turner, A.J., 2005. Membrane-Associated Zinc Peptidase Families: Comparing ACE and ACE2. Biochimicaet Biophysica Acta (BBA)-Proteins and Proteomics, 1751(1), pp.2-8.
36. Lu, C.W., Liu, X.F. and Jia, Z.F., 2020. 2019-nCoV Transmission through the Ocular Surface must not be Ignored. Lancet (London, England), 395(10224), p.e39.
37. To, K.K.W., Tsang, O.T.Y., Yip, C.C.Y., Chan, K.H., Wu, T.C., Chan, J.M.C., Leung, W.S., Chik, T.S.H., Choi, C.Y.C., Kandamby, D.H. and Lung, D.C., 2020. Consistent Detection of 2019 novel Coronavirus in Saliva. Clinical Infectious Diseases.
38. Belser, J.A., Rota, P.A. and Tumpey, T.M., 2013. Ocular Tropism of Respiratory Viruses. Microbiol. Mol. Biol. Rev., 77(1), pp.144-156.
39. Bastola, A., Sah, R., Rodriguez-Morales, A.J., Lal, B.K., Jha, R., Ojha, H.C., Shrestha, B., Chu, D.K., Poon, L.L., Costello, A. and Morita, K., 2020. The First 2019 Novel Coronavirus Case in Nepal. The Lancet Infectious Diseases, 20(3), pp.279-280.
40. Wax, R.S. and Christian, M.D., 2020. Practical Recommendations for Critical Care and Anesthesiology Teams Caring for Novel Coronavirus (2019-nCoV) Patients. Canadian Journal of Anesthesia/Journal Canadiend'anesthésie, pp.1-9.
41. Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W.H., Ou, C.Q., He, J.X., Liu, L., Shan, H., Lei, C.L., Hui, D.S. and Du, B., 2020. Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine, 382(18), pp.1708-1720.
42. Slots, J. and Slots, H., 2011. Bacterial and Viral Pathogens in Saliva: Disease Relationship and Infectious Risk. Periodontology 2000, 55(1), pp.48-69.
43. Corstjens, P.L., Abrams, W.R. and Malamud, D., 2012. Detecting Viruses by Using Salivary Diagnostics. The Journal of the American Dental Association, 143, pp.12S-18S.
44. Corstjens, P.L., Abrams, W.R. and Malamud, D., 2016. Saliva and Viral Infections. Periodontology 2000, 70(1), pp.93-110.
45. Ireland, A.J., Hosein, I. and Sherriff, M., 2005. Enamel Loss at Bond-up, Debond and Clean-up Following the use of a Conventional Light-Cured Composite and a Resin-Modified Glass Polyalkenoate Cement. The European Journal of Orthodontics, 27(4), pp.413-419.
46. Dashti-Khavidaki, S. and Khalili, H., 2020. Considerations for Statin Therapy in Patients with COVID-19. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy

47. Crawford, B., Kasmidi, M., Korompis, F. and Pollnac, R.B., 2006. Factors Influencing Progress in Establishing Community-Based Marine Protected Areas in Indonesia. Coastal Management, 34(1), pp.39-64.
48. Del Rio, C. and Malani, P.N., 2020. 2019 Novel Coronavirus—Important Information for Clinicians. Jama, 323(11), pp.1039-1040.
49. Sabino-Silva, R., Jardim, A.C.G. and Siqueira, W.L., 2020. Coronavirus COVID-19 Impacts to Dentistry and Potential Salivary Diagnosis. Clinical Oral Investigations, pp.1-3.
50. Corstjens, P.L., Abrams, W.R. and Malamud, D., 2016. Saliva and Viral Infections. Periodontology 2000, 70(1), pp.93-110.
51. Corstjens, P.L., Abrams, W.R. and Malamud, D., 2012. Detecting Viruses by Using Salivary Diagnostics. The Journal of the American Dental Association, 143, pp.12S-18S.
52. Corstjens, P.L., Abrams, W.R. and Malamud, D., 2016. Saliva and Viral Infections. Periodontology 2000, 70(1), pp.93-110.
53. Ireland, A.J., Hosein, I. and Sherriff, M., 2005. Enamel Loss at Bond-Up, Debond and Clean-up Following the use of a Conventional Light-Cured Composite and a Resin-Modified Glass Polyalkenoate Cement. The European Journal of Orthodontics, 27(4), pp.413-419.
54. Ireland, A.J. and Sherriff, M., 2002. The Effect of Pumicing on the In Vivo Use of a Resin Modified Glass Poly (Alkenoate) Cement and a Conventional No-mix Composite for Bonding Orthodontic Brackets. Journal of Orthodontics, 29(3), pp.217-220.
55. Ireland, A.J., Knight, H. and Sherriff, M.2003. an in Vivo Investigation into Bond Failure Rates with a New Self-Etching Primer System. American Journal of Orthodontics and Dentofacial Orthopedics, 124(3), pp.323-326.
56. Barker, C.S., Soro, V., Dymock, D., Sandy, J.R. and Ireland, A.J., 2014. Microbial Contamination of Laboratory Constructed Removable Orthodontic Appliances. Clinical Oral Investigations, 18(9), pp.2193-2202.
57. Freeman, J., 2012. Testing Decontamination Equipment in Dental Practice. Dental Nursing, 8(12), pp.772-779.
58. Ireland, A.J., Wilson, A.A., Blythe, L., Johnston, N.J., Price, R. and Sandy, J.R., 2011. Particulate Production During Conventional Light-Cured Composite and a Resin-Modified Glass Polyalkenoate Cement. The European Journal of Orthodontics, 27(4), pp.413-419.
59. MacIntyre, C.R., Wang, Q., Rahman, B., Seale, H., Ridda, I., Gao, Z., Yang, P., Shi, W., Pang, X., Zhang, Y. and Moa, A., 2014. Efficacy of Face Masks and Respirators in Preventing Upper Respiratory Tract Bacterial Colonization and Co-Infection in Hospital Healthcare Workers. Preventive Medicine, 62, pp.1-7.
60. Caprioglio, A., Pizzetti, G.B., Zecca, P.A., Fastuca, R., Maino, G. and Nanda, R., 2020. Management of Orthodontic Emergencies During 2019-NCOV.
61. Popat, H., Thomas, K. and Farnell, D.J., 2016. Management of Orthodontic Emergencies in Primary Care–Self-Reported Confidence of General Dental Practitioners. British Dental Journal, 221(1), p.21.