



Oral Manifestations of Coronavirus Disease 2019–An Insight

Amutha S¹, Selva Kumar R², Sai Lakshmi L.J³, Ananthalakshmi R⁴, N.Anitha^{5,*}

¹Department of Oral Pathology & Oral Microbiology,

Dr MGR Educational and Research Institute, Thai moogambigai Dental College& Hospital, Chennai.

²Department of oral & maxillofacial surgery, Asan Memorial Dental college & Hospital, Chengalpattu.

³Dr MGR Educational and Research Institute, Thai moogambigai Dental College&Hospital, Chennai.

⁴Dr MGR Educational and Research Institute, Thai moogambigai Dental College&Hospital, Chennai.

⁵Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Pallikaranai, Chennai

*Email : dranitha.nnr@gmail.com

ABSTRACT

Coronavirus 2019 disease (Covid-19) initially affects respiratory, gastrointestinal and neurological systems. But later oral, olfactory and other systems are also involved. In humans, Angiotensin converting enzyme 2 (ACE2) was identified as a functional receptor for SARS-CoV-2 virus. Angiotensin-converting enzyme 2 (ACE2) cell receptors are expressed in many cell types and tissues including the lungs, heart, blood vessels, kidneys, liver, gastrointestinal tract in the lining epithelium of the nose, mouth. This review elaborately discusses about the structure of the virus, mode of transmission, various oral manifestations of Covid-19 which has been reported in the literature and the underlying mechanisms. The reported manifestations include oral mucosal changes, gustatory dysfunctions, and salivary gland disorders. The exact pathogenesis of these oral symptoms is not completely understood yet. Knowledge of these oral manifestations helps the dental health care personnel to identify cases and prevent further spread of infection to the patients

Keywords: Coronavirus 2019; Oral manifestations in Covid-19; Angiotensin converting enzyme 2 (ACE2); gustatory dysfunctions in Covid-19

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2), emerged in late 2019, and it has been there as an ongoing pandemic threat in many countries and territories. Its first outbreak was identified in Wuhan City, Hubei Province, China, on 12 December 2019[1]. Coronaviruses (CoVs) belong to the family *Coronaviridae* (Subfamily *Coronavirinae*), the members of which infect a broad range of hosts, producing symptoms and diseases ranging from the common cold to severe and ultimately fatal illnesses such as SARS, MERS, and, presently, COVID-19[2].

Patients infected by CoV-2 shows some more common symptoms like fever, non-productive cough, myalgia, or fatigue and less common symptoms like sputum production, headache, haemoptysis, and diarrhoea[3]. Along with these systemic manifestations, there are many oral manifestations which could enable the dentists and others to identify 87.5% of symptomatic COVID-19 cases[4]. Thus, knowledge of these oral manifestations helps to identify cases and prevent further spread of infection to the patients and dental health care personnel.

METHODS

Literature search was done in google scholar, pubmed for relevant studies published upto December 2020 using the key words “oral manifestation of covid-19”, “oral findings in covid -19 patients”, “oral lesions in covid” and covid -19.

STRUCTURE OF THE VIRUS

SARS-CoV-2 belongs to the same lineage of CoVs, which are structurally enveloped, the positive-strand RNA viruses. The structures of the coronavirus are more spherical in shape, but their structure has the potential to modify its morphology in response to environmental conditions, being pleomorphic[5]. It has

four major structural proteins, namely, spike (S), membrane (M), envelope (E), and nucleocapsid (N)[6] shown in figure1[6].

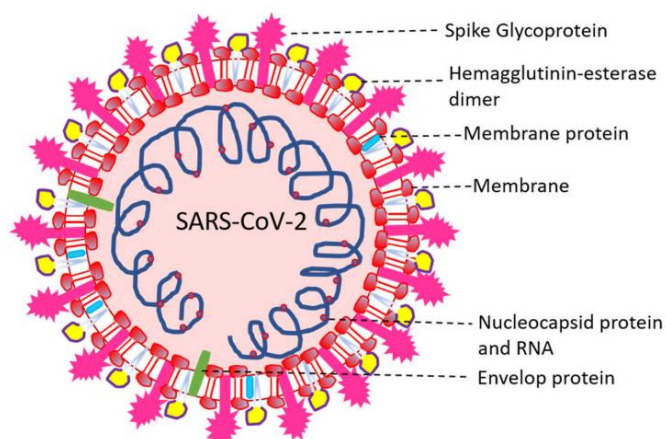


Figure 1: Virion structure and its genome[6]

S protein is large, multifunctional class I viral transmembrane protein and varies from 1,160 amino acids to 1,400 amino acids. It lies in a trimer on the virion surface, giving the virion a corona or crown-like appearance. It is required for the entry of the infectious virion particles into the cell through interaction with various host cellular receptors[7].

The M protein is the most abundant viral protein, giving a definite shape to the viral envelope[8].

The E protein is the most enigmatic and smallest of the major structural proteins which plays a multifunctional role in the pathogenesis, assembly, and release of the virus. It is a small integral membrane polypeptide that acts as a viroporin, whose inactivation or absence will be responsible for the altered virulence of coronaviruses due to changes in morphology and tropism[9].

The N protein of coronavirus is a multifunctional protein. It plays a role in complex formation with the viral genome and it facilitates the M protein interaction needed during virion assembly, and enhances the transcription efficiency of the virus[10].

MODE OF TRANSMISSION

Epidemiologic data suggest that the virus can spread from infected person to others (within 6 feet for at least 15 minutes) via droplets expelled during face-to-face exposure during talking, coughing, or sneezing[11]. Transmission may also occur via aerosols (smaller droplets that remain suspended in air), but it is unclear. The existence of aerosols in contact surface is also another possible mode of transmission[12].

Based on recent literature, older people above age 65 are at high risk and more susceptible. Patients with immunodeficiency, organ transplant, medical staff / workers, Dentists and other individuals who are in close contact with these patients are more susceptible to this virus and considered as high-risk groups[5].

PATHOGENESIS

The life cycle of the virus within the host includes 5 steps (I) Attachment (II) Penetration (III) Biosynthesis (IV) Maturation and (V) Release[11, 13].

First, the virus gets attached to the host receptors (attachment), then it enters the host cell by membrane fusion or endocytosis (penetration). Once, it enters and releases its content inside the host cell, viral RNA enters the nucleus for replication and start to synthesize the viral proteins (biosynthesis) and the new viral particles are made (maturation) and released[14].

The spike protein protruding from the viral surface, determines the diversity of coronaviruses and host tropism. In humans, Angiotensin converting enzyme 2 (ACE2) was identified as a functional receptor for SARS-CoV-2 virus. ACE2 is present in many cell types and tissues including the lungs, heart, blood vessels, kidneys, liver and gastrointestinal tract. It is present in the epithelial cells and act as a protective barrier. It is also present in the lining epithelium of the nose, mouth and lung[14, 15].

CLINICAL PRESENTATIONS

The incubation period ('pre-symptomatic' period) is 5–6 days, but can be up to 14 days. During this period the infected individuals can be contagious and transmit the virus to healthy individuals in the population[16].

COVID-19 patients have various clinical manifestations like fever, dry cough, shortness of breath, fatigue, nausea/vomiting, diarrhoea and myalgia. Complications include impaired function of the heart, brain, lung, liver, kidney, and coagulation system. It can lead to respiratory failure, myocarditis,

cardiomyopathy, ventricular arrhythmias, hemodynamic instability, acute cerebrovascular disease, encephalitis, venous and arterial thromboembolic events[11].

ORAL MANIFESTATIONS

Based on reported cases so far, oral manifestations included oral mucosal lesions like ulcer, erosion, bulla, vesicle, pustule, fissured or de-papillated tongue, dysgeusia, macule, papule, plaque, pigmentation, halitosis, whitish areas, haemorrhagic crust, necrosis, petechiae, swelling, erythema, and spontaneous bleeding[17]. Oral lesions were nearly equal in both genders. Latency time between appearance of systemic symptoms and oral lesions varies for about 4 days before and 12 weeks after onset of systemic symptoms. In some few cases oral lesions preceded systemic symptoms and few appeared simultaneously[18].

ORAL MUCOSAL LESIONS:

Patients presented with blisters, ulcers, erosion, macule, and plaques. Four Studies have reported oral lesions in patients with COVID-19 such as ulcers or blisters or diffuse reddish lesions affecting both keratinized and non-keratinized tissues of the oral cavity. These lesions can be observed in the palate, lip mucosa, buccal mucosa, and tongue[19, 20]. The lesions appeared as multiple, small, shallow, painful ulcers with erythematous halos covered by yellow-white pseudo membrane resembling herpetic lesions. Most of the lesions healed after 5-15 days in association with systemic symptoms[17, 18, 21]. These ulcers may be related to the side effects of anti-viral drugs [22].

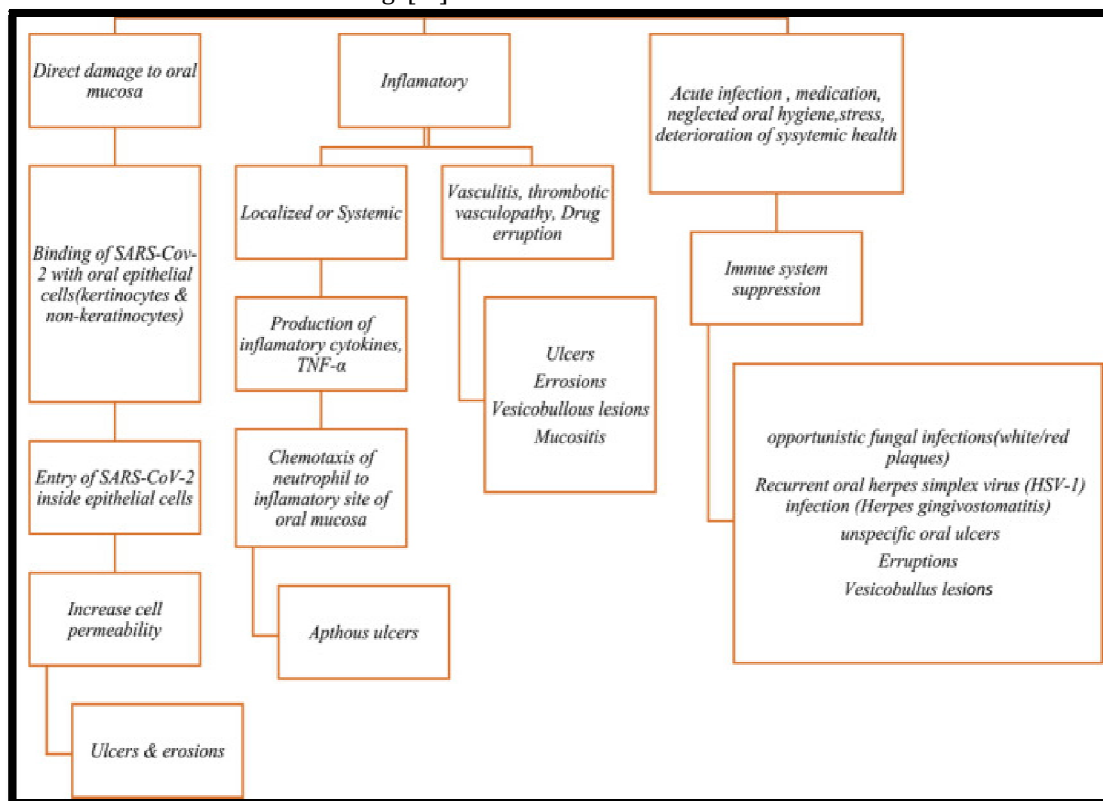


Figure 2: Proposed mechanisms of oral mucosal lesion due to Covid-19. SARS-CoV-2, severe acute respiratory virus syndrome coronavirus 2; TNF, tumour necrosis factor (Adapted from[23])

GUSTATORY DYSFUNCTIONS

Gustatory dysfunctions are one of the most common manifestations in covid-19 patients. The taste disturbance includes loss of taste (complete ageusia or partial hypogeusia) and altered taste (dysgeusia)[4]. Loss of taste is more common (91%) before hospitalization, whereas after hospitalization, taste and olfactory alteration appeared with an equal percentage[22].

Pathogenesis of gustatory dysfunction in covid -19 is not completely understood yet. Several hypotheses have been put forth by many authors, this could be due to the interaction between virus and ACE2 receptors. The expression of ACE2 was found to be higher in the tongue[22]. Keyhan et al. described that the presence of dysosmia and dysgeusia can be related to damage caused to the olfactory nerve and trigeminal nerve by the virus invasion or excessive exposure to chemicals and disinfectant agents that are used by people during this viral epidemic[24].

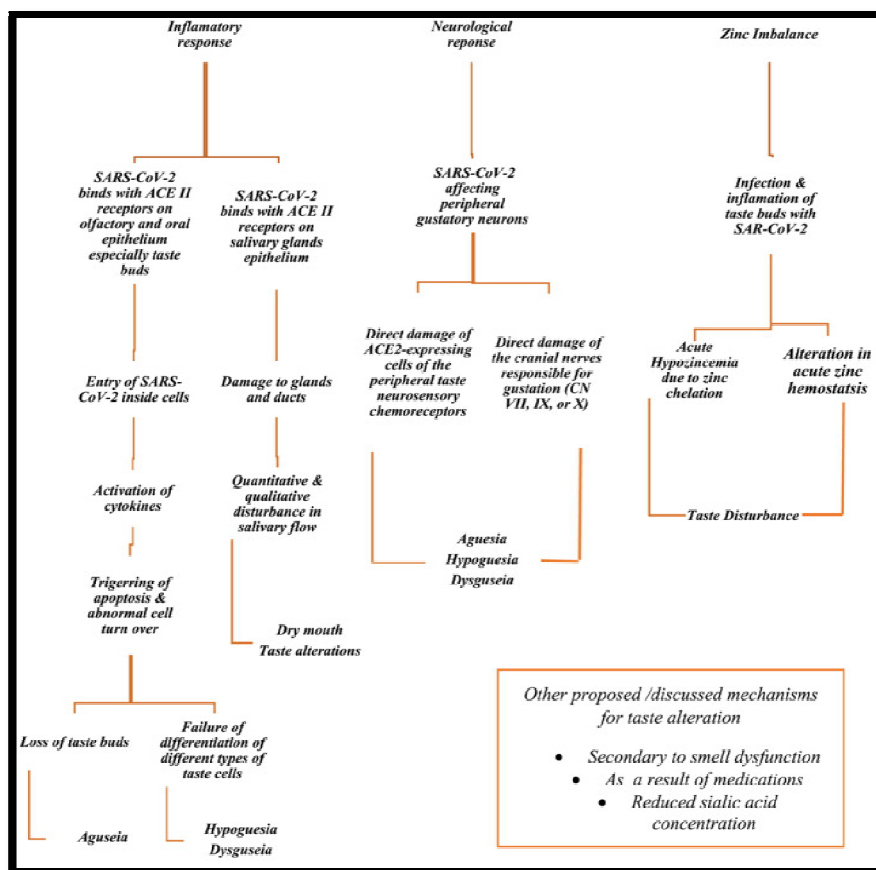


Figure 3: Proposed mechanisms for taste alteration in Covid-19. ACE2, angiotensin-converting enzyme 2; SARS-CoV-2, severe acute respiratory virus syndrome coronavirus 2 (Adapted from [23])

SALIVARY GLAND DISORDERS

Cov-2 virus causes acute nonsuppurative sialadenitis, so far two cases one with parotitis and other with submandibular gland sialadenitis has been reported in literature [25]. Many studies demonstrated that Cov-2 virus tropism for epithelial cells lining the salivary gland duct. It has been detected in saliva and used for diagnostic test. So, these findings suggest that cov-2 directly infects the salivary glands[25]. Cov-2 sialadenitis responded well to the antibiotic treatment with complete resolution[26].

CONCLUSION

COVID-19 patients manifest with certain oral manifestations. Only few cases have been reported in the literature. Dentist should be aware of these manifestations for early diagnosis and prevent further spread of infection to the patients and dental health care personnel. Further research has to be done to understand the pathogenesis of these manifestations.

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