Review Article

COVID 19-AN UPDATE ON ORAL CHANGES

ABSTRACT

The Severe Acute Respiratory Syndrome (SARS) coronavirus-2 is a novel coronavirus belonging to the family Coronaviridae originating in Wuhan, China has created a impact across the globe. The disease has been declared a pandemic by the WHO on March 11, 2020. In this review, an update on virology, pathophysiology, clinical presentation with detailed update on oral manifestations

Key words: SARS COV2,COVID,ORAL, MANIFESTATIONS

INTRODUCTION

A series of acute atypical respiratory disease occurred in Wuhan, China in dec 2019 which rapidly spread from Wuhan to other areas. The pathogen responsible for such diseas was found to be a novel coronavirus belonging to the family Coronaviridae. Hence the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was coined by WHO) due to its high similarity to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and high mortality during 2002–2003 [1].

Comment [U1]: SPELLING

World Health Organization (WHO) declared COVID 19 as a Pandemic on March 11, 2020 . The SARS-CoV-2, which started initially as severe pneumonia outbreak in China, has now quickly spread all throughout the globally, COVID-19 has affected large number of people being reported in approximately 200 countries and territories [2,3]. As of Dec 7th, 2020, there have been 66,729,375 confirmed cases of COVID-19 with 1.5 million deaths(4).

VIRAL ENTRY AND INVASION INTO HOST CELL (PATHOPHYSIOLOGY)

Coronaviruses are enveloped containing single-stranded RNA viruses of ~30 kb. a wide variety. They are largely divided into four genera; α, β, γ, and δ based on their genomic structure. α and β coronaviruses infect only mammals [5]. Human coronaviruses such as 229E and NL63 are alpha coronavirus which are responsible for common cold . whereas SARS CoV, Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-2 belong to β coronaviruses.

The virus is transmitted via respiratory droplets and aerosols from person to person. Once inside the body, the virus binds to host receptors and enters host cells through endocytosis or membrane fusion [6]. The virus follows series of steps after gaining entry into the host cells: attachment, penetration, biosynthesis, maturation and release. After getting attached to the host receptors, penetration happens through endocytosis or membrane fusion into the host cell. Once viral contents are released inside the host cells, viral RNA enters the nucleus for replication. viral proteins (biosynthesis) are synthesized by viral MRNA Then, new viral particles are made (maturation) and released. Coronaviruses has four structural proteins; Spike (S) glycoprotein protruding from the viral surface, which determines the diversity of coronaviruses and host tropism. Spike comprises two functional subunits; S1 subunit is responsible for binding to the host cell receptor and S2 subunit is for the fusion of the viral and cellular membranes Membrane (M), envelop (E) and nucleocapsid (N) [7]. Angiotensin converting enzyme 2 (ACE2) was identified as a functional receptor for SARS-CoV [8]. ACE2 receptor is highly expressed in various body organs like nasal and oral mucosa, especially the tongue, salivary glands, lung, heart, ileum, kidney and bladder [9]. In lung, ACE2 was highly expressed on lung epithelial cells.

After getting attached to ACE-2, which is highly expressed in adult nasal epithelial cells, the virus undergoes local replication and propagation, along with the infection of ciliated cells in the conducting airways. [10]. Then, there is migration of the virus from the nasal epithelium to the upper respiratory tract which causes symptoms of fever, malaise and dry cough. About one-fifth of all infected patients progress to next stage of disease and develop severe symptoms.(ref?) The virus invades and enters the type 2 alveolar epithelial cells via the host receptor ACE-2, undergoes replication which releases multiple cytokines and inflammatory markers such as interleukins (IL-1, IL-6, IL-8, IL-120 and IL-12), tumour necrosis factor-α (TNF-α), IFN-λ and IFN-β, CXCL- 10, monocyte chemoattractant protein-1 (MCP-1) and macrophage inflammatory protein-1α (MIP-1α) causing 'cytokine storm' which further attracts neutrophils, CD4 helper T cells and CD8 cytotoxic T cells.(ref?) These cells fights against the virus also cause inflammation and diffuse alveolar damage eventually culminating in an acute respiratory distress syndrome. [11]

Comment [U2]: ADD REFERENCE

Comment [U3]: REFERENCE?

CLINICAL FEATURES [12] ??

Comment [U4]: WHY REFERNECE HERE

The incubation period of COVID-19 is roughly 5–6 days, but can be up to 14 days. During this period, the infected individuals may not show any symptoms but can be contagious and transmit the virus to healthy individuals in the population. The common symptoms are fever, body aches, breathlessness, malaise and dry cough, can be categorised as mild, moderate or severe disease based on the severity. Some patients may also present with gastrointestinal symptoms such as abdominal pain, vomiting and loose stools.(ref??)

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TABLE1 : SHOWING DIFFERENT STAGES IN COVID

Comment [U6]: Reference ?? if table taken from any source whether prior permission taken ?

STAGES	SYMPTOMS	RADIOLOGICAL FINDINGS

Asymptomatic	NO SYMPTOMS	Positive nasal swab test Normal chest X-ray
Mild	fever, body aches, breathlessness, malaise and dry cough abdominal pain, vomiting and loose stools.	Normal chest Xray
Moderate	Symptoms of pneumonia (persistent fever and cough) with normal oxygen saturation	Significant lesions on high-resolution CTchest
Severe	Pneumonia with reduction in oxygen saturationlevel (SpO2<92%),neurological manifestations such as acute cerebrovascular diseases, skeletal muscle injury and impaired consciousness	lesions on high-resolution CTchest
Critical	Acute respiratory distress syndrome, hypovolemic shock, coagulation defects, encephalopathy, heart failure and acute kidney injury	

NASAL SYMPTOMS [13]. ???

Comment [U7]: WHY REFERENECE HERE

Hyposmia and Anosmia can happen with COVID infected patients which lasts for more than 7 days . The main suspected mechanism is invasion of the olfactory receptors centrally or damage of the olfactory epithelium which leads to post olfactory loss. Anosmia is usually associated with frontal headache. The frontal headache could be due to an acute rhinosinusitis with a mucosal inflammation due to SARS-CoV-2. Anosmia is seen in 68% to 85% of affected population.(ref??)

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EAR SYMPTOMS [13,14].

Comment [U9]: WHY REFERENCE HERE

Patients with COVID-19 may present rhinolaryngological ??? symptoms such as tinnitus and hearing loss. Kilic et al.(2020)(ref?) concluded that sudden sensorineural hearing loss (SSNHL) may be one of the symptoms of COVID19 and can also be considered to be a neurologic symptom. The reasons could be neuritis caused by viral involvement in the cochlear nerves, cochleitis due to viral involvement in the cochlea and perilymphatic tissues.

ORAL SYMPTOMS

DYSGEUSIA[15,16,17]????

Dysgeusia can be an early symptom of COVID-19 infection with prevalence of 71% to 88.8%. Angiotensin-converting enzyme 2 (ACE2) receptors have been found in the epithelium of taste buds and salivary glands , resulting in salivary gland dysfunction with subsequent salivary flow impairment, in both quality and quantity, and the resultant dysgeusia as an early symptom in asymptomatic patients with COVID-19.(ref)????

A direct damage to nonneuronal cells in the olfactory epithelium where numerous ACE2 receptors are expressed can also result in taste disturbance. There can be a direct damage of ACE2-expressing cells of the taste buds or direct damage of any of the cranial nerves responsible for gustation (CN VII, IX, or X) especially Chorda tympani . Also, the oral mucosa is lined with ACE2 receptors, can trigger an inflammatory response, which leads to cellular and genetic changes that could alter taste ultimately lead to the development of taste dysfunction. There could be tissue hypoxia in patients with COVID-19 who are clinically conscious which may also result in tissue injury leading to disturbance in taste. stages of COVID-19.?? Another possible mechanism may involve zinc, which has an important role in taste perception. Chelation of Zinc can happen through immune mechanisms result in acute hypozincemia leading to gustatory dysfunction. Finally, xerostomia can also causes alteration in taste preception.(ref??)

Comment [U10]: HOW HEARIING LOSS IS RELATED TO RHINOLARYNGEAL SYMPTOMS

Comment [U11]: ADD REFERNECE

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XEROSTOMIA [18]???.

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Xerostomia or dry mouth syndrome has been linked with COVID-19 as most of the patients have xerostomia. It is a sign of dehydration which could occur secondary to underlying illness such as COVID-19. Also neuroinvasive and neurotropism potential of SARS-CoV-2 can also leads to Xerostomia. Angiotensin-converting enzyme (ACE2) receptor 2 in epithelial cells of the salivary gland are the primary site for coronavirus which leads to viral induced infection and inflammation causing xerostomia(REF?)

Comment [U18]: PLZ ADD REFEENCE HERE

BURNING MOUTH SYNDROME [19??]

Comment [U19]: WHY REFERNECE HERE

Burning mouth syndrome was also seen many COVID positive patients. Xerostomia along with gustatory dysfunction could have a strong association in causing Burning mouth syndrome.(ref??)

Comment [U20]: PLZ ADD REFEENCE HERE

OPPORTUNISTIC INFECTIONS [20??]

Comment [U21]: WHY REFERNECE HERE

Also, COVID-19 acute infection, when treated with medications could potentially contribute to various oral lesions due secondary opportunistic fungal infections, recurrent oral herpes simplex virus (HSV-1) infection. There can be non-specific oral ulcerations, mucosal bullous eruptions, fixed drug eruptions, gingivitis as a result of the impaired immune system and/or susceptible oral mucosa.Geograhic tongue has also been reported(REF??)

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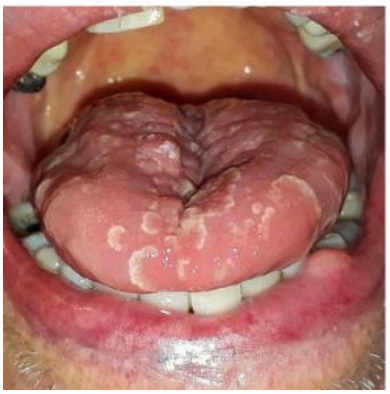

FIG 1 SHOWING GEOGRAPHIC TONGUE IN COVID INFECTED PATIENT(image taken from??? Permissions??

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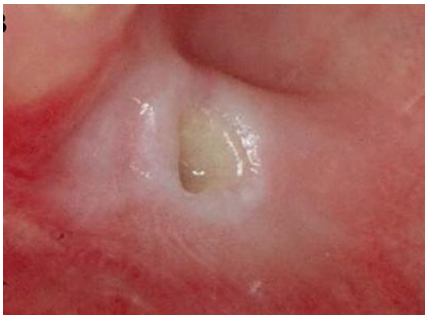

FIG 2 SHOWING ULCER IN BUCCAL MUCOSA(image taken from ???permissions?)

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HYPERPIGMENTATION [21???]

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There has also been hyperpigmentation in labial gingiva noted in asymptomatic covid positive patient. Immunoinflammatory processes leading to inflammatory mediators like prostaglandins, leukotrienes, cytokines (TNF alpha,IL-1) and inflammatory mediators, may play a role in this response and increased melanogenesis and cause hyperpigmentation. (ref???)

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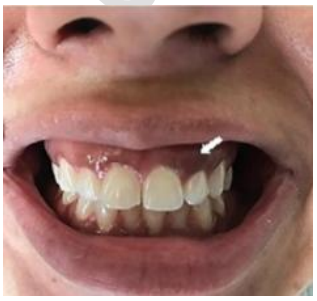

FIG 3 SHOWING PIGMENTATION IN GINGIVA IN COVID INFECTED PATIENT(image taken from ???? permissions??)

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CONCLUSION

There can be a wide array of oral manifestations in covid 19 patients, some may be an initial sign of COVID without showing symptoms. A thorough examination of the oral cavity is recommended and practised for better understanding of should pathobiology of these oral alterations.

Comment [U28]: GRAMMER

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