International Journal of Research in Health and Allied Sciences

Journal home page: www.ijrhas.com

Official Publication of "Society for Scientific Research and Studies" [Regd.]

ISSN: 2455-7803 Index Copernicus value [ICV] = 68.10;

Review Article

Oral and Salivary Gland Manifestations in COVID-19 Patients

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ABSTRACT

Several scientific literature has been published since the outbreak of the novel coronavirus disease 2019 (COVID-19)which is caused by SARS-CoV-2, few published articles called the attention to the oral cavity as the potential route of infection, leading to various implications for dental practice and the use of saliva as a diagnostic tool for the COVID-19. In this article we would review the available literature on the salivary glands, salivary flow and oral manifestations in the context of SARS-CoV-2 infection.

Keywords: Sars-CoV-2, Salivary glands, Salivary outcome, Oral manifestations, infectious diseases.

Received: 4 April, 2020 Accepted: 28 April, 2020

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This article may be cited as: Parmar S, Gautam A, Gautam A. Oral and Salivary Gland Manifestations in COVID-19 Patients. Int J Res Health Allied Sci 2020; 6(3):70-72.

INTRODUCTION

COVID-19, is caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) which was transitionally named as 2019-nCoV, belongs to the genus Betacoronavirus and it has affected human species for the third time.[1] COVID-19 was first reported and confirmed in Wuhan, China in December 2019.[2] Since 2002, beta coronaviruses (CoV) have caused SARS-CoV in 2002-2003, MERS-CoV in 2012, and the newly emerged SARS-CoV-2 in December 2019 which is highly contagious.[3] Previously it was reported that, both SARS coronavirus (SARS-CoV) and MERS coronavirus (MERS-CoV) were considered to be originated from bats. The genetic sequence of SARS-CoV-2 has been shown to be 79.6% identical to that of SARS-CoV and 96% identical to a bat coronavirus.[4] The SARS-CoV-2 is mainly transmitted from man to man by droplet infection through close contact and is highly infectious, leading to rapid global spread from infected Chinese travellers .[5] On January 30, 2020, the World Health Organization (WHO) declared that COVID-19 a public health emergency of international concern or a pandemic as it was killing thousands of people worldwide.[6]

Coronavirus Morphology and Structure

Coronaviruses are enveloped, single stranded RNA viruses with high rates of mutation and recombination.[7] The structural proteins include the spike surface glycoprotein(S), small envelope protein (E), matrix protein (M), and nucleocapsid protein (N).[8] It is the spike surface protein that plays a critical role in binding of the virus to the host cell receptors. SARS-CoV primarily binds to the angiotensin converting enzyme 2(ACE2) receptor on the host cell.[8]In case of SARS-CoV-2, it has been confirmed that human ACE2 is the main receptor where the virus get attached and enter into the host cell.[9]The entry of coronavirus into the host cell is a multi-step process as it engages multiple distinct domains in the spike protein that facilitates attachment of the virus to the surface of the cell, leading to sequence of events i.e. engagement of the receptor, processing of proteases and membrane fusion. Genomic analysis of the SARS-CoV-2, also divulge the presence of an activation site on the spike protein, which is activated by furin, an enzyme which is found abundantly in many human tissues, which can be attributed to its rapid spread.[10]

Salivary Glands and Saliva

Coronaviruses, including the SARS-CoV, have been detected previously in saliva, almost with the same levels found in nasopharyngeal specimens.[11]Therefore, saliva plays an important role in the transmission of infection from person to person by contact with the droplets.[12]In one of the cases, SARS-CoV-2 has been detected in saliva of COVID-19 positive patients, even upto the 11th day after hospitalization. The presence of the COVID-19 in the saliva can have its source either from the salivary glands ducts or from the gingival crevicular fluid (from gingiva) or from secretions of the lower and upper respiratory tract.[13] During the early onset of SARS-CoV disease in rhesus macaques the ACE 2 epithelial cells of the salivary glands have been shown to be an initial target.[14] The mRNA, protein levels of the cellular protease and enzyme furin, vary according to the cell type and high levels have been found in the salivary glands.[15] In one study, saliva was collected from the floor of the mouth directly from the submandibular duct, which drains saliva from each bilateral submandibular and sublingual glands. Interestingly, the expression of SARS-CoV-2 was found in four out of 31 (12.90%)COVID-19 patients.[16]Another important finding of the study of Chen and Colleagues was that expression of SARS-CoV-2 was higher in critically-ill patients (3/4), which suggest greater virus invasion or destruction of salivary glands at the late stage of the disease. Overall, the literature suggests that SARS-CoV-2 could infect salivary glands.

Xerostomia

Hyposalivation, the reduction of unstimulated salivary flow rate, is a common finding in patients mainly reported as an outcome of the use of medication and psychological processes.[17] Dry mouth was shown to be reported in a relatively high proportion of COVID19 patients.[16] Hyposalivation might result in reduction of presence of many proteins with antiviral properties resulting in exposing the patients to a higher risk of getting coronavirus disease (COVID 19).[18] In evident studies it was reported that, the SARS-CoV-2 infection was more severe in individuals over 50 years of age associated with comorbidities such as diabetes, cardiovascular problems and diseases involving the nervous system.[19,20] It is a known fact that salivary flow reduces with age and is not explained based on medications used by older adults.[21] It is known that infectious and inflammatory processes might also lead to hyposalivation and, thus, the chances of qualitative and quantitative disturbances in saliva secretion by SARS-CoV-2 infection should not be discarded.

Taste Disorders

Taste disorders have been reported in a variety of clinical problems.[22] Amblygeustia, a diminished sensitivity of taste, was manifested by a relatively high proportion of COVID-19 patients.[16] In COVID-19 positive patients it was suggested that chemosensory dysfunction should be considered while screening symptoms as it was reported in a study where patients with influenza like symptoms had 68% (40/59) olfactory loss and 71% (42/59) taste loss, respectively.[23] Low salivary flow rate and disturbances in salivary biomarkers were suggested to cause xerostomia[24,25] which has been further associated with altered taste sensorial. Moreover, oral neuropathy or neurological transduction interruption induced by alterations in salivary composition were responsible for oral sensory complaints and loss of taste function.[26] Possible taste alterations as result of the direct effect of SARS-CoV-2 infection in sensory neurons or other components of the gustatory system should also be considered.

Cutaneous Manifestations

Cutaneous manifestations were evident as erythematous rash in fourteen patients, widespread urticarial in three patients and chickenpox-like vesicles in one patient. Trunk was the mainly involved region. Itching was less or absent and usually lesions healed in few days. Apparently, there was not any correlation with disease's severity.

Oral findings

Oral cavity may exhibit manifestations of many underlying diseases such as oral ulcerations, gingival bleeding, glossitis, oral pain, or halitosis.[27] Viral infections usually manifest as either ulceration or blisters in the oral cavity.[28] A case report suggested that recurrent oral ulcers could be an inaugural symptom of COVID-19.[29] Also, a report of three covid patients showed that pain and intraoral manifestations such as oral ulcers or blisters was a common finding in COVID-19 before seeking any medical advice. Thus, it encouraged to perform intraoral examinations in patients with suspected SARS-CoV-2.[30]As these oral findings were new and found in limited group of people, their occurrence may vary significantly among COVID-19 patients such as in those with systemic diseases and/or with poor oral health which might be the contributory factor to the oral findings. Given the possibility of immunocompromised status of the patients, it was also possible that the oral manifestations may be related to other viruses or bacteria.

Conclusion

The SARS-CoV-2 infection manifest various oral findings affecting salivary glands resulting in reduction in salivation and further altered taste sensorium. However, further studies are needed to understand the role of salivary glands and saliva in COVID-19 patients.

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