

An Overview On Oral Manifestations Of Covid-19

Research Article

John Abraham^{1*}

Department of Family Medicine/Geriatrics, Marathahalli-Sarjapur Rd, beside Bank of Baroda, John Nagar, Koramangala, Bengaluru, Karnataka 560034 India.

Abstract

Background: Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) or COVID-19 was characterized as a pandemic before been declared as a Public Health Emergency of International Concern (PHEIC). The outbreak has affected more than 148 million people affecting the respiratory system, skin, and digestive system. Hence, the present study aims to find the preponderance of oral manifestations of COVID-19 and to suggest the management of those affected with the same.

Method: In the present review, search engines such as PubMed, Scopus, ScienceDirect, and Web of Science were used. Gray literature was also included by performing a manual search on Google Scholar. All the articles that were published till April 25, 2021, were included. The search keywords include: "Symptoms", "Oral Manifestation", "Mouth disease", "COVID-19", "SARS-CoV-2", and "India".

Results: The most common oral manifestations are: sore throat (25.43%) followed by dysgeusia (27.84%). The other common symptoms are enanthema (58.5%), oral lesions (48.5%), and oral bleeding (22.95%). Chlorhexidine mouthwash, topical or systemic corticosteroids, normal saline gargling, and artificial saliva are used in managing the manifestations.

Conclusion: Looking out and identifying the oral manifestation can help in timely diagnosis and treatment of COVID-19. So, Therefore, it is important to include dentists in the multi-disciplinary team assisting the COVID-19 patients.

Keywords: SARS-CoV-2; COVID-19; Oral Manifestation; Management.

Introduction

Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) or COVID-19, were at the start, reported in December 2019 by the officials in Wuhan City, China (WHO, 2020-a). Concerned by the continuous rise in the cases, WHO on March 11, 2020, assessed the situation could be characterized as a pandemic before declaring the outbreak as a Public Health Emergency of International Concern (PHEIC) on April 27, 2020 (WHO, 2020-b). The outbreak has affected more than 148 million people causing more than 3.1 million deaths worldwide (WHO, n.d.). Commonly seen symptoms include fever, dry cough, and fatigue, loss of taste or smell, diarrhea, nasal congestion, nausea or vomiting, headache, chills or dizziness, conjunctivitis different types of skin rashes, sore throat, and muscle or joint pain (WHO, 2020-c).

As with any other viruses, COVID-19 is also evolving overtime, resulting in thousands of mutations (WHO, 2021). The three widely known mutations are B.1.1.7 (first reported in the United

Kingdom), B.1.351 (first reported in South Africa), and P.1 (first reported in Brazil) ("How Many New Coronavirus," 2021). The United States has discovered about 677 mutants whereas India has detected over 24,000 mutants in 7,000 variants (Haseltine, 2021; IANS, 2021).

Pathogenesis

In early infection, SARS-CoV2 attacks specific cells like bronchial epithelial, nasal cells and pneumocytes. This is mainly via the viral structural spike(S) protein that binds to the angiotensin-converting enzyme 2 (ACE2) receptor. Corona virus entry into the host cells is mediated by SARS-CoV2 S protein which is activated by cleavage of ACE2. Also, The viral uptake is upgraded by, Type 2 trans-membrane Serine Protease (TMPRSS2) existing in the host cells.

SARS-CoV-2 infects and destroys the T lymphocytes. The viral inflammatory response, impedes lymphopoiesis and enhances lym-

***Corresponding Author:**

John Abraham,
Department of Family Medicine/Geriatrics, Marathahalli-Sarjapur Rd, beside Bank of Baroda, John Nagar, Koramangala, Bengaluru, Karnataka 560034, India.
E-mail: drjohnabraham1988@gmail.com

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phocyte apoptosis. During later stages of viral infection, especially when viral replication is rushed, epithelial-endothelial barrier integrity is found to be compromised. Also, dysfunctional alveolar-capillary oxygen transmission, and diminished oxygen diffusion capacity is caused due to bradykinin-dependent lung angioedema. When COVID-19 infection is severe, the immediate activation of coagulation and exhaustion of clotting factors occurs in inflamed lung tissues and pulmonary endothelial cells may result in micro-thrombi formation and contribute to the thrombotic complications, such as deep venous thrombosis, pulmonary embolism stroke and Myocardial Infarctions.

Concerning to the oral cavity, presence of ACE2 in the cells of oral mucosa and tongue, indicates that the mouth is likely infectious route of SARS CoV2 and therefore advocates an a relatedness between this viral infections and oral ulcers associated with COVID-19.

Clinical features: The newer variants of COVID-19 have a wide range of symptoms and medical complications (ANI, 2021). The primary symptoms of the variants include fever, muscle pain, loss of smell and taste, and dry and persistent cough. The additional symptoms which is seldom found include conjunctivitis, sore throat, headache, rashes, upset stomach, and discoloration of fingers and toes (Pandey, 2021).

Oral Manifestations: According to Froum (2020), physicians are examining the direct connection between COVID-19 and oral disease, as the survivors who battled against the disease for weeks to months, found a decline in their oral health resulting in sensitive gums, teeth cracking, teeth falling out, and teeth turning grey. Some studies suggest that the mouth might be the most vulnerable area to the virus because of the abundant Angiotensin Converting Enzyme (ACE2) receptors found in the oral tissue. The common oral manifestations associated with COVID-19 are gingival inflammation, xerostomia (dry mouth), oral ulcerations and gingival tissue breakdown, and loss of taste and smell. Thus considering the importance of oral health and the relationship between oral health and COVID-19, the present study aimed at examining out the prevalence of oral manifestations of COVID-19 and the suggested management.

Method

Information search

Electronic search engines such as PubMed, Scopus, ScienceDirect, and Web of Science were used. To access the gray literature, a manual search was performed on Google Scholar. All the articles that were published till April 25, 2021, were included.

The search keywords include: “Symptoms”, “Oral Manifestation”, “Mouth disease”, “COVID-19”, “SARS-CoV-2”, and “India”.

Study selection

Those studies which included oral manifestation of COVID-19, preferably in prevalence, and those which included details about management at different levels were included in this review.

Inclusion and exclusion criteria

The studies which were published on oral manifestations with the percentage indicated, preferably in the Indian context were included in the review. Studies that were published in languages other than English were excluded from the review.

Analysis

Author(s), year of publication, type of publication, country where the study was done, different types of oral manifestations, and the methods used to manage the symptoms were collected for the present review. Frequencies, the average (mean), largest observation (maximum), and smallest observation (minimum) were calculated from the available data.

Result

The present review sampled 22 papers which include 13 research articles, 7 review articles, 1 short communication, and 1 general article.

As shown in table 1, most of the papers were published in 2020 (63.6%) while the rest were published in 2021 (36.4%). More than

Table 1. Characteristics of the studies.

		N	%
Year	2020	14	63.60%
	2021	8	36.40%
Country	India	8	53.30%
	The United States	2	13.30%
	Singapore	1	6.70%
	Israel	1	6.70%
	Brazil	1	6.70%
	France	1	6.70%
	Unknown	1	6.70%
Type of publication	Research articles	13	59.10%
	Review articles	7	31.82%
	Short communication	1	4.54%
	Article	1	4.54%

Table 2. Prevalence of the oral manifestations in COVID-19 diagnosed.

	N	Mean	Maximum	Minimum
Papers with prevalence	10			
Sore throat	9	25.43	58.9	9.8
Dysgeusia	5	27.84	39.3	10.5
Enanthema	2	58.5	88	29
Oral lesions	2	48.5	68	29
Oral bleeding	2	22.95	41.2	4.7

Table 3. Descriptive characteristics of the studies included.

Sl.No	Author(s) & Year	Country	Type of publication	Major Findings	Management
1	Kumar, S., Rathore, P., Choudhary, N., Singh, N., et al (2020)	India	Research article	1. Sore throat: 14% in both - 16-30 years and 31-45 years, 9% in 46-60 years. 2. Expectoration: 2% in >60 years.	
2	Chew, N. W., Lee, G. K., Tan, B. Y., Jing, M., et al (2020)	Singapore and India	Research article	1. The commonly reported symptoms included throat pain - 33.6% (304) 2. Symptoms were mild in severity.	
3	Yadav, V., Bhagat, S., Sharma, D. K., Sibia, R. P. S., et al (2021)	India	Research article	Dysgeusia - 13.1% Dryness of throat - 10.5% Soreness of throat - 9.8% Posterior nasal discharge - 5.2%	
4	Biadsec, A., Biadsec, A., Kassem, F., Dagan, O., et al (2020)	Israel	Research article	Impaired sense of taste - 38.3% (49) Sore throat - 26.6% (34) Dry mouth - 56.3% (72) Plaque-like changes in the tongue - 7% (9) Swelling: oral cavity - 7.8% (10), palate - 3.1% (4), tongue - 3.1% (4), gums - 1.6% (2) Current oral bleeding - 4.7% (6)	
5	Goel, N., Spalgais, S., Mrigipuri, P., Khanna, M., et al (2020)	India	Research article	Sore throat - 14.9% (5)	
6	Gupta, V., Rajanna, L. B., Upadhyay, K., Bhatia, R., et al (2021)	India	Research article	Sore throat - 58.9% Gustatory Dysfunction (sense of taste) - 39.53%	
7	Sahoo, P. R., Sabu, M., Surapaneni, P. S., Maiti, A., et al (2021)	India	Research article	Altered taste - 10.5% (76) Throat pain - 14.2% (102 [combined]) The prevalence of altered taste was much lower compared to Europeans and similar to East Asians.	
8	Iranmanesh, B., Khalili, M., Amiri, R., Zartab, H., et al (2020)		Review paper	1. Oral manifestations included macule, papule, pustule, plaque, erosion, ulcer, hemorrhagic crust, petechiae, erythema, fissured or depapillated tongue, pigmentation, and halitosis 2. The most common sites of involvement is tongue (38%), followed by labial mucosa (26%), palate (22%), gingiva (8%), buccal mucosa (5%), oropharynx (4%), and tonsil (1%). 3. Oral lesions were painful, with burning sensation, or pruritus in 68% of the cases. 4. Swelling of oral cavity (including palatal, lingual, and alveolar mucosa) was reported by 8% of the patients. 5. Enanthema was reported in 29% COVID-19 confirmed cases in a study	Different types of therapies including chlorhexidine mouthwash, nystatin, oral fluconazole, topical or systemic corticosteroids, systemic antibiotics, systemic acyclovir, artificial saliva, and photobiomodulation therapy (PBMT) were prescribed for oral lesions depending on the etiology.
9	Gupta, S., Mohindra, R., Chauhan, P. K., Singla, V., et al (2020)	India	Research article	Oral findings - 51.51% Sore throat - 39.4% Ageusia - 5.9% Petachiae - 5.9% Gingival recession - 5.9% Gingival erythema - 47.1% Dental caries - 35.3% Perioral swelling - 23.5% Gingival bleeding - 41.2% Only ageusia, petechiae, and perioral swelling were found to be associated with COVID-19	
10	Drago, F., Ciccarese, G., Merlo, G., Trave, I., et al (2021)		Review paper	Oropharyngeal mucosa - was reported by only a few patients Painful oropharyngeal ulcers were reported. (5 cases) Blisters and gingivitis - 1 case palatal petechiae, erythema, and pustules (2 cases) 29% of 21 Spanish patients were found to have oral-pharyngeal lesions. 88% of patients with enanths with petechial pattern was found to be strongly associated with COVID-19	
11	Singh, C. V., Jain, S., & Parveen, S. (2021)	India	Research article	For anosmia and dysgeusia caused due to the disease, use of fluticasone nasal spray and triamcinolone medication was reported with the recuperation of smell and the taste sensation within a week.	Gustatory dysfunction was treated triamcinolone paste TDS, normal saline gargle.
12	Singh, G., Priya, H., Mishra, D., et al (2021)		Review paper	Common manifestations include - ageusia, non-specific anosmia (not associated with rhinitis), and hyposalivation. Other symptoms include ulcers in the oral cavity, desquamative gingivitis, herpetic ulcers on attached gingiva, blisters/irregular ulcers on the tongue's dorsal surface, enlargement of submandibular glands, and cervical lymphadenopathy. Dysgeusia or ageusia and anosmia are frequent in COVID-19 and varies from 5.6% to 88.8%	
13	Halepas, S., Lee, K. C., Myers, A., Yoon, R. K., et al (2020)	The United States		23 patients (48.9%) were presented with erythematous lips and/or angioedema while only 5 (10.6%) were noted to have a strawberry tongue. Oral or oropharyngeal findings were significantly associated with the presence of systemic rash (p=0.04) and conjunctivitis (p=0.02). Cervical lymphadenopathy- 19.2%	

14	Dos Santos, J. A., Normando, A. G. C., da Silva, R. L. C., De Paula, R. M., et al (2020)	Brazil	Research article	Symptoms: Hypogeusia White plaque and multiple pinpoint ulcers resembling the late stage of herpetic lesions were found on the dorsum of the tongue Reactive lesion (fibroma) of approximately 1 cm	Was treated with: Intravenous Fluconazole (Zoltec 200 mg/100 mL, for ten days) and oral nystatin (100,000 IU/mL, 8/8 h, for 30 days), Antifungals and chlorhexidine digluconate (0.12%) alcohol-free mouth rinses, and daily applications of 1% hydrogen peroxide showed almost complete resolution.
15	Amorim dos Santos, J., Normando, A. G. C., Carvalho da Silva, R. L., Acevedo, A. C., et al (2020)		Review paper	Gustatory impairment - 45% Dysgeusia - 38% Hypogeusia - 35% Ageusia - 24% Tongue, palate, lips, gingiva, and buccal mucosa were affected with irregular ulcers and petechiae.	
16	Chaux-Bodard, A. G., Deneuve, S., &Desoutter, A.(2020)	France	Research article	Inflammation of a tongue papilla that may be accompanied by pain and development of erythematous macule within 24 hours , which advances into irregular ulcer.	
17	Halboub, E., Al-Maweri, S. A., Alanazi, R. H., Qaid, N. M., et al (2020)		Review paper	The most common orofacial manifestations were vesiculobullous ulcerative lesions, and acute sialadenitis of the parotid gland . In four cases, oral manifestations were the first signs of COVID-19.	The management of oral mucosal lesions included one or more of the following: topical or systemic corticosteroids, diphenhydramine, mouthwashes, and antibiotics. In all cases, the reported orofacial manifestations completely resolved within a couple of days (range: 3-21 days) from the day of diagnosis.
18	Corchuelo, J., & Ulloa, F. C. (2020)	The United States	Research article	Symptoms: Mild candidiasis in the posterior tongue Painless petechiae	Nystatin Oral Suspension was used with a dose of 3 ml (300,000 international units) every 6 hours. Rinses with chlorhexidine (Chlorhexidine gluconate 0.12%) patient was instructed to immerse the tooth brush brush in sodium hypochlorite solution (1:100 dilution of 5% sodium hypochlorite) for 30 min, then to rinse with water.
19	Mortazavi, H., Rezacifar, K., &Nasrabad, N. (2020)		Mini-review paper	Salivary gland disease Xerostomia Taste/smell alterations Oral mucosal lesions	
20	La Rosa, G. R. M., Libra, M., De Pasquale, R., Ferlito, S., et al (2021)		Review paper	Various oral lesions associated with COVID-19, includes, aphthous-like ulcerations and macules. The tongue, lips, and palate were the most frequently affected sites. The lesions could be related to the direct or indirect effect of SARS-CoV-2 due to the oral mucosa cells, and coinfections, caused due to compromised immunity.	
21	Stefania, D.M., (2020)		Short communication	Widespread clinical signs: Enanthema of the mouth mucosa, presenting point-like blisters surrounded by an erythematous halo. In some cases, foot-and-mouth-like injuries have been found in the intra-oral mucosa starting as widespread small 1-2 mm spots which in a few days are joined together to form a single ulcer covered by pseudo-membranes on the lip surface. The lips appear swollen, chapped, and covered by bleeding eschars turning necrotic, clearly bordered by hard erythematous tissue and fibrin.	
22	Karunakaran (2021)		Article	Multiple palatal and oropharyngeal petechial lesions Dysgeusia Palatal and oropharyngeal erosions and ulcerative lesions Severe pain over the lesion area Partial paresthesia surrounding the lesions Irregular areas of blanching involving the palate Burning sensation of palate and oropharynx, and dysphagia Palatal and oropharyngeal tenderness and soreness Necrotic pseudo membranes covering the erosive/ulcerative lesions	1. Topical triamcinolone acetonide (Kenacort) 0.1% paste (applied by the patient three times daily) 2. Doxycycline and benzalkonium chloride mouthrinses (applied by the patient three times daily) 3. Topical benzocaine 5% gel (applied by the patient three times daily)

half the papers sampled the Indian population (53.3%) followed by The United States (13.3%).

As shown in table 2, the most common oral symptoms are enanthema (58.5%), oral lesions (48.5%), dysgeusia (27.84%) followed by the sore throat (25.43%) followed by. The other common symptoms are and oral bleeding (22.95%).

Discussion

The present systematic review was to find the prevalence of oral manifestations and to suggest the management to those affected with COVID-19. The results based on 10 papers show that sore throat and dysgeusia are the most common oral manifestations. The others include enanthema, oral lesions and bleeding.

Sore throat

Though sore throat is very common, it can be the result of a non-serious illness to a dangerous one. Sore throat as a sole symptom can be rare as only 5-10% of COVID-19 patients have it, when in other cases, it is accompanied by other symptoms (Harris, 2021).

Dysgeusia

Dysgeusia which is the distortion of the sense of taste can be caused by numerous medical conditions like heart disease, Alzheimer's disease, upper respiratory viral infection, etc. (Lozada-Nur, Chainani-Wu, Fortuna & Sroussi, 2020). Zahra, Iddawela, Pillai, et al., (2020) found that symptoms of dysgeusia are not enough to diagnose an individual with COVID-19, even though it is frequently reported. But if dysgeusia is present for a longer duration, it could lead to an increase in the severity of COVID-19.

Enanthema

Enanthema or enanthen is the result of viral infections causing rashes or spots on the mucous membranes. The cause of the symptom might be due to different diseases like chickenpox, measles, hand-foot, and mouth disease, and also COVID-19. Considering the short time in which some COVID-19 patients show enanthema, the symptom suggests a strong association with the virus (Lubell, 2020).

Oral lesions and bleeding

Oral lesions, gingival inflammation and bleeding or simply are suggested to be the result of the inflammation initiated by COVID-19 (Froum, 2020). Whereas there are also claims that these manifestations are not the result of viral infection but rather a secondary infection caused by the deteriorating health or medications used for COVID-19 treatment. (Dos Santos, Normando, da Silva, et al., 2020).

Fungal infections

A few cases were reported related to fungal infection, mostly mucor mycosis as a post covid manifestation. It was mainly found in patients with altered immunity and in patients with pre-existing immunosuppression.

Management

General manifestations are managed by: Broad spectrum systemic antibiotics (ceftriaxone, doxycycline), antivirals (oseltamivir, favipiravir, remdesivir), antihistamines (Diphenhydramine). The use of fluticasone nasal spray and triamcinolone medications were found to be helpful in the recovery of smell and taste sensation within a week (Singh, Jain & Parveen, 2021).

Iranmanesh, et al., (2020), Halboub, et al., (2020), and Corchuelo & Ulloa (2020) observed the various management protocols for oral manifestation of COVID 19 and found that chlorhexidine, an antiseptic mouthwash, is effectively used to reduce the gingival inflammation. Other managements involves application topical or systemic corticosteroids, benzalkonium chloride mouth rinses, normal saline gargling, use of artificial saliva, topical antifungals (nystatin, oral fluconazole), topical anesthetics (benzocaine 5% gel).

Conclusion

Even though enough researches are required to establish a relationship between the oral manifestation and COVID-19, looking out for the oral symptoms might also play a vital role in the timely

diagnosis of COVID-19. The surge in the oral manifestations among COVID-19 patients might be the result of the direct effect of virus in the oral cavity, due to secondary infection as a result of compromised immunity or due to adverse reaction of medications used. Therefore, it is important to include dentists in the multi-disciplinary team assisting the COVID-19 patients so that the clinical dental examination could be accentuated, considering the requirement for support and pain control for the patient and thereby improving their quality of life.

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