



Oral Findings in Patients with COVID-19 Infection: Report of Two Cases and Review of Literature

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Few reports have been published highlighting oral findings in COVID-19 patients. Since the outbreak of the recent pandemic caused by SARS-CoV-2, it is important to illustrate in the very near future how recurrent these oral findings are in the symptomatic COVID-19 patients in contrast to those asymptomatic ones, as there are multiple findings reported. This case study reports a new combination of oral findings in two COVID-19 patients from India, one symptomatic, and other asymptomatic. Cases presenting oral findings in asymptomatic COVID-19 patients are the rarest. Moreover, till now, petechial or purpuric lesions, solely as the oral findings without any associated skin lesions and oral mucosal hyperpigmentation of our patients are the rare oral findings to be reported in COVID-19 patients. These cases provide evidence for a deeper understanding of the oral alterations seen in COVID-19 patients that need to be addressed at present.

Keywords: COVID-19; oral manifestations; SARS-CoV- 2; petechiae; purpura.

1. INTRODUCTION

Coronavirus Disease 2019 (COVID-19), is an ongoing pandemic which has spread to the whole world. It is an illness caused by the novel Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) which is the seventh type of coronavirus family to affect humans. According to WHO, the most probable diagnostic clinical features are- fever, cough, and an acute respiratory infection, which spreads from human to human via droplet transmission and direct contact with oral, nasal, and eye mucosal membranes [1].

The virus has been reported to dysregulate immune mechanisms. Till now, only a few reports have been published in the literature emphasizing on the oral findings in these patients like ulcerations, blisters, gingivitis, dysgeusia, fungal co-infections, halitosis, xerostomia associated with reduced saliva secretion, erythema, dry mouth etc.

We describe two cases of COVID -19 patients from India. The main objective of this article is to report a new combination of oral manifestations in two COVID-19 patients (one symptomatic and the other asymptomatic).

2. CASE PRESENTATION

2.1 Patient 1

A 70-year-old male patient from India, complained of fever with progressive cough and shortness of breath. He was confirmed COVID-19 positive after testing reverse-transcription polymerase chain reaction (RT-PCR). The patient's SpO₂ was 74-75%, advised nasal cannula (60 l/min, 60% O₂) and a treatment course of ramdesivir (100 mg IV), favipiravir (400 mg), paracetamol (650 mg), atorvastatin (20 mg PO), clexane (prophylactic dose- 60 mg I.V), pantoprazole (40 mg), vitamin C (8000 mg), vit E and zinc supplementations (50 mg) after getting admitted in a tertiary care hospital in Delhi, India. The patient was healthy before this infection.

After two days of hospitalization, the patient complained of burning sensation all over the mouth during eating. After taking written consent from the patient, oral examination was done. White membranous plaques were found on the

left buccal mucosa and posterior part of the hard palate .The provisional diagnosis for these white lesions was made to be oral candidiasis as clinically these lesions were scrappable and left erythematous areas behind after scrapping (Fig. 1C). Use of chlorhexidine mouthrinses (0.2%), twice daily was advised to the patient. With this, small reddish vesiculobullous lesions were also present on the buccal mucosa. (Fig. 1C) for which patient was advised Anabel Ir 0.2% (choline salicylate) and lidocaine gel for topical application 3-4 times a day. Also, small hemorrhagic lesions, suggestive of petechiae or purpuric spots were found on the upper and lower labial mucosa (Fig. 1A & B). Patient was an upper denture wearer for the past 6 years. Patient's RT-PCR on the 10th day of hospitalization was negative. Follow-up after two weeks (Fig. 1D, E, F) and three weeks after negative RT-PCR (Fig. 1-G, H, I) revealed that white plaques were resolved and hemorrhagic lesions were reduced in number.

2.2 Patient 2

A 64 year-old-female, tested COVID-19 positive on being tested by a nasopharyngeal and oral swab following RT-PCR for SARS CoV-2 RNA amplification. Commenting on the general health, the patient was healthy before this infection and was not on any long-term medications. She was in direct contact with the first patient but did not present any symptoms. This patient underwent all the investigations similar to patient 1, but the findings were within normal range. The patient was advised a similar course of treatment except for antivirals – ramidesivir and favipiravir. She was hospitalized for observation and isolation. On day-3 of hospitalization, oral examination revealed presence of a pale ulcer, 2-3 mm in diameter on the lower labial mucosa (Fig. 2-B). The patient 2 reported complaint of burning sensation after having any kind of oral intake after getting admitted in the hospital . Clinically ,there were no signs of candidiasis . Also, in the oral cavity, there was pigmentation present on buccal mucosa and soft palate (Fig. 2-A). Resolution of the ulcer without any scarring can be appreciated on labial mucosa, two weeks after repeating RT-PCR for (Fig. 2-C, D) COVID-19 infection was negative. Patient was on follow-up for three weeks after negative RT-PCR to check for the complete resolution of lesions (Fig. 2-E, F).

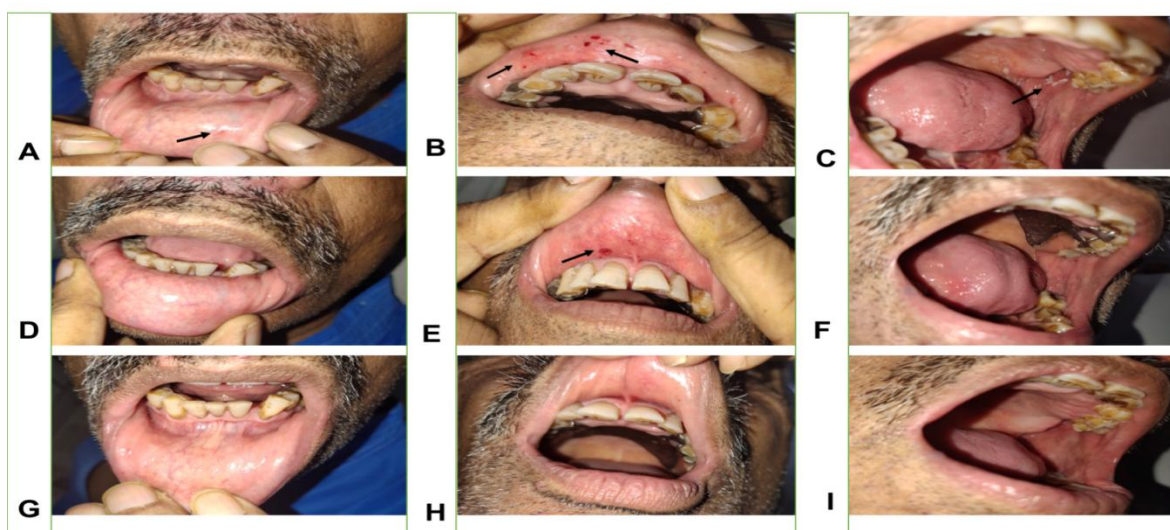


Fig. 1. Clinical pictures of oral manifestations of COVID-19 in patient 1 (A&B) – petechiae and purpuric lesions on labial mucosa. (C) – Candidal lesions and blisters on left buccal mucosa. (D,E,F) – resolving lesions on labial and buccal mucosa, 2 weeks after negative RT-PCR. (G,H,I) – resolved lesions, 3 weeks after negative RT-PCR

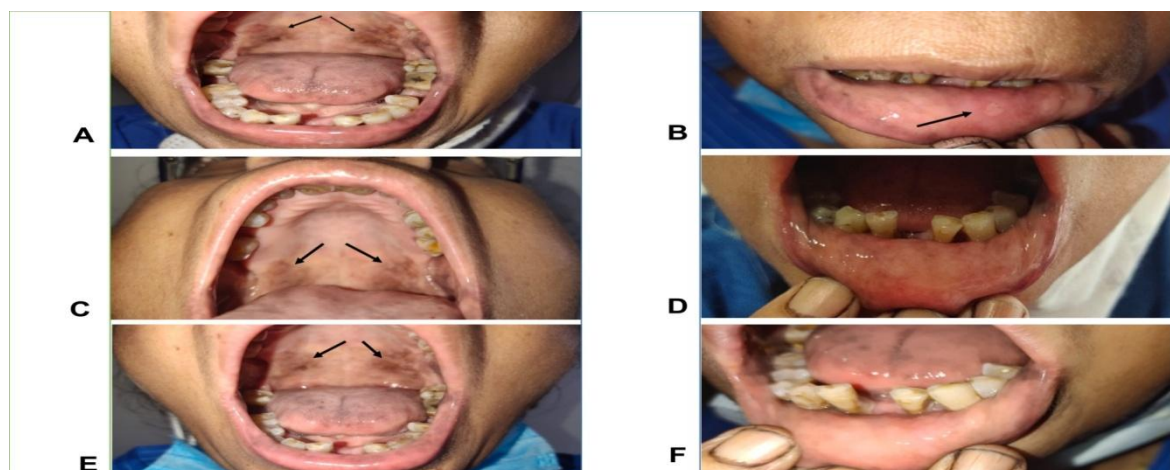


Fig. 2. Clinical pictures of oral manifestations of COVID-19 in patient 2. (A)- Brownish hyper pigmentation in palatal region. (B)- Ulcer or blister on lower labial mucosa. (C)- Slight reduction in palatal hyper-pigmentation, 2 weeks after negative RT-PCR. (D)– Healing of ulcer without any scarring, 2 weeks after negative RT-PCR. (E)- further reduction in palatal hyper pigmentation, 3 weeks after negative RT-PCR. (F)- Healthy lower labial mucosa,3 weeks after negative RT-PCR

3. DISCUSSION

The total number of reports on oral findings in COVID-19 patients suggests that the oral lesions associated with this disease are common manifestations (e.g. candidal lesions, ulcers etc) which may be seen as a secondary effect of therapeutic treatment given to the patients. Therefore, cases of associated oral findings are reported less in number. This could also be possible due to a lack of intraoral examinations

because of the recommended protective measures for SARS-CoV-2 infections. Dysgeusia is the only well-known recorded oral manifestation of COVID-19 infection in the literature.

Studies reporting oral manifestations of COVID-19 infections are limited. Table 1 presents a comprehensive list of all reported oral findings till date. All the mentioned studies in the table suggested various etiologies for the occurrence

of these oral findings involving both the keratinized and non keratinized mucosa of the oral cavity like cytokine storms due to COVID-19, immunocompromised states, co-infections, undergoing variety of drugs treatment and other viral etiologies, e.g. study by Ansari et al. reported role of COVID-19 infection for the occurrence of oral lesions in COVID-19 patients [6].

3.1 Petechial or Purpuric Lesions

In Patient 1, rare oral finding in COVID-19 patients was found on the upper and lower labial mucosa, i.e. small rounded reddish petechiae and purpuric lesions without any other mucocutaneous manifestations on the body, suggestive of having a recent viral infection like COVID-19 infection. Petechiae in febrile conditions, and milder forms of thrombocytopenia are commonly found in viral infections, and have also been mentioned in 36% of COVID-19 patients [13,14,15].

The patient was on a prophylactic-dose of Clexane, a low molecular weight heparin (LMWH). So, this could also be a drug reaction and a cause for thrombocytopenia leading to oral petechiae and purpuric lesions. However, these lesions started to disappear much before the prescribed medicine (LMWH) was stopped giving to the patient. A study on the occurrence of enanthems in COVID -19 patients, suggests that these types of spots are associated more with viral etiology rather than an adverse drug reaction [9]. But that study reported the palatal enanthems along with other dermatological manifestations like skin rash on the bodies which were not observed in our patient.

3.2 Oral Candidiasis

Pseudo-membranous white plaques on left buccal mucosal lining in patient 1 suggest fungal infection- candidiasis, may be due to dysregulated immune system. Oropharyngeal candidiasis(OPC) was reported in hospitalized COVID -19 patients within 8 days of onset of this disease [11]. On the other hand, study by Abanoub Riad et al., it has been mentioned that most of the reported candidiasis cases in COVID-19 patients are the oral white pseudo membranous plaques that extend over the regions like oral mucosa, tongue etc. and these lesions can start occurring from day 1 since COVID-19 symptoms emergence [16]. Broad-spectrum antibiotics, ICU admission,

lymphocytopenia, mechanical ventilation and systemic corticosteroids are the potential risk factors for hospitalized COVID-19 patients to develop OPC.

Chronic denture use could be linked to candidal lesions. However, in patient 1, these lesions resolved in 14 days when the patient turned COVID-19 negative, suggesting that the candidal lesions may not have been due to denture wearing. The whitish plaques resolved after the patient turned negative for the infection, suggesting that the candidal lesions may not have been due to denture wearing. However, it must be noted that these lesions resolved after giving oral hygiene instructions to the patient about the usage of chlorhexidine mouthwash 0.2%, twice daily. The patient was also observed for signs of improvement. The resolution of these lesions could also be due to antioxidants like vit C and vit E, which are believed to be effective in reducing the production of cytokines storm in COVID-19 patients. Clinical studies and reports demonstrate that prompt administration of high-dose i.v. Vit-C improves the outcome of COVID-19 infection. Moreover, it has been documented that vitamin C boosts immunity by keeping high levels of disease-fighting white blood cells in the body, so that the body can fight against infections, especially opportunistic ones such as candidiasis.

3.3 Burning Sensations, Dry Mouth and Dysgeusia

Both the patients reported burning sensations during eating along with dryness in mouth which supports the study conducted in COVID -19 patients assessing the first symptoms of olfactory and taste functions [10] as 51.4% of the patients experienced dry mouth which had a strong association with burning sensations in mouth, although the exact cause for these burning sensations is not known. However, there was no diffuse enanthem or depapillation of tongue and no lesion on palate in both of our patients.

The patients also experienced altered taste sensations (dysgeusia) possibly due to the suggested mechanism of SARS-CoV-2 i.e. the virus can bind angiotensin-converting enzyme -2 receptor expressing cells which may act as target cells for its entry, and is readily expressed in the epithelial cells of tongue surface more than the other parts of oral cavity, causing alteration in taste sensations [17].

Table 1. Reported oral manifestations, associated with COVID-19 infection

	Authors	Location at which the study was conducted	Age , gender	SARS CoV-2 Status	Any associated co-morbidities	Reported Oral manifestation	Suspected Aetiology	Skin Manifestation
1.	Chaux-Bodard et al. [2]	France	45, female	Positive	-	Ulcer on the dorsal aspect of tongue following reddish macule.	Viral aetiology	Erythematous lesion on big toe.
2.	Carrera-Presas et al. [3]	Spain	56, male	Suspected	-	1. Complained sore throat 2. Herpetic like ulcers causing pain in palate.		No skin lesions
3.	Carrera-Presas et al. [3]	Spain	58, male	Suspected	Diabetes and Hypertension	1. Pain in palate 2.Unilateral presence of ulcers surrounded by erythematous halo on hard palate.		No skin lesions
4.	Carrera-Presas et al. [3]	Spain	65, female	Positive	Obesity and Hypertension (controlled).	1. Desquamative gingivitis. 2. Blisters in the lower labial mucosa. 3.Complained tongue pain	Viral aetiology	Rashes were reported under the breasts, back and genital areas.
5.	Patel and Wooley [4]	England	35, female	Suspected	-	1.Erythematous , edematous gingivae 2.Necrotic interdental papillae 3.Severe halitosis. 4.Complained pain in gingiva.	Necrotizing Gingivitis	No skin lesions
6.	Kahraman and Çaşkurlu [5]	Turkey	51, male	Positive	-	1.Erythematous surface in the oropharynx and on hard palate. 2.Petechiae and numerous pustular enanthen near the soft palatal region. 3.Complained sore throat	--	Not mentioned
7.	Ansari et al. [6]	Iran	75, male	Positive	Hypertension	On tongue, irregularly margined ulcers in non-hemorrhagic red background.	Viral aetiology	No skin lesions
8.	Ansari et al. [6]	Iran	56, female	Positive	Diabetes mellitus	On almost entire palate, irregular ulcers in non-haemorrhagic red background	Viral aetiology	No skin lesions

	Authors	Location at which the study was conducted	Age , gender	SARS CoV-2 Status	Any associated co-morbidities	Reported Oral manifestation	Suspected Aetiology	Skin Manifestation
9.	Ciccarese et al. [7]	Italy	19, Female	Positive	-	1.Lesions on lips- erosions, ulcerations and blood crusts. 2. Palatal and gingival petechial lesions.	-	Erythematous macules, papules and petechiae on the lower extremities of the body.
10.	Soares et al. [8]	Brazil	42, male	Positive	Diabetes and Hypertension	1.Ulcers in buccal mucosa. 2.Macules (reddish) on hard palate, tongue and lips.	Viral aetiology	1. Petechiae- like and small sized vesiculobullous lesions
11.	Juan Jimenez-Cauhe et al. [9]	Spain	21 patients (Age between 40-60)	Positive		Macular enanthem in one patient, petechial in two patients, and macular-petechial in three patients, located in the palatal region.	Infectious aetiology, most frequently viral	Skin rashes were present in form of papulovesicular, purpuric periferle xural and erythema multiforme like.
12.	SaygoTomo et al. [10]	Brazil	37 , female	Positive	-	1.Complained burning sensations and dysgeusia. 2. Dry Mouth 3.Painful Bilateral erythema(diffused)and depapillation in the tongue.	Oral mucositis	No skin lesions
13.	M. Salehi et al. [11]	Iran	-	Positive	Cardiovascular Disease (52.8%) and Diabetes (37.7%)	Oropharyngeal candidiasis(OPC) in 53 COVID 19 positive patients with or without the complaints of dry mouth and glossalgia.	Oropharyngeal Candidiasis	No skin lesions
14.	Santos et al. [12]	Brazil	67, male	Positive	1.Revascularise d coronary artery disease 2. Hypertension 3. Polycystic kidney disease with history of kidney transplant.	1.White colored plaques and numerous yellowish small ulcers in the tongue dorsum resembling of herpetic recurrents late stage with candidiasis. 2.Complained hypogeusia.	Saccharomyces cerevisiae infection	No skin lesions

	Authors	Location at which the study was conducted	Age , gender	SARS CoV-2 Status	Any associated co-morbidities	Reported Oral manifestation	Suspected Aetiology	Skin Manifestation
15.	Present Study	India	70, male	Positive	-	1.White pseudomembranous plaques suggestive of candidiasis on the buccal mucosa. 2.Petechial and purpuric lesions on upper and lower labial mucosa. 3. Complained burning sensations and dysgeusia. 4.Blisters or ulcers on buccal mucosa. 5. Dry Mouth.	Viral aetiology	No skin lesions
16.	Present study	India	64, female	Positive	-	1. Blister or ulcer present on lower labial mucosa. 2.Pigmentation on the soft palate and buccal mucosa. 3.Complained burning sensation and dysgeusia. 4. Dry Mouth.	-	No skin lesions

3.4 Vesiculobullous Lesions

Patient 1 presented with upper labial ulceration, also on the left buccal mucosa while a blister was on the lower labial mucosa in Patient 2. Oral ulcerations have been reported in several studies in COVID-19 patients. Moreover, the histology of an ulceration in a COVID-19 patient, after excluding all other etiologies, suggested that it may be a primary reaction to the SARS-CoV-2.

Similarly, Dominguez Santas M et.al. also held COVID-19 responsible for the occurrence of minor aphthous in four COVID-19 patients of age 19, 37, 33 and 43 years old having a latency period of 0, 5, 3, and 4 days, respectively, from COVID-19 symptoms onset [18]. The researcher group also excluded other potential causes for these oral findings in all the patients by doing serological testing. Psychosocial stress should also not be neglected while assessing these oral ulcers. Therefore, all patients positive for this virus should have a complete oral examination to better understand these oral alterations.

3.5 Mucosal Pigmentation

Oral mucosal hyperpigmentation was another finding in patient 2, which should be linked with post-inflammatory pigmentation. SARS CoV-2 has the potential to damage cells of oral mucosa, further causing inflammatory reactions like cytokine surge in which the serum levels of inflammatory mediators such as IFN- γ , IP-10, TNF- α , IL-15 and IL-1 β are increased [17]. This might be the chief reason for increased mucosal discoloration in these patients, especially if there is a presence of comorbidities. Drug reactions should also be considered as a cause for mucosal hyperpigmentation. However, pigmentation was markedly reduced than earlier in later follow-ups (Fig. 2A). So, the incidence of this finding could be more likely to be post-inflammatory pigmentation after SARS-CoV-2 infection.

4. CONCLUSION

Cases presenting oral findings associated with asymptomatic COVID-19 patients are the rarest in the literature. Oral ulcers or blisters have been reported in more than half of the cases. For suspected diagnosis, more than 43% of the reported cases suggest the viral etiologies like SARS-CoV-2 virus could be held responsible for

the occurrence of these oral lesions. Pre-existing comorbidities can also be ruled out as causative factors of oral lesions as nearly half the reported cases presented with co-morbidities like diabetes and hypertension. Cells with ACE-2 receptor distribution can become host cells for the SARS-CoV-2 virus and further cause various reactions in the cells of the oral cavity [17].

Thus, we are reporting these oral findings in the COVID-19 patients and conclude with that (i) These cases provide the dental professionals with comprehensive information about the oral findings seen in COVID-19 patients and emphasize on the importance of intraoral examinations in these patients (ii) Co-infections, lack of oral hygiene, impairment in immunity, variety of drug reactions alone or aggravated in viral infection like COVID-19 and hyper-inflammatory response after COVID-19 infection need to be considered while evaluating these type of findings in the COVID-19 patients. (iii) Also, the collection of these findings to update the community rapidly is important, as well as these findings are still new in the literature and their exact association with COVID-19 is currently unclear.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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