

Oral Findings in Institutionalized COVID-19 Patients- A Preliminary Survey

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Abstract

Original Research Article

Introduction: Since its discovery in December 2019 in Wuhan, China, the SARS-CoV-2 virus has rapidly spread the world over. Much research involving the virus, disease and its pathogenesis is now published. However, apart from some case studies, there is no large scale reporting done of the oral findings in patients infected by the virus. **Aims:** To record the oral soft tissue findings, report significant or peculiar findings, if any, and correlate laboratory and clinical findings, in patients suffering from Covid-19 disease. **Methods and material:** 101 COVID -19 patients admitted at a tertiary healthcare and medical teaching institute were clinically examined by a trained single investigator (House officer from the department of Dentistry of LTMMC & LTMGH, Sion Mumbai) in September 2020. **Results:** Thirty-nine patients had oral findings. A majority (twenty-two) had ulcers, seven showed signs of inflammation of their oral mucosa, five had white oral mucosal patches, three had bald tongues, four had angular cheilitis, and two patients had spontaneous bleeding due to oral lesions. Eight patients also had atypical ulcers, mostly on their tongue. These ulcers have, to the best of our knowledge, not yet been reported elsewhere. They could be a manifestation of COVID -19 infections, and the topic of further research. **Discussion:** COVID-19 patients do exhibit certain oral signs and symptoms, with majority on the tongue.

Keywords: COVID-19, oral findings, ulcers.

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1. INTRODUCTION

The first case of COVID-19 infection (caused by the SARS-CoV-2 virus) in India was reported in Kerala on 30th January, 2020. At the time of writing this article, India stands at over 1 crore total cases.

COVID-19 mainly presents as a respiratory tract infection, but the virus affects other systems too. Among the common oral symptoms are chemosensory changes (anosmia and dysgeusia) [1].

Since the start of the pandemic, much research has been done on COVID-19. Some case reports and literature do mention oral signs and symptoms [2, 3]. However, no large scale study has been done to identify the oral findings in confirmed COVID-19 patients in

India. Hence, we conducted a preliminary survey in Mumbai, India.

Our aim was to identify the oral findings in patients infected with SARS-CoV-2 virus, if any, and analyze any correlation between laboratory findings and clinical findings in the oral cavity.

2. MATERIALS AND METHODS

Using the formula $n = N/1 + N(n)^2$ where n is the sample size and N is the total population, which in this case was the total number of COVID+ve patients admitted at Lokmanya Tilak Municipal Medical Hospital, Mumbai, we arrived at a sample size of ninety- eight patients. The confidence interval was kept at 90% with a 10% margin of error. The study was carried out from 8th through 15th September, 2020.

After obtaining the permission of the IEC of LTMMC & LTMGH, 112 patients admitted in the isolated COVID wards and COVID Intensive Care Unit at Lokmanya Tilak Municipal Medical College & Hospital in Mumbai, India were identified for the study from amongst all patients admitted with the disease in various areas. These patients were explained about the survey in a language they understood and given a chance to ask questions before their written informed consent were sought.

The patient's demographic details (name, age, gender, occupation, address, phone number) were noted. Their medical history was taken to check for any comorbidity. They were then asked if they had any oral symptoms prior to examination.

The hard and soft palate, buccal mucosa, lips, gingiva, tongue, floor of the mouth, tonsillar pillars and oropharynx were thoroughly examined by the trained investigator (House officer from the department of Dentistry of LTMMC & LTMGH, Sion, Mumbai).

The oral examination focused on soft tissue findings, as those were expected to be more relevant, given the viral infection, and prior review of literature [2-5]. Each patient's oxygen requirement status, cytokines, as well as medications were noted.

3. RESULTS

Of the one hundred and twelve patients identified, one hundred and one consented to participate in the survey. There were sixty-one males and forty females [Table 1]. Two patients were below 18 years of age, eight were 18-25 years, nineteen were 25-35 years, fifteen were 35-45 years, thirty-seven were 45-60 years, and twenty were above the age of 60 [Table 2].

Twelve patients were admitted to the Intensive Care Unit, the remaining were in the wards. Forty-two patients were judged to have mild COVID disease severity, forty-four had moderate, and fifteen had severe disease severity [Table 3]. This was judged based on their CORAD score, COVID score on CT scan, and clinical and laboratory findings. The CORAD and COVID scores are both determined after examining the HRCT scan of a patient. (The CORAD and COVID scores are both determined after examining the HRCT scan of a patient. The CORAD score is given from 1 to 6, with increasing score denoting higher suspicion of COVID-19 infection. The COVID score is from 1 to 25, with 5 points for each lobe of the lung. Each lobe is scored according to the extent of involvement, with 5 being the highest involvement for that lobe. The scores for 5 lobes are then totalled to give the COVID score).

Laboratory investigations including CRP and D-Dimer levels, LDH and Serum Ferritin and Interleukin- 6 were raised in all patients in the study.

Sixty-two patients had no obvious oral signs while thirty-nine did [Table 4]. Of these thirty-nine, a majority (twenty two patients) had ulcers [Table 5]. Four had traumatic ulcers attributable to sharp teeth and lip biting habits.

Nine patients had what appeared to be minor aphthous ulcers on the gingiva, tongue, corner of the mouth and lip [Figures 1 and 2]. These patients gave prior history of mouth ulcers.

One patient appeared to have herpetic ulcers in the corner of the mouth and the lower lip [Figure 3]. This patient gave prior history of the ulcers appearing along with fever.

One patient appeared to have a drug induced ulcer on the lateral border of the tongue. This ulcer was symptomatic, and the patient also complained of a burning mouth [Figure 4]. The patient was given Ivermectin, Doxycycline, Favipiravir, Methyl Prednisolone, and Metered dose inhaler of Budesonide, Aspirin, Azithromycin, Enalapril, Low Molecular Weight Heparin, Vitamin B complex, Vitamin C, and Zinc.

Nine patients had ulcers that appeared to have no etiology or attributable cause [Figures 5, 6, 7, 8]. Four of these did not complain of the ulcers when asked initially, but when the ulcer was noted on examination, gave history of ulcer appearing with the initial symptoms of COVID-19, or on hospitalization. Two patients had completely asymptomatic ulcers in the pharyngeal region. Three patients were symptomatic and aware of the ulcers.

These ulcers were mostly regular, oval to circular in shape, along the lateral border of the tongue, or oropharynx with white slough at the base, mild induration, and mostly with an inflammatory halo surrounding them.

Four patients presented with single ulcers, while five presented with multiple. There was no common medication or finding among all of the patients who presented with this kind of ulcer.

Seven patients showed signs of inflammation of their oral soft tissues [Figure 9], of which two were generalized, while five were localized- two patients had tonsillitis, two had an erythematous, inflamed red patch in the buccal sulcus (one of these patients had a tobacco chewing habit) [Figure 10]. One patient had an erythematous bald tongue.

Three patients' mucosa appeared pale clinically; Hb was not evaluated using lab tests. Four patients had angular cheilitis [Figure 11].

Five patients had white patches on their mucosa, of which one was suggestive of oral candidiasis [Figure 12], and four were non scrapable [Figures 13 and 14]. Two of these were due to traumatic cheek bite, the other two needed to be further investigated.

Two patients demonstrated spontaneous bleeding due to oral lesions on their lips and tongue, gingiva and buccal mucosa [Figure 15].

Three patients had a bald tongue with evident depapillation [Figures 16 and 17]. Three patients had intra-oral swelling. One was due to inflammation in the gingiva of the lower anteriors leading to swelling of the interdental and papillary gingiva as well as bleeding and loss of attachment in a diabetic patient, the second patient had a swelling on his lower right posterior alveolar ridge, and one patient had a gingival swelling with respect to decayed upper first molar. All these swellings were symptomatic, and reported by the patients themselves prior to oral examination.

One patient had a yellowish discoloration in the floor of his mouth. This patient gave a history of alcoholic liver disease and viral hepatitis in the past [Figure 18].

One patient complained of edema in lips concurrent with Ritonavir medication. One patient reported burning mouth after starting Favipiravir, which subsided on stopping the medication, and improved in a few days, when he was given Methylprednisolone injections. On examination of this patient, no ulcers were found, but areas of redness could be appreciated on the lower lip.

Apart from the thirty-nine who showed oral signs, nineteen other patients complained of burning mouth or xerostomia.

A majority of the lesions examined were on the tongue, followed by the lips, angle of mouth, gingiva and buccal mucosa, oropharynx, palate and buccal sulci, and alveolus and floor of the mouth [Table 6].

Of the patients presenting oral signs and symptoms, thirteen patients had mild disease severity, nineteen had moderate, and seven had severe COVID disease severity. Hence, we observe with increasing disease severity, the chances of oral signs and symptoms presenting increase. No strong correlation was noted with raised cytokines and CRP levels and oral signs.

Table-1: Gender distribution among sample population

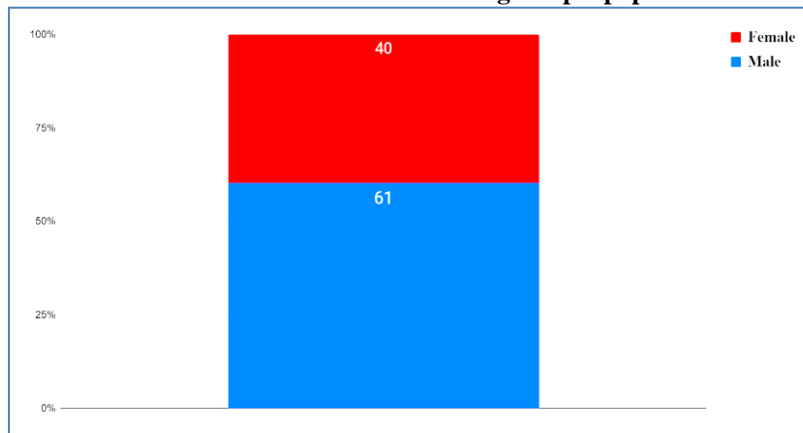


Table-2: Age distribution of participants

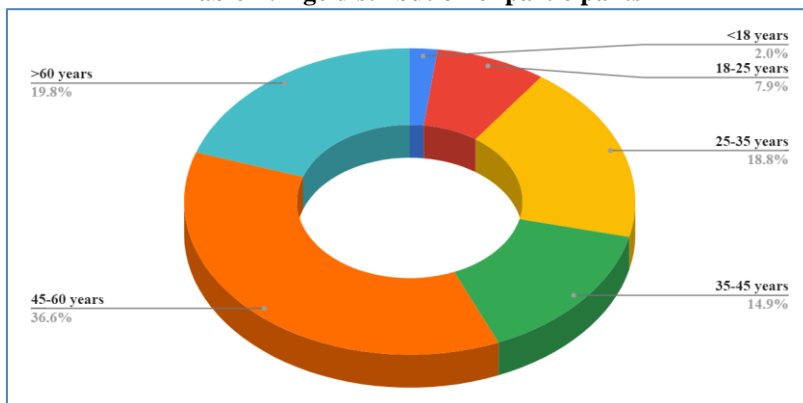


Table-3: COVID severity of participants

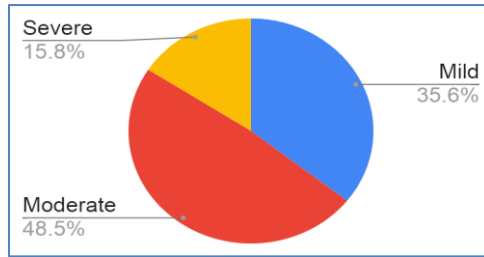


Table-4: Oral signs observed in participants

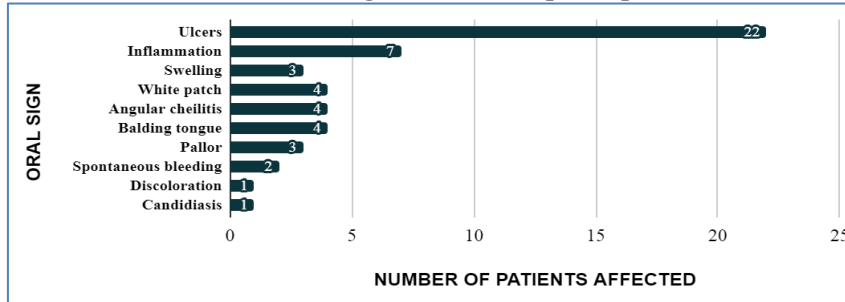


Table-5: Types of ulcers seen in COVID-19 patients

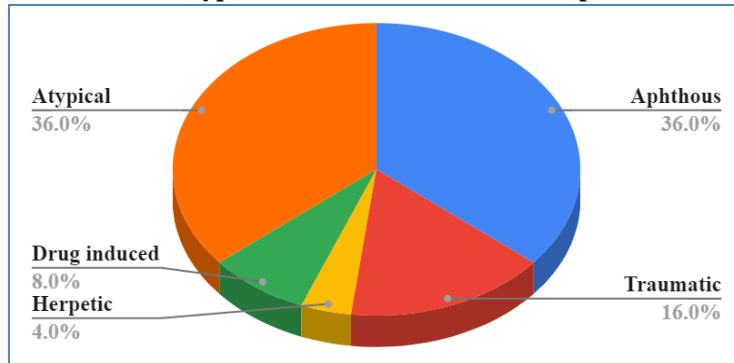


Table-6: Number of lesions observed per area examined in the participants CLINICAL PICTURES

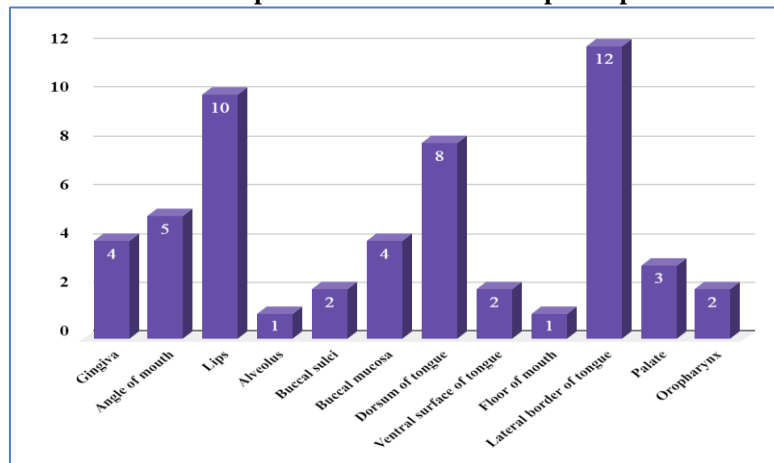




Fig-1: Minor aphthous ulcers along the lateral border and ventral surface of tongue



Fig-4: Drug induced ulcer on the right lateral border of tongue



Fig-2: Minor aphthous ulcer on the left lateral border of tongue



Fig-5: Atypical ulcer on left ventral surface and lateral border of tongue



Fig-3: Recurrent herpes labialis in the right corner of the mouth and lower lip



Fig-6: Atypical ulcer along right lateral border, ventral surface and dorsum of tongue

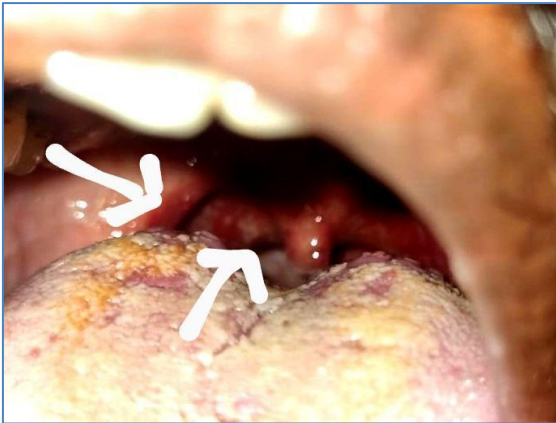


Fig-7: Atypical ulcer and inflammation in the oropharynx



Fig-11: Angular cheilitis



Fig-8: Atypical ulcer in the oropharynx

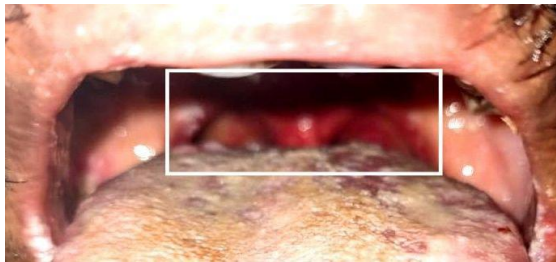


Fig-9: Inflammation of tonsillar pillars



Fig-12: Scrapable white lesion suggestive of candidiasis on the palate and buccal mucosa

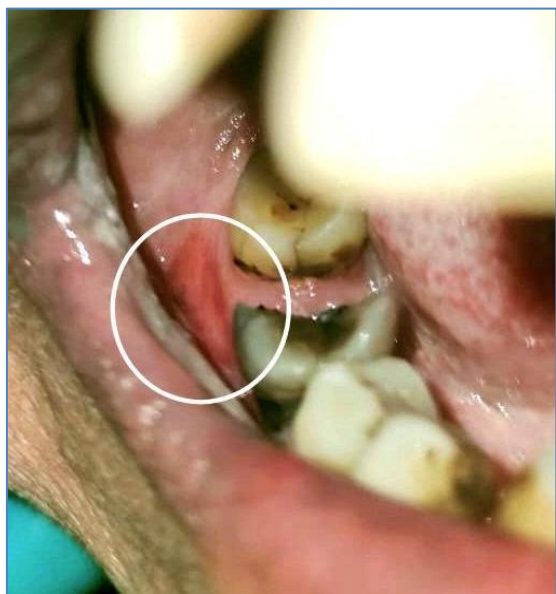


Fig-10: Erythematous, inflamed patch in buccal sulcus of patient with tobacco chewing habit

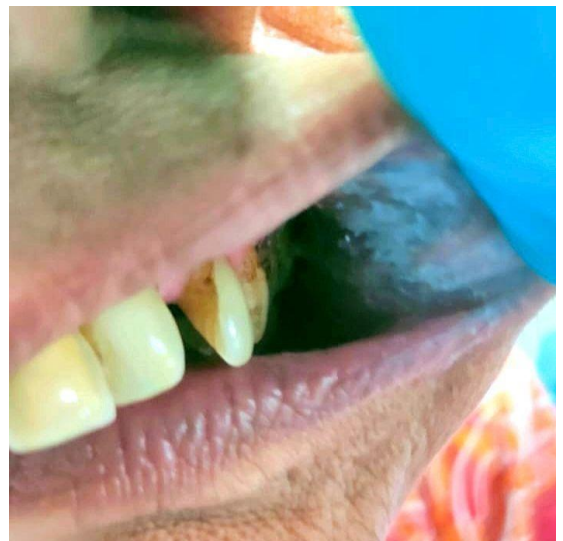


Fig-13: White patch on buccal mucosa



Fig-14: White patch in buccal sulcus

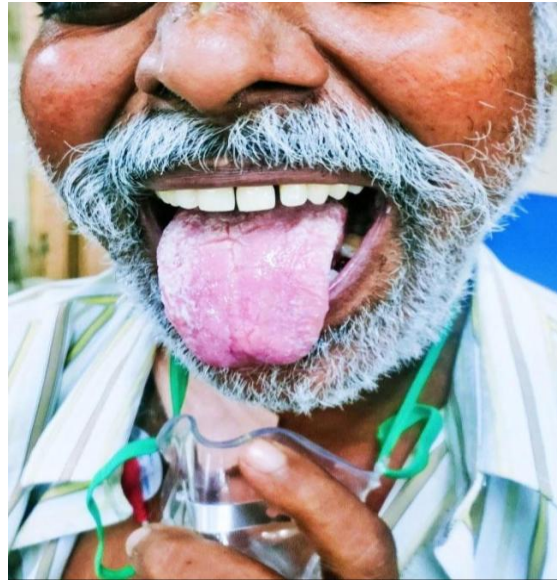


Fig-17: Depapillation on dorsum of tongue in a patient with suspected candidiasis



Fig-15: Spontaneous bleeding from lesions on tongue, gingiva and buccal mucosa

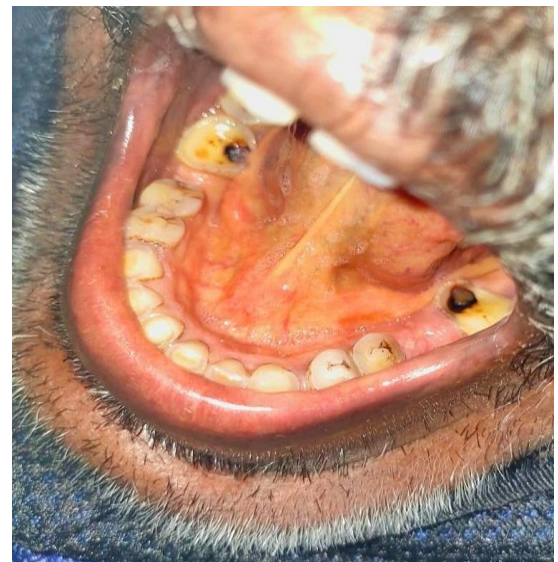


Fig-18: Yellowish discoloration of floor of the mouth in a patient suffering from jaundice

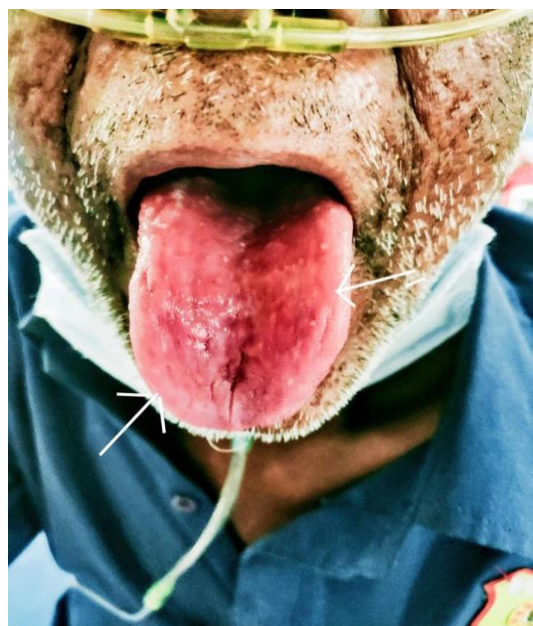


Fig-16: Depapillated bald tongue

4. DISCUSSION

SARS-CoV-2 has a plethora of effects on various body systems. The cytokine storm is well established and researched. Patients that we examined had elevated levels of the following cytokines.

1. CRP, an acute phase protein produced by the liver in response to inflammation
2. D-Dimer, a fibrin degradation product (or FDP)- a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It indicates activation of the coagulation cascade. The presence of elevated D-Dimer levels in COVID could indicate pulmonary embolism, increased risk of disseminated intravascular coagulation, or a hypercoagulable state.

3. Ferritin, an acute phase reactant which, if elevated, indicates a state of inflammation.
4. Interleukin-6, a nonspecific inflammatory marker that could indicate an ongoing inflammatory response.
5. Lactate dehydrogenase (LDH), an enzyme required during the process of turning sugar into energy for your cells. LDH is present in many kinds of organs and tissues throughout the body, including the liver, heart, pancreas, kidneys, skeletal muscles, lymph tissue, and blood cells. High levels of LDH in the blood point to acute or chronic cell damage.

Previous reviews of literature suggest that oral manifestations in COVID-19 patients could be due to the cytokine storm; however we found no strong correlation between elevated cytokines and oral signs. In fact, some patients with oral signs did not have remarkably raised levels of cytokines.

The results clearly suggest that a large number of symptomatic COVID patients also present oral signs, with increasing occurrence in severe cases.

The impact of the coronavirus infection on oral soft tissues seems to be attributable to a number of causes. Patients diagnosed with COVID-19 experience psychological [6] as well as neuroendocrine [7] mediated stress [6, 7], anxiety and insomnia, which could be the cause of the aphthous ulcers observed in the patients. Recent studies show that the SARS-CoV-2 virus affects neurons [8] as well. This, coupled with stress, and immune suppression [9] (due to infection as well as corticosteroids given as part of the treatment) are known to reactivate herpetic lesions.

Some observed lesions might also be a result of the complex pharmacotherapy administered to patients. This explanation was mostly reinforced by the lesion observed, the history provided by the patient, and knowledge of what treatment they have undergone. Corticosteroids are known to cause immune suppression, and secondary fungal infections like candidiasis. One would expect a change in the oral microflora due to COVID and its pharmacotherapy. This, too, could lead to opportunistic infections.

A large number of patients showed poor oral hygiene, either because of personal neglect or restricted movement due to their need for supplemental oxygenation. This, coupled with xerostomia predisposes patients to oropharyngeal infections [10]. Xerostomia, interestingly, has also been linked to increased chances of acute respiratory infections [11].

It is now known that the SARS-CoV-2 virus attaches by its S protein to ACE2 receptors. Oral, pharyngeal and nasal epithelial cells also express this receptor [4, 5]. Literature suggests that of all oral epithelial cells, the expression of ACE2 is most in the

tongue [40]. A majority of the lesions we observed in our survey, especially depapillation and atypical ulcers, were on the lateral borders of the tongue. We noticed that a number of ulcers that were not attributable to any obvious cause were mostly on the tongue and oropharynx. These ulcers were mostly asymptomatic.

Further research and firm evidence would, however, be required to suggest a correlation between COVID-19 infection and these lesions, and validate our findings.

While taking history, in some cases, patients reported an inability to eat, or a lack of interest in eating. While this was mostly due to chemosensory changes (anosmia and dysgeusia) [1, 2] noted in COVID-19, some reported an inability to ingest food due to ulcers and dry mouth. Coupled with insomnia and sub-optimal mental health, dietary changes due to anorexia, or inability to consume food due to oral ulcers could further worsen the health of a patient.

If a large part of the infected population suffers from them (as we found in our survey), studying these signs could reveal more about COVID-19, the SARS-CoV-2 virus and the effect it has on the body. Hence, these oral signs and symptoms are of importance and worth taking a note of.

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