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Estimating the Prevalence of Oral Manifestations in Covid-19 Patients: A Systematic Review

By Dr. Ankita Gupta

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Methods: An extensive literature search of several electronic bibliographic databases (PubMed, Scopus, Science direct, Litcovid) was done to retrieve all articles published in the English language from January 1, 2020, to June 30, 2022, reporting the prevalence of oral manifestations among COVID-19 individuals.

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Results: Based on their eligibility, a total of 75studies comprising 11,321 patients were included. Most of the articles were published in the year 2020 (n=33) and were from Italy (n=13). Among the patients affected, most of them were in the range of more than 50 years and females (58.1%). Taste alteration (n=43; 57.3%) was found in most people followed by vesiculobullous lesions (n=41; 54.6%) and tongue manifestations (n=26; 34.6%). The most common sites of involvement in descending order were tongue (n=62), oral mucosa (n=27), lips (n=19), and others. In most of the studies, oral symptoms followed the general symptoms.

Conclusion: COVID-19 patients show various oral manifestations that may help clinicians for early identification of the disease. Recognition of signs and symptoms of COVID-19 is critical for early diagnosis and better prognosis.

Keywords: COVID-19, COVID tongue, oral ulcers, oral lesions, SARS-CoV-2.

I. Introduction

The novel Coronavirus 2019 disease (COVID-19) has become a global crisis and a challenge to public health owing to its fast rate of dissemination and increased mortality rate. Although the disease was first observed in December 2019 in the Hubei Province of China, soon it circulated hastily around the world. On March 2020, the disease has been declared as a 'pandemic emergency' by the World Health Organization. The outbreak is responsible for more than 608,328,548 confirmed cases and 6,501,469 deaths worldwide till September 2022 [1].

The incubation period of disease ranges from 1-14 days with fever, cough, shortness of breath or difficulty in breathing, or fatigue as the most common presenting symptoms. Less common features, such as headache, loss of taste or smell, sore throat, diarrhea, and nausea or vomiting, may also be present [2]. The severity of symptoms varies from person to person as it depends upon the time of exposure to the virus, the patient's age and gender as well as the coexisting diseases.

It was found that the coronavirus invades human cells with the help of receptors known as Angiotensin-converting enzyme 2 (ACE 2) and transmembrane protease serine 2 (also called transmembrane serine protease or TMPRSS2) [3]. Among these two, the ACE 2 receptor is found mainly in the cells of the lung, liver, kidney, gastrointestinal (GI) and even on the salivary glands and dorsum of the tongue of the oral cavity [4]. These cells with the receptors act as host cells for the virus through which, the virus invades these cells of the body and starts an inflammatory response in these organs.

Previously, it was assumed that COVID-19 lacks oral manifestations unlike other viral exanthema but after some years, SARS-CoV-2 was detected from the saliva of the patients suggesting a possibility that oral manifestations could be clinical characteristics of COVID-19. Also, the presence of the ACE 2 receptor in some specific organs of the oral cavity such as the tongue and salivary glands confirms the possibility of the involvement of the oral cavity in coronavirus infection. The frequency of oral manifestations among COVID-19 patients is unknown but some previous studies have tried to provide the incidence and prevalence of these manifestations. A huge study conducted by Nuno-Gonzalez on 666 patients suggests that oral cavity findings are present in 25.65% of cases [5]. The commonly occurring oral manifestations found in a case series conducted by Sinadinos and Shelswell were blisters, ulcerations, and desquamative gingivitis [6]. In the oral cavity, the most commonly involved sites in COVID-19 disease are the palate and tongue followed by the gums and the lips [7]. In the tongue, the ulcerations are quite common specifically on the dorsum surface or sides of the tongue. Rarely, only in 15% of patients, the ulcerations develop on the ventral surface [8]. Additionally, multiple pinpoint yellowish ulcers and white plaque can also be present on the tongue [3]. The occurrence of white plaque on the dorsal surface of the tongue is due to the occurrence of fungal infections which is also one of the common oral manifestations of SARS-CoV-2, probably caused by lower immunity. Dima et al reported a case of a neonate with COVID-19 having oral cavity candidiasis [9]. These oral manifestations are accompanied with pain in 75% of

Author: e-mail: ankitag@lnctrishiraj.ac

cases [7]. In another study, 25% of patients reported impaired taste, 15% had burning sensations, and 20% had difficulty in swallowing. Ageusia was observed in 24% of patients, hypogeusia in 35%, and dysgeusia in 38% of the COVID-19 patients. Taste disorders are more common in women than men [10].

A proper understanding of the dentist regarding oral manifestations of COVID-19 is very important as it helps in the early diagnosis of the disease and hence prevents transmission. The present systematic review aims to summarize the findings of the available past literature regarding oral manifestations of COVID-19 to highlight the role of the dentist in intervening the severity of this deadly pandemic disease.

II. Methods

a) Outcome

The primary outcome of this study was the systematic evaluation and characterization of currently reported cases and studies of oral manifestations associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11].

b) Eligibility criteria

The clinical evidence was searched in the form of original peer-reviewed journal articles which include observational and cross-sectional studies investigating the prevalence of oral disorders in patients with COVID-19. Apart from these, case reports and case series were also included in the systematic review. The range of data publication was limited fromJanuary 1, 2020, to June 30, 2022. Conference papers, book reviews, book chapters, letters to the editor and replies, newspaper and newsletter articles, expert opinions, and theses or dissertations were not used. Articles that are not published in English were also excluded.

c) Data sources and search strategy

We conducted an extensive literature search in several electronic bibliographic databases (PubMed, Scopus, Science direct, Litcovid) and retrieved all articles published from January 1, 2020, to June 30, 2022. Observational cross-sectional, case-control and cohort studies, case reports/ series reporting MIS-C, and letters to the editor were screened. The surveillance studies were also included.

PUBMED [search until 30.06.2022]

((((((((((((((((((((((((oral manifestations) OR (oral involvement)) OR (oral lesions)) AND (gingival lesions)) OR (gingival bleeding)) OR (gingival ulcer)) AND (buccal mucosa involvement)) OR (buccal ulcer)) AND (lip ulcer)) OR (lip mucosa involvement)) AND (tongue lesions)) OR (tongue ulcer)) OR (tongue involvement)) OR (ageusia)) OR (hypogeusia)) OR (dysgeusia)) OR (loss of taste)) OR (altered taste)) OR (gustatory impairment)) AND (burning sensation)) AND (aphthous stomatitis)) AND (ulcers on palate)) AND (COVID-19)) OR (coronavirus)) OR (corona pandemic)) OR ((SARS-CoV-2)

LITCOVID [search until 30.06.2022]

"Oral manifestations in COVID-19" OR "tongue lesions in coronavirus" OR "gingival involvement in coronavirus pandemic" OR " buccal mucosa involvement in COVID-19"

SCOPUS [search until 30.06.2022]

(tongue lesions OR mucosal lesions OR oral lesions AND COVID-19 OR coronavirus)

SCIENCE DIRECT [search until 30.06.2022]

Oral manifestations in COVID-19 OR oral involvement in coronavirus

d) Data collection

The inclusion of studies was done in two phases. In phase I, the titles of all the studies were screened first, followed by the screening of abstracts, based on the inclusion and exclusion criteria. Articles eligible based on the title and abstract would then be read in full and judged for their eligibility. Duplicates were eliminated and irrelevant articles were excluded from the systematic review. The full-text articles of all potential studies were obtained and evaluated for inclusion. In phase II, the references of all the included studies, case reports, and case series were again screened to search for any new potentially eligible studies.

All studies that reported orofacial manifestations in patients with laboratory-confirmed COVID-19 were included. Studies with suspected COVID-19 cases were excluded. To provide a systematic overview of these studies, we evaluated the included studies in terms of their demographic details such as author, year, country, study type, sample size, gender, age, study duration, medical history, admission in the ICU, and severity of the disease. Apart from this, the details related to the oral manifestations such as the site affected, onset of the orofacial manifestations, general symptoms, any special investigations performed, treatment of oral lesions, and outcome of the disease were also recorded. In the end, a total of 75 articles were included in this systematic review. The article inclusion flow diagram is shown in figure 1

e) Outcome measures

The primary outcome was estimating the prevalence of oral manifestations among COVID-19 patients. The secondary outcome was the most common type of oral manifestation and site affected in the oral cavity.

f) Statistical analysis

Qualitative data were resynthesized by grouping and comparing information reported in newly included

studies. Oral and mucosal conditions were summarized in schematic representations.

III. Results

A lot of studies along with the literature reviews have evaluated the oral mucosa involvement in COVID-19. We got 268 articles on the preliminary search, out of them, 75 articles were included in the final analysis [5,6,9,10,12-82].

The demographic characteristics of the included studies (n=75) are shown in table 1. We retrieved the data from 75 studies [5,6,9,10,12-82] including 11,321 patients with individual sample sizes of studies ranging from 14 [47] to 1172 [35]. All the articles (n=75) were published in year 2020 [6,9,12-27,56-69], 2021 [5,28-43,70-79], and 2022[44-55,80-82] but most of the articles (n=33) were from 2020 followed by the year 2021 (n=31) and 2022 (n=15).

The 75 articles included data from 27 countries around the globe. Most of the studies were conducted in Italy (n=13) [16,19,20,22,23,28,29,36,37,58,66,72,81], followed by Brazil (n=7) [10,47,49,52,56,75,77], India (n=7) [17,33,44,45,50,55,80], Egypt (n=5) [34,38,41,68,71], Turkey (n=5) [26,39,42,48,64], Iran (n=4) [25,54,62,79], Spain (n=4) [5,53,59,60], USA (n=4) [27,57,65,67], Saudi Arabia (n=3) [40,46,51], New York (n=2) [30,31], China (n=2) [15,35], Iraq (n=2) [12,43], Israel (n=2) [13,74], Europe (n=2) 18,70], Copenhagen (n=1) [14], California (n=1) [21], France (n=1) [24], Qatar (n=1) [32], Romania (n=1) [9], United Kingdom (n=1) [6], Colombia (n=1) [61], Norway (n=1) [63], Indonesia (n=1) [69], Afghanistan (n=1) [73], Czech Republic (n=1) [76], Ukraine (n=1) [78], and Poland (n=1) [82].

Among 75 studies, most of them were cross-sectional studies (n=36) [5,12-26,29,30,33,34,37-42,44-46,48-51,53-55] followed by case report (n=20) [10,61-75,78-81], case series (n=10) [6,9,56-60,76,77,82], retrospective studies (n=6) [27,28,35,36,47,52], prospective study (n=2) [31,43], and case-control study (n=1) [32].

A total of 11,321 patients were evaluated in the systematic review, of which 6581 (58.1%) were females. Three studies did not report the gender of the patients in their studies [5,22,35]. The age group of most of the studies (n=39) was in the range of more than 50 years followed by less than 30 years (n=12). Three studies did not report the age group of the patients [5,34,35] and one study was conducted among newborns [9]. The detailed age distribution is shown in figure 2.

Only 33 studies have reported the medical history of the patient. Among those studies, most patients were having hypertension (n=25), diabetes (n=19), respiratory disease and asthma (n=7), cardiovascular disease (n=6), allergy (n=4), and others. Regarding hospitalization, 21 studies reported that COVID-19 patients were admitted to the hospital, 11 studies reported hospitalization in ICU, and 5 of the studies also showed that the patients were ventilated (Table 1).

The oral manifestations were divided into 12 categories: taste alteration, tongue manifestation, xerostomia, red and white lesions, vesiculobullous lesions, periodontal changes, burning sensation, bleeding disorders, lip lesions, TMJ disorders, salivary gland disorders, and fungal infections. Most of the patients were having multiple signs and symptoms. Hence, we have calculated the oral manifestation individually. Taste alteration (n=43; 57.3%) was found in most people followed by vesiculobullous lesions (n=41; 54.6%) and tongue manifestations (n=26;34.6%). The detailed results of the type of oral manifestation is shown in figure 3.The most common sites of involvement in descending order were the tongue (n=62) followed by oral mucosa (n=27) and lips (n=19) (Figure 4). Descriptive characteristics of the oral lesions are shown in Table 2.

Taste Disorders and tongue manifestation: The prevalence of taste disorders and tongue manifestation was assessed with data from 43 (57.3%) and 26 (34.6%) studies respectively. Loss of taste or ageusia and was reported by 21 studies [12,14,20,23,35,40-42,44,49, 53,55,56,58,63,65,67,70,72,74]. Taste alteration or dysfunction was reported by [5,13,16-19,21,22,29, 36,38,46,51,54,66,78], Amblygeustia [15], dysgeusia [24,28,37,50,54,59,60]

Three studies [29,36,51] reported geographic tongue and one study [30] reported strawberry tongue among the COVID-19 patients. Other tongue manifestations are shown in table 2.

Vesiculobullous lesions: Forty one (54.6%) included studies and case reports or case series were having the vesiculobullous lesions [5,6,10,26,27,29,31,33,34,37-44,46-51,53,55,56,57,59-62,64,69,70,75-77,79,81,82].

Xerostomia: Xerostomia was noted in 18cross-sectional studies [13,15,28,34,37,38,40,42,44,45,46,48,50-55] and 2 case reports[60,78] constituting 26.6% of the included studies.

Red and white lesions: Eighteen studies(24%) reported red and white lesions in COVID-19 positive patients [9,24-26,29,33,36,37,39,43,49,51,53,57,61,68,80,82].

Periodontal involvement: Twelve studies (16%) were found having the involvement of gingiva and periodontium among the patients of COVID-19 of the present systematic review [6,26,29,32,38,39,42,44, 51,55,59,78].

Burning sensation: Eleven studies (14.6%) reported the complaint of burning sensation [5,33,38,42-44,53,55, 57,60,78].

Bleeding disorders: A total of six studies (8%) reported the incidence of bleeding disorders in COVID-19-positive patients [29,51-53,64,82].

Other findings: Salivary gland disorders (4%) [37,38,52], fungal infection (2.6%) [43,82], and dental pain (2.6%) [34,42] was found in three, two, and two studies respectively.

The latency time between the appearance of systemic symptoms and oral lesions was between 2 weeks before to 10 days after the onset of systemic symptoms. In most of the studies (n=14), general symptoms followed the oral symptoms (Table 2).

General treatment, as well as the treatment for the oral lesions among COVID-19 patients, is given in supplementary table 1. Oral lesions healed between 7 and 21 days after appearance. 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 severity and etiology.

IV. Discussion

COVID-19 has become a public health problem around the world. Initially, it was thought that the lack of involvement of the oral mucosa is a differentiating feature of COVID-19 as compared to other viral infections but in April 2020, a case report published by Chaux-Bodard et al have shown the association of COVID-19 with the oral mucosa in a 45-year-old female having painful inflammation of the papilla of the tongue, which ultimately healed as an asymptomatic ulcer in 10 days without a scar along with a skin lesion in the toe and was tested positive on Day 8 [83]. Since then, many observational studies and case reports were published in the literature depicting the involvement of oral mucosa among COVID-19 patients. The present systematic review was conducted with the same intent to elaborate the association between COVID-19 and the oral cavity with the help of previously published studies.

SARS-CoV-2 invades human cells of the lower respiratory system with the help of receptors known as ACE 2 and transmembrane protease serine 2 [3]. Among these two, the ACE 2 receptor is found mainly in the cells of the lung, liver, kidney, gastrointestinal (GI) and even on the cells of nasal epithelium and oral mucosa [4]. These cells act as host cells for the virus through which, the virus invades these cells of the body and starts an inflammatory response in these organs which, in turn, causes the smell and taste dysfunctions early in the course of the disease [15]. Hence, the mechanism of development of oral lesions can be directly through the effects of the replicating virus in these cells (lesions will be SARS-CoV-2-specific) and indirectly as a sequel of possible drug reactions that may develop during the latency period, viral exanthem, through physical and psychological stress of the COVID-19 or its treatment, or co-infection with other bacterial infections enhancing the severity of COVID-19[59]. According to Amorim dos Santos et al [4], the deterioration of the general health of COVID-19 patients along with the longer period of hospitalization and several treatment procedures also predispose the occurrence of oral lesions. Chaux-Bodard et al. hypothesized that oral lesions may arise as a sequel of various inflammatory reactions that induce vascular inflammation [83]. Previously published reports of the Italy and United Kingdom stated the temporary association of pediatric inflammatory multisystem syndrome with SARS-COV-2 cases [84]. Various diseases like Kawasaki disease and erythema multiforme can itself predispose to oral manifestations. Hence, we have excluded such conditions from our systematic review.

Talking about the oral lesions, the most common sites of involvement in descending order were the tongue (n=62), oral mucosa (n=27), lips (n=19), entire oral cavity (palate (n=12), gingiva and periodontium (n=12), and salivary gland (n=3). Sousa et al found the palate and tongue followed by the gums and the lips as the most commonly involved sites in COVID-19 patients [7]. Description of the oral manifestations among COVID-19 patients are as follows:

a) Taste disorders

According to the various published studies, smell and taste changes are the early indicators of the COVID-19 pandemic which are effective in early diagnosis and decision making. Though these symptoms are not life-threatening, they may hamper the quality of life of the patient. Prof C. Hopkins, President of the British Rhinological Society has stated that loss of smell/taste can be the only symptom of COVID-19 [85]. Several public health surveillance organizations such as the European Centre for Disease Prevention and Control, Centre for Disease Control and Prevention (CDC), WHO [86], and Public Health England included the sudden onset of anosmia, ageusia, or dysgeusia in the list of main clinical criteria for the case definition of COVID-19 [87]. In our systematic review also, general symptoms followed the oral symptoms, especially loss of taste. The possible explanation for the taste disturbances in COVID-19 patients is the higher expression of ACE 2 receptor in the tongue as compared to the buccal and gingival tissues resulting in the damage to mucosal epithelial cells of the oral cavity [88].

In the present systematic review, the incidence of taste disorders and tongue manifestation was assessed with data from 43 (57.3%) and 26(34.6%) studies respectively. Al-Zaidi et al in their cross-sectional study found the overall prevalence of taste dysfunction

in 83.08% of COVID-19 patients. The taste recovers at one week for 50% of the participants followed by less than a week (25%), within 2 weeks (18.75%), and within 3 weeks (6.25%) [12]. Amorim dos Santos et al in their living systematic review (LSR) found taste disorder as the most prevalent oral symptom in this population with a prevalence of 45% [4] but in their second LSR, the prevalence decreased to 38%. They stated that the prevalence of taste disorders among COVID-19 patients varies from 14% in Africa to 49% in Europe [89]. Yan CH et al found taste loss in 71% of COVID-19–positive subjects and the association was strongly associated with COVID-19 positivity (OR 10.2; 95% CI, 4.74-22.1) [21]. A total of 52% reported changes in taste sensation in Biadsee A et al study with 52 patients reporting a change in spicy taste perception, 54 in salty taste, 53 in sour taste, and 61 patients in sweet taste [13]. Bodnia NC et al reported a total loss of taste in 70% of patients which resolved within 1-3 weeks for 78% and 3-6 weeks for 22% [14]. A meta-analysis conducted by Tong JY et al have shown that gustatory changes are noted in 43.93% of these individuals [90]. The prevalence of taste alterations was estimated to be around 54.73% [95% CI: 46.28–63.04%] in another meta-analysis conducted by Nijakowski K et al [91].

Three studies conducted by Favia G et al [29], Bardellini E et al [36], and Binmadi NO et al [51] reported geographic tongue in our systematic review. Bardellini E et al conducted a pediatric retrospective cohort study and reported oral pseudomembranous candidiasis (n=2), coated tongue (n=2), taste alteration (n=3), and geographic tongue (n=1) as the most common oral lesions of which, geographic tongue appeared concurrently with the high fever according to the patient's mother [36]. The etiopathogenesis of the geographic tongue is still unclear but some authors reported the association of several non-genetic multifactorial factors, including viral infections [92]. A study conducted by Halepas S et al [30] reported strawberry tongue among COVID-19 patients. Other tongue manifestations are plaque-like changes in the tongue [13,52,61], macroglossia [24,32], ulcerations on tongue [10,24,26,56,73,76,80,81], fissured tongue [29,44,73], lingual papillitis, white tongue and glossitis with patchy depapillation [5], burning sensation in tongue [42,68,78], white coat, numbness, and black discoloration of tongue [43], depapillation of tongue [45,60], hairy tongue [46], Greasy tongue coat [71], and smooth tongue and mycosis of the tongue [82].

b) Vesiculobullous lesions

Forty one included studies and case reports/case series (54.6%) have mentioned the incidence of vesiculobullous lesions [5,6,10,26,27, 29,31,33,34,37-44,46-51,53,55,56,57,59-62,64,69,70,75-77,79,81,82]. Favia G et al widely describes the histological aspect of oral SARS-CoV-2-related lesions and found ulcers (52.8%) as the most detected oral manifestation [29]. Presas CMC et al reported three cases with ulcers, of which one was infected by the SARS-CoV-2 virus and two were suspected patients infected by the SARS-CoV-2 virus. The lesions resemble herpes simplex infection but were not confirmed by biopsies [59]. Painful oral ulcers were the most common orofacial manifestations in patients with COVID-19 in a review conducted by Halboub E et al [93]. Tapia ROC et al [57] and Dalipi ZS et al [70] found bullous and lesions on the palate and oral mucosa respectively. Riad A et al found multiple ulcers (1 and 7 ulcers per patient) with their size ranging between 1 and 5 mm, of which the majority (92.3%) were not bleeding, and all of them (100%) were manifested on the dorsum or side of the tongue. They found a statistically significant association between the number of ulcers and gender, onset, duration, Ct value, and pain score [8]. A systematic review conducted by Orilisi G stated that oral ulcers, cheilitis, and tongue lesions were more common in patients before hospitalization, while perioral pressure ulcers, macroglossia, blisters, and oral candidiasis were more recurrent in patients during hospitalization [94].

Regarding the mechanism of the formation of the ulcer, it was proposed that an increased level of tumor necrosis factor (TNF)-α in COVID-19 patients can lead to chemotaxis of neutrophils to oral mucosa and the development of aphthous-like lesions. Stress and immunosuppression secondary to COVID-19 infection could be other possible reasons for the appearance of such lesions in COVID-19 patients [10].

Red and white lesions: Eighteen studies (24%) reported red and white lesions in COVID-19 positive patients [9,24-26,29,33,36,37,39,43,49,51,53,57,61,68,80,82].

The various types of red and white lesions reported in the included studies are cheilitis and oral lichenoid reaction [24], white plaques on the intraoral mucous layer [25,37,43,68,80], rash and erythema [26], candidiasis [9,29,36,49,51,53], reddish-white spots on the palate [33,57], erythema and lichen planus [39], angular cheilitis [53,82], and reddish plaques on the lower lip [61].

Xerostomia Xerostomia was noted in 18 cross-sectional studies [13,15,28,34,37,38,40,42,44,45,46,48,50-55] and 2 case reports [60,78] with 26.6% of studies reporting the complaint of dry mouth. In a study conducted by Biadsee et al, 56% of patients reported xerostomia which was assessed by the question ''Do you feel the need to drink more (dry mouth)?'' [13]. In the updated version of the LSR performed by dos Santos et al [89], xerostomia was the most prevalent oral symptom identified in patients with COVID-19, whereas, taste disturbances were the predominant feature in the original LSR [4]. In a meta-analysis conducted Nijakowski K et al, xerostomia was prevalent

among 37.58% [95% CI: 26.35–49.53%] of the COVID-19 patients [91].

Periodontal involvement: Twelve studies (16%) [6,26,29,32,38,39,42,44,51,55,59,78] have shown the prevalence of gingivitis and periodontitis. The gingival manifestations found among the COVID-19 patients of our systematic review were the gingivitis [29], desquamative gingivitis [6,59], ulceronecrotic gingivitis [29], and gingival bleeding [6,38,42,44,55,78]. Periodontitis [32] and necrotizing periodontal disease [51] were reported in two studies.

Other findings: Red and/or swollen lips was observed by Halepas S et al in 48.9% of patients [30]. Pale lips [33], reddish plaques on the lower lip [61], nodule in the lower lip [10], and reddish macules [42] were the findings related to lip involvement in COVID-19 patients. Reddish-white spots on the palate [33], ulcerations on the palate [6,39,56,59,60,81,82], white coat of the palate [43,68], bulla on the left and right palatal mucosa [57], an erythematous surface on the hard palate [64], and angioma type lesion on the right side of the palate [82] were the palatal findings among COVID-19 patients. Eleven studies (14.6%) included in the systematic review found the complaint of burning sensation also [5,33,38,42-44,53,55,57,60,78]. Biadsee A et al found a statistically significant strong association between burning mouth and taste change ($p=0.002$, $p=0.009$, respectively) [13].

Although we have tried to summarize the findings of the studies reporting oral manifestations among COVIOD-19 patients, one of the biggest limitations of this systematic review was the lack of temporal dimension. We were not able to say that these oral manifestations are directly connected to COVID-19, or due to indirect manifestations of other factors such as stress, immunosuppression, and/or medications. Another shortcoming was the lack of definitive diagnosis as most of the included cases have not undergone biopsy for confirmation of the diagnosis.

V. Conclusion

Our systematic review shows a higher prevalence of oral manifestation, specifically taste alteration (57.3%) followed by vesiculobullous lesions (54.6%), and tongue manifestations (34.6%). COVID-19 patients show various oral manifestations that may help clinicians with early identification of the disease. Recognition of signs and symptoms of COVID-19 is critical for early diagnosis and better prognosis. Dental practitioners can play an important role not only in the prevention of COVID-19 transmission but also in breaking the chain of COVID-19 disease. Raising awareness of these symptoms is important to initiate early diagnosis and treatment of this deadly COVID-19 disease.

Declarations

Ethics approval and consent to participate-Not required.

Availability of data and material-Can be made available whenever required.

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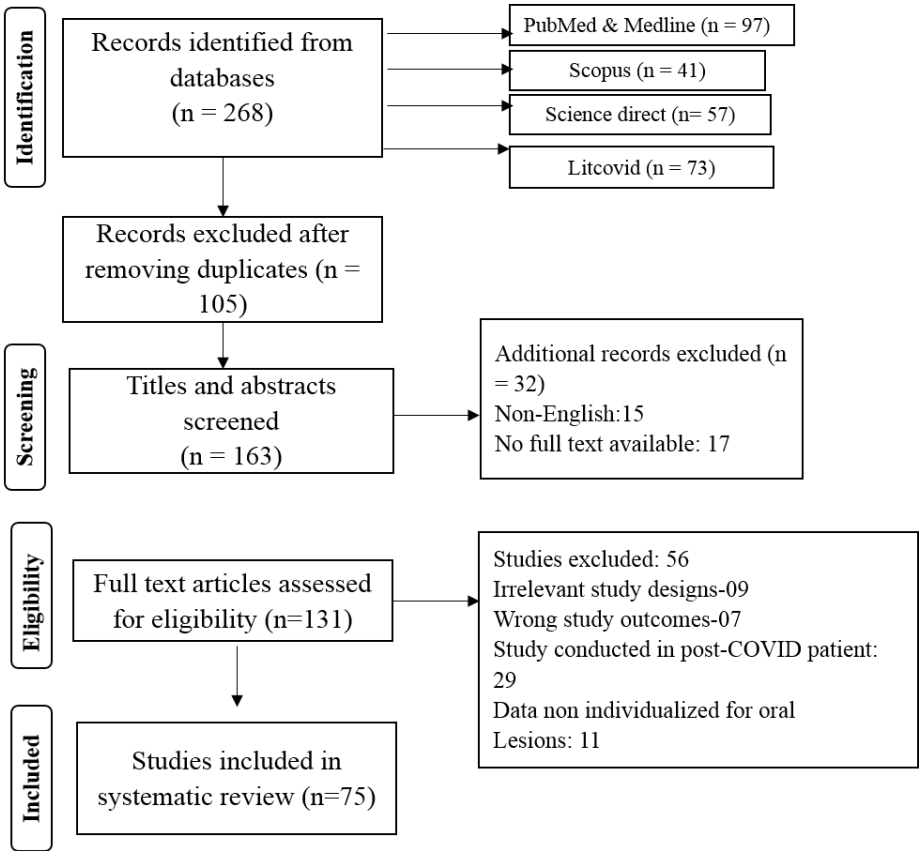

Figure 1: Flow diagram of literature search and selection criteria of the included studies (n=75)

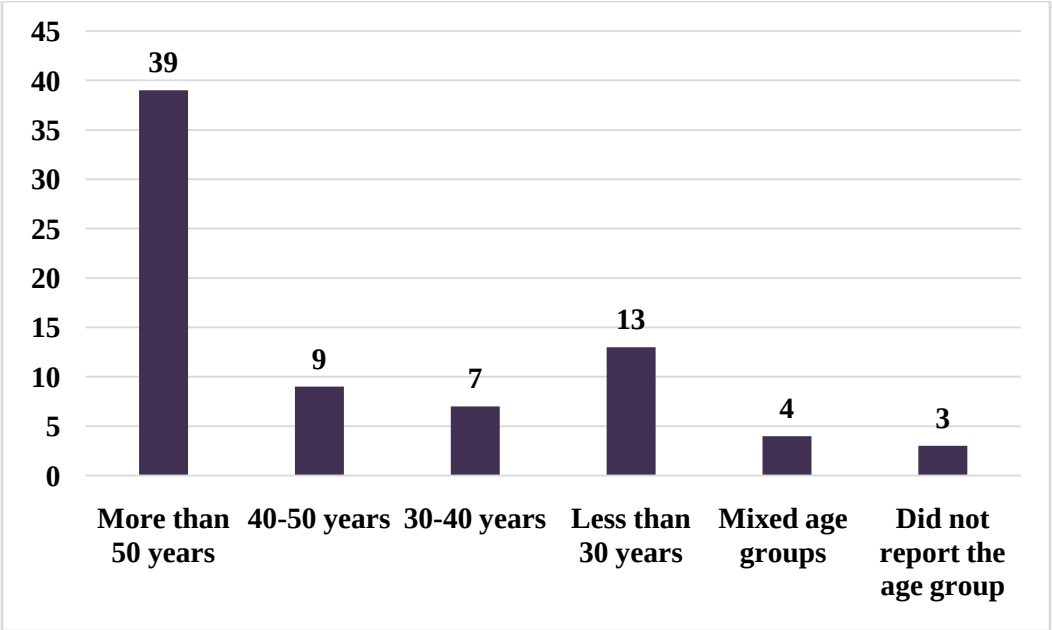

Figure 2: Age distribution of the patients included in the systematic review (n=75)

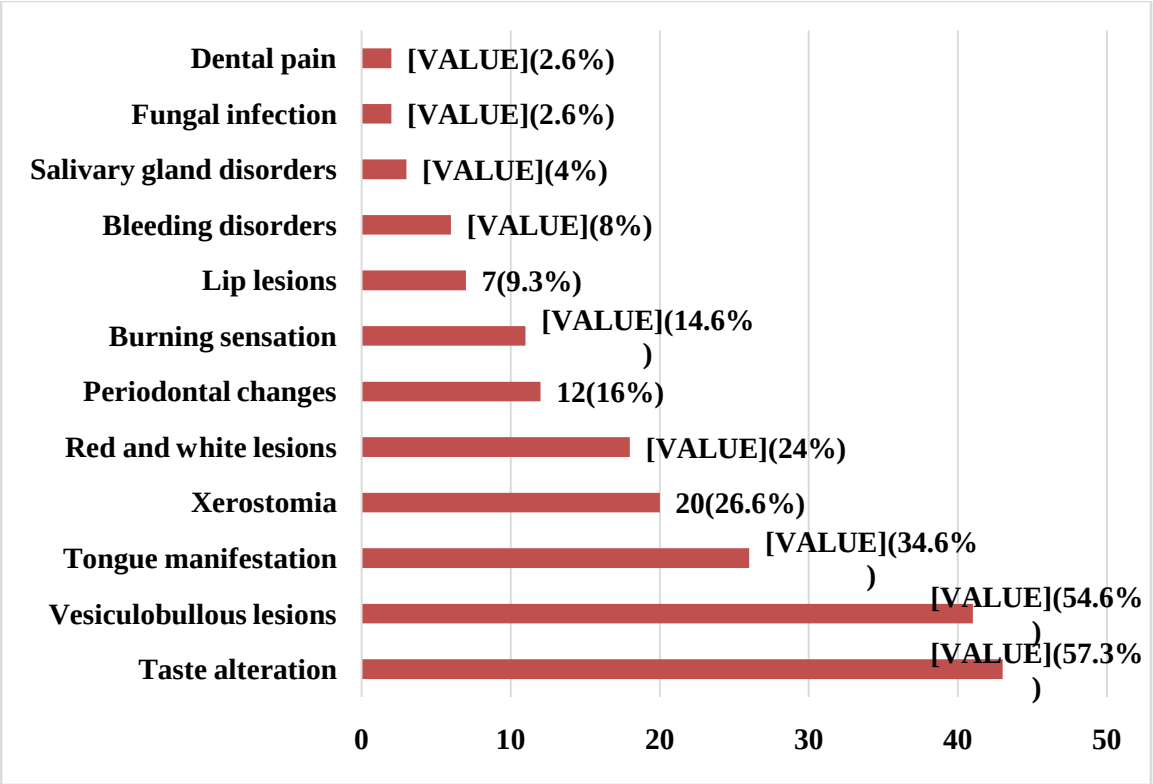

Figure 3: Categories of oral manifestation among the patients with COVID-19

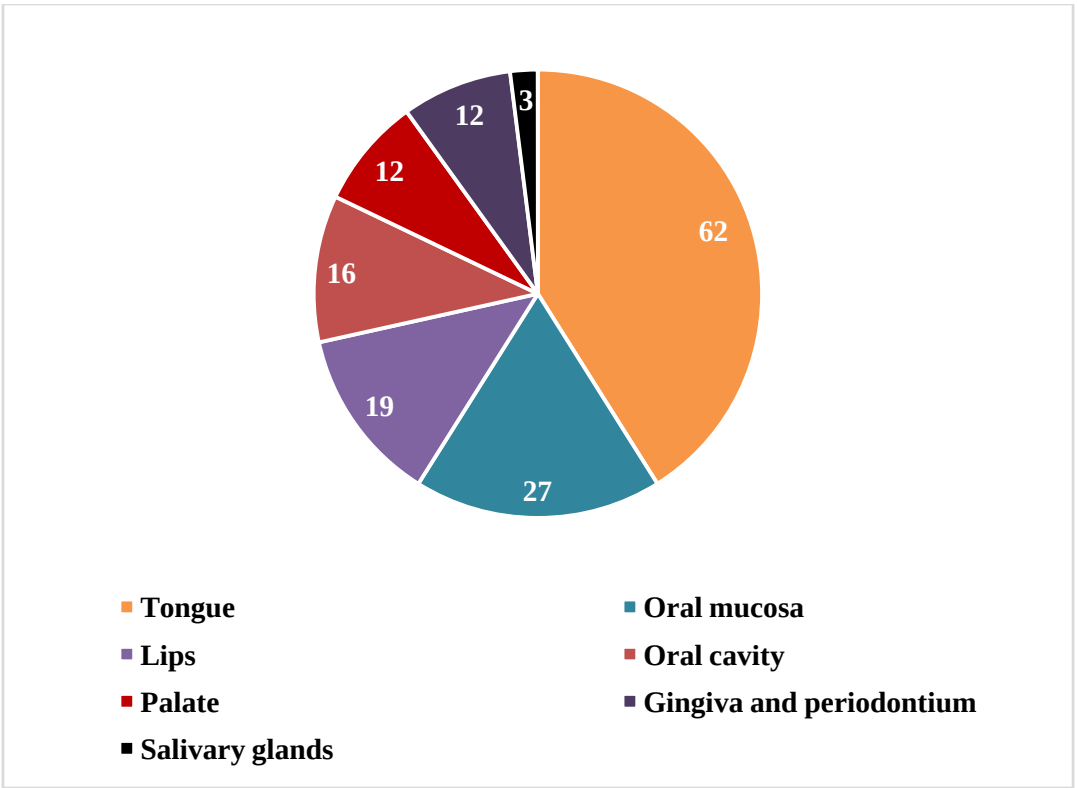

Figure 4: Intraoral sites of involvement among COVID-19 patients

Table 1: Demographic characteristics of the included studies (n=75)

S. No.	Author & Year	Study location	Study design	Sample size	Gender	Age	Study duration	Medical history	Admission in the ICU	Severity of the disease
1.	Al-Zaidi and Badr (2020) [12]	Iraq	Cross-sectional	65	M- 41.6% F- 58.4%	41.2 yrs	5 April 2020 - 17 May 2020	-	-	Moderate
2.	Biadsee et al (2020) [13]	Israel	Cross-sectional	140	M-58; F-70	36.5 yrs	March 25, 2020, and April 15, 2020.	-	-	Mild
3.	Bodnia and Katzenstein (2020) [14]	Copenhagen	Cross-sectional	65	F-22; M-28	45 yrs	March 2020	-	-	Mild
4.	Chen L et al (2020) [15]	China	Cross-sectional	31	M-15 F-16	60.6 yrs	28 February 2020 to 4 March 2020	-	-	-
5.	Dell V et al (2020) [16]	Italy	Cross-sectional	355	M-54%	50 yrs	March10 to 30, 2020	Cardiovascular disease, allergic (Sinusitis)	-	Mild to Moderate
6.	Kumar L et al (2020) [17]	India	Cross-sectional	141	M-58.9%; F-41.1%.	15.2 yrs	May to August 2020	-	-	Mild to Moderate
7.	Lechien JR et al (2020) [18]	Europe(Multi Centre)	Cross-sectional	417	F-263; M-154	36.9 ± 11.4 yrs	-	Allergic Rhinitis Asthma Hypertension Hypothyroidism	Hospitalisation of severe cases	Mild Moderate Severe
8.	Paderno A et al (2020) [19]	Italy	Cross-sectional	508	M-56% F-44% (55±15 years)	55±15 years	March 27 to April 1, 2020	-	Hospitalisation of severe cases	Mild Moderate Severe
9.	Rizzo PB et al (2020) [20]	Italy	Cross-sectional	202	F-55.1% M-44.9%	56 yrs	March 19 and March 22, 2020	-	-	Mild
10.	Yan CH et al (2020) [21]	California	Cross-sectional	59 and 203 (Covid +ve and –ve)	M&F-49.2% (Covid +ve); M-34%, F-65% (covid –ve)	54 yrs	March 3, 2020, and March 29, 2020	Allergic Rhinitis, immunocompromised state, hypertension, DM, Cardiac Disorders, Cancer CLD, History of Head Trauma, Neurological disease	Hospitalisation of severe cases	Mild Moderate Severe

11.	Sinjari B et al (2020) [22]	Italy	Cross-sectional	20	-	-	May 2020 to June 2020)	DM, Cardiovascular conditions	-	Mild to Moderate
12.	Giacomelli A et al (2020) [23]	Italy	Cross-sectional	59	M-40% F-60%	60 yrs	March 19,2020	-	-	Mild
13.	Mascitti H et al (2020) [24]	France	Cross-sectional	59	M:F-3:1	Median age (IQR) was 57.6 (49.4–69.1) years.	March 31, 2020	-	-	Mild
14.	Salehi M et al (2020) [25]	Iran	Cross-sectional	53	M-43.4%; F-56.6%	<50 yrs-20.7%; ≥50 yrs-79.3%	1 March 2020 to 30 April 2020	Cardiovascular diseases (52.83) and DM (37.7%; Chronic kidney disease-20.7%	-	Mild to Moderate
15.	Askin O et al (2020) [26]	Turkey	Cross-sectional	210	M-58.6%; F-41.4%	7.44 ± 17.259 yrs	April 2020.	Comorbidties	29 in ICU 129 in wards	Moderate and Severe
16.	Katz J et al (2020) [27]	USA	Retrospective study	889	F-509 M-386	18-34 yrs-66%	Registry Study	-	-	-
17.	Fantozzi PJ et al (2021) [28]	Italy	Retrospective study	326	M-52.3% F-47.7%	Median age- 57 (48–67) days	6 March to 30 April 2020	Hypertension (n = 29), chronic pulmonary disease (n = 11), DM (n = 10), cardiovascular disease (n = 9), cancer (n = 5)	Hospitalized (median no of days-12.5 days)	Moderate and severe
18.	Favia G et al (2021) [29]	Bari, Italy	Cross-sectional	123	M:F ratio 1.3:1	Median age 72 yrs	October 2020 to December 2020	-	History of Hospitalization and ICU	Moderate and severe
19.	Halepas S et al (2021) [30]	New York	Cross-sectional	47	M-51.1%; F-48.9%	9.0 ± 5.0 yrs	March 15 through June 1, 2020	-	History of Hospitalization, ICU	Mild Moderate Severe

20.	Rekhtman S et al (2021) [31]	New York	Prospective cohort study	296	M-71% F-29%	Median age- 64 (57-77)	May 11, 2020 and June 15, 2020	CAD-23%; Congestive heart failure-14%; Asthma 9%; COPD-14%; DM-34%; Hypertension-71%	History of Hospitalization	Moderate and Severe
21.	Maraouf N et al (2021) [32]	Qatar	Case control	Cases-40; Control-528	Cases-M-50%; F-50% Controls-M-54.9%; F-45.1%	Cases-53.6 yrs Controls-41.5 yrs	February and July 2020	DM-Cases-42.5% Controls-27.8%	Hospitalization and ICU admission	Mild Moderate Severe
22.	Nuno-Gonzalez A et al [5] (2021)	Spain	Cross-sectional	666	-	55.7yrs	10 and 25 April 2020	-	History of Hospitalisation	Mild Moderate
23.	Subramaniam T et al (2021) [33]	India	Cross-sectional	713	M:F-6:3	69 yrs	May 2020 and June 2020	DM Hypertension	-	Mild Moderate
24.	Abubakr N et al (2021) [34]	Egypt	Cross-sectional	573	408 females and 165 males.	36.19 ±9.11 years	May 1, 2020 to July 1, 2020	-	-	Mild Moderate
25.	Song J et al (2021) [35]	China	Retrospective	1172	-	-	December 2019	-	History of Hospitalization	Mild
26.	Bardellini E et al (2021) [36]	Italy	Retrospective	27	M;F-19:8	4.2 yrs	March to April 2020	-	-	Mild
27.	Gherlone EF et al (2021) [37]	Italy	Cross-sectional	122	M-75.4% F-24.6%	62.5 yrs	July 23, 2020 to September 7, 2020	CAD, DM, Chronic kidney disease, active neoplasia COPD	History of Hospitalization and ICU and Ventilation	Moderate Severe
28.	El Kady DM et al (2021) [38]	Egypt	Online survey	58	M-53.4%; F-46.6%	18-46 yrs	May 15 to June 10, 2020	-	History of Hospitalisation	Mild
29.	Fidan V et al (2021) [39]	Turkey	Cross-sectional	74	M-66.2% F-33.8%	51.4 ± 6.3 yrs	April to October 2020	-	Hospitalized	Mild Moderate

30.	Natto ZS et al (2021) [40]	Saudi Arabia	Cross-sectional study	109	M-67% F-33%	39.3±12.4 yrs	July-October 2020	DM (10.1%); hypertension (7.3%); asthma and arthritis (1.7%)	-	-
31.	Elamrousy WAH et al (2021) [41]	Egypt	Cross-sectional	124	M-74.2%; F-25.8%	50.32 ± 12.47 yrs	2 September 2020, to 10 June 2021	DM (n = 52), hypertension (n = 16), cardiac disease (n = 8), renal disease (n = 4), liver disease (n = 4)	Hospitalized	Severe (58.1%)
32.	Bulut DG et al (2021) [42]	Turkey	Cross-sectional	200	M-75 F-125	20–30 yrs: 89 (62/27), 31–40: 65 (43/22), 41–50: 27 (14/13), 51–60: 15 (4/11), 61–70: 4 (2/2)	September 2020 to March 2021	-	Hospitalized (11.5%)	Moderate Severe
33.	Naser Al et al (2021) [43]	Iraq	Prospective study	338	M-59%; F-41%	Mean age-45 yrs	August 2020 to March 2021	Respiratory diseases, DM, hypertension, heart disease, urogenital diseases, hematological diseases, gastrointestinal diseases	Hospitalized	critical admitted cases-38.6%
34.	Muthyam AK et al (2022) [44]	India	Cross-sectional	100	M-51% F-49%	More than 35 yrs-54%; Less than 35 yrs-46%	-	Immunocompromised state, Multidrug therapy	Hospitalisation	Mild to Moderate
35.	Ganesan A et al (2022) [45]	India	Cross-sectional	500	M-73.4% F-26.6%	53.46 ± 17.50 years	-	-	-	-

36.	El Tantawi M et al (2022) [46]	Multicountry study (Saudi Arabia)	Cross-sectional	434	M-41.5% F-58.5%	18-23 yrs	August 2020 to January 2021	Cancer and COPD	-	Mild
37.	Soares CD et al (2022) [47]	Brazil	Retrospective	14	M-71.5% F-38.5%	58 yrs	-	-	-	-
38.	Tuter G et al (2022) [48]	Turkey	Cross-sectional	204	M-37.3% F-62.7%	53.3 yrs	February 2021 to March 2021	DM hypertension Immunosupression	Hospitalisation ICU	Mild Moderate Severe
39.	Schwab G et al (2022) [49]	Brazil	Cross-sectional	154	M-59.7% F-40.3%	54.60 ± 13.93 years	January 13 to May 28 of 2021	-	Hospitalisation ICU Ventilation	Moderate to Severe (discharged /death)
40.	Chawla J et al (2022) [50]	India	C Cross-sectional	217	M-70% F-30%	50-60 yrs	September and December 2020	DM, hypertension CAD, bronchial Asthma	-	Mild Moderate
41.	Binmadi NO et al (2022) [51]	Saudi Arabia	Cross-sectional	195	M-25% F-75%	33% were 18 to 24 years old and 33% were 25 to 34 years old.	March of 2020 and March of 2022	Immunosupression, hormonal modulation	Hospitalisation ICU Ventilation	Mild Moderate Severe Critical
42.	de Paula Eduardo F et al (2022) [52]	Brazil	Retrospective	519	M-68.2% F-31.8%	51-80 yrs	May 2020 to February 2021	-	ICU	Severe
43.	Villarroel-Dorrego M et al (2022) [53]	Spain	Cross-sectional	55	M-54.5% F-45.5%	51 ± 23.24 y	-	-	-	-
44.	Manifar S et al (2022) [54]	Iran	Cross-sectional	140	M-44.2% F-55.8%	53.78 ± 17.44 yrs	1 September 2020 to 17 October 2020	-	Hospitalisation	Moderate Severe
45.	Bhuyan R et al (2022) [55]	India	Cross-sectional	169 (first wave) 211 (2nd wave)	1st wave- M-35.5%; F-64.5% 2nd wave- M-45.5%; F-55.5%	63 ±17 and 57 ± 18 (1st and 2nd wave)	-	Comorbidities	Hospitalisation ventilator	Mild Moderate Severe
46.	Brandao TB et al (2020) [56]	Brazil	Case series	08	M-05; F-03	53 yrs	-	Hypertension COPD (case 1); DM, obesity,	Hospitalisation	Mild Moderate Severe-Critical

								renal Failure, bariatric surgery, fibromyalgia (case 2); obesity, Parkinson disease, hypertension, COPD (case 3) DM and Hypertension (case 4)		
47.	Dima M et al (2020) [9]	Romania	Case series	03	M:F-2:1	Newborns	May 2020	Diaper erythema	Neonatology Ward	Mild
48.	Tapia ROC et al (2020) [57]	Latin America	Case series	04	F:M--3:1	47.2 ± 6.8 yrs	-	-	Case 2- Hospitalised	Mild (case 1 & 3); hospitalized (case 2); moderate (case 4)
49.	Vaira LA et al (2020) [58]	Italy	Case series	72	M-27; F-45	49.2 yrs	March 31, 2020 and April 6, 2020.	History of head trauma, allergic rhinitis, chronic rhinosinusitis, and psychiatric or neurological disorders.	-	Mild Moderate
50.	Presas CMC et al (2020) [59]	Spain	Case series	03	M:F-2:1	59 yrs	last week of March and the first week of April 2020	DM & hypertension (case 2); Obesity and Hypertension (case 3)	Case 3- Hospitalisation	Case 1- Mild Case 3- Moderate to severe
51.	Sinadinosand Shelswell (2020) [6]	United Kingdom	Case series	03	M:F-2:1	58 yrs		DM and Hypertension (case 2); obesity (case 3)	-	Mild to Moderate
52.	Rodríguez MD et al (2020) [60]	Spain	Case series	03	F:M-2:1	53 yrs	-	-	Case 1 – Home quarantine Case 2 & 3- Hospitalisa	Case 1- Mild Case 2- Moderate Case 3- Moderate

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53.	Corchuelo and Ulloa (2020) [61]	Colombia	Case report	01	Female	40 yrs	-	-	-	Moderate
54.	Dos Santos et al (2020) [10]	Brazil	Case report	01	Male	67 yrs	March 31, 2020	CAD, autosomal dominant polycystic kidney disease, and kidney transplant, immunosuppression, venous thromboembolism	Hospitalisation in ICU	Severe
55.	Zarch and Hosseinzadeh (2020) [62]	Iran	Case report	01	Female	56 yrs	October 2020	-	-	-
56.	Hjelmeseth J (2020) [63]	Norway	Case report	01	Female	60 yrs	-	-	-	-
57.	Kahraman and Çaşkurlu (2020) [64]	Turkey	Case report	01	Male	51 yrs	18 March 2020	-	-	Moderate
58.	Smith AC et al (2020) [65]	United States	Case report	01	Male	21 yrs	March 19, 2020	-	-	Mild
59.	Maniaci A et al (2020) [66]	Italy	Case report	01	Male	15 yrs	-	-	-	Mild
60.	Melley LE et al (2020) [67]	USA (Pennsylvania	Case report	01	Female	59 yrs	May 2020	-	-	-
61.	Riad A et al (2020) [68]	Egypt	Case report	01	Female	47 yrs	-	Cardiovascular disease DM	-	Moderate

62.	Putra BE et al (2020) [69]	Indonesia	Case report	01	Male	29 yrs	-	Cardiovascular diseases	-	Moderate
63.	Dalipi ZS et al (2021) [70]	Europe	Case report	01	Male	17 yrs	-	-	-	-
64.	Eita AAB et al (2021) [71]	Egypt	Case report	01	Female	31 yrs	-	Irritable Bowel Syndrome Atopy	-	Severe
65.	Cirillo and Colello (2021) [72]	Italy	Case report	01	Female	36 yrs	March 2020	-	-	Mild
66.	Nejabi MB et al (2021) [73]	Afghanistan	Case report	01	Male	62 yrs	-	-	-	Mild
67.	Klein H et al (2021) [74]	Israel	Case report	01	Female (pregnant)	40 yrs	-	-	-	Mild
68.	Ramires MCCH et al (2021) [75]	Brazil	Case report	01	Female	50 yrs	-	Obesity, hypertension, and type2 DM	Hospitalisation Ventilation	Severe
69.	Hocková B et al (2021) [76]	Czech Republic	Case series	03	M:F-3:0	62 yrs		Arterial hypertension, hypercholesterolemia, GERD (case 1); Arterial hypertension, history of MI and septic shock (case 2)	ICU	Severe
70.	Teixeira IS et al (2021) [77]	Brazil	Case series	04	M:F-1:3	57 yrs, 84 yrs, 70 yrs, 64 yrs	-	Hypertension, hypothyroidism, and rectal tumor (case 2); hypertension, hypothyroidism (case 3); bipolar disorder (case 4)	-	-
71.	Emelyanova N et al (2021) [78]	Ukraine	Case report	01	Female	38 yrs	-	-	-	-
72.	Fathi Y et al (2021) [79]	Iran	Case report	01	Female	22 yrs	April 2020	-	Hospitalization (2nd day)	

73.	Shenoy P et al (2022) [80]	India	Case report	01	Female	55 yrs	-	-	-	-
74.	Palaia G et al (2022) [81]	Italy	Case report	01	Female	30 yrs	-	-	-	-
75.	Rafałowicz B et al (2022) [82]	Poland	Case series	06	M-4 F-2	43 yrs, 72 yrs, 53 yrs, 48 yrs, 66 yrs; 71 yrs	January-June 2021	Hypertension and insulin resistance (case 2)	No	

CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; GERD: Gastroesophageal reflux disease; DM: Diabetes mellitus; CLD: Chronic lung disease

Table 2: Oral manifestations of the included studies (n=75)

S. No.	Author & year	Oral manifestation	Site	Type of oral manifestation	Occurrence/duration of oral manifestation	Systemic manifestation
1.	Al-Zaidi and Badr (2020) [12]	Loss of taste (83%)	Tongue	Taste alterations	1 week before systemic symptoms	Fever (63.08%), cough (60.00%), dyspnea (47.69%), sore throat, diarrhea (32.31%), chest pain (30.77%).
2.	Biadsee et al (2020) [13]	Taste alteration (n=67), dry mouth (72), plaque-like changes in the tongue (9), swelling in the oral cavity (10)	Tongue, oral cavity	Taste alteration, tongue manifestation, xerostomia	Along with systemic symptoms	Cough and runny nose (p = 0.018), olfactory dysfunction
3.	Bodnia and Katzenstein (2020) [14]	Total loss of taste (70%)	Tongue	Taste alterations	1-3 weeks (78%), 3-6 weeks (22%)	Fatigue, headache, fever, dry cough and disturbance of the sense of smell
4.	Chen L et al (2020) [15]	Amblygeustia (47.2%), dry mouth (11.1%)	Tongue, oral cavity	Taste alteration, xerostomia	Along with systemic symptoms	Submandibular lymph node enlargement (1); cough (21); fever (20); diarrhea (04); chest tightness (13)
5.	Dell V et al (2020) [16]	Taste disorders (65.5%)	Tongue	Taste alterations	Mean duration: 10 days	Fever (72.1%); cough (47.9%); fatigue (40.3%); dyspnea (21.7%); diarrhea (19.7%)
6.	Kumar L et al (2020) [17]	Taste Dysfunction (28.4%)	Tongue	Taste alterations	Duration: 2-15 days	Malaise (14.2%), sore throat (19.9%), cough (20.6%), fever (48.2%), diarrhea (5.7%), nasal discharge (3.5%) headache (5.7%)
7.	Lechien JR et al (2020) [18]	Gustatory dysfunction (88.8%)	Tongue	Taste alterations	Mean duration: 9.2 ± 6.2 days	Olfactory dysfunction (85.6%)
8.	Paderno A et al (2020) [19]	Gustatory dysfunction (group a-51.9% Group b-78.9%) Partial-36.8% Total-60.1% Unable to assess-3.1%	Tongue	Taste alterations	First symptom in 11.9% (group a) and 10.2% (group b) Mean duration: 9.2 ± 5.4	Olfactory dysfunction, fever, cough, headache, dyspnea, asthenia, diarrhea, nausea, nasal congestion, pharngodynia
9.	Rizzo PB et al (2020) [20]	Loss of taste (n=113)	Tongue	Taste alterations	Mean duration: 9.5 days	Dry cough, fever, headache, sore throat, chest pain, nausea, abdominal pain
10.	Yan CH et al (2020) [21]	Gustatory impairment -71% (p<0.001)	Tongue	Taste alterations	-	Fatigue (81%), fever (70%), anosmia (68%), myalgia or arthralgia (63%), diarrhea (48%), nausea (27%).

11.	Sinjari B et al (2020) [22]	Impaired taste (25%), burning sensation (15%), difficulty in swallowing (20%), dry mouth (30%) (p=0.02)	Oral cavity, tongue	Taste alterations	-	-
12.	Giacomelli A et al (2020) [23]	Dysgeusia (8.5%) Ageusia (1.7%)	Tongue	Taste alterations	Before hospitalization (91%)	Fever (72.8%), cough (37.3%), dyspnea (25.4%), sore throat (1.7%), arthralgia (5.1%), headache (3.4%), asthenia (1.7%), abdominal symptoms (8.5%)
13.	Mascitti H et al (2020) [24]	Oral lichenoid reaction 32.5%; oral enanthema 27.5%; macroglossia 25.0% cheilitis 12.5%; ageusia-20.5%; extensive ulcerations of the tongue2.5%	Lips, tongue, oral cavity and oral mucosa	Red and white lesions, tongue manifestation, taste alteration, vesiculobullous lesion	-	Macular exanthema (80%), face edema (32%), livedo (13%), urticarial rash (8%), purpura (5%), oral lichenoid lesions (33%), and conjunctivitis (18%)
14.	Salehi M et al (2020) [25]	White plaques on the intraoral mucous layer	Mucous membrane	Red and white lesions	-	-
15.	Askin O et al (2020) [26]	Necrosis on maxillary arch (1 case); apthous stomatitis 5.8%; rash and erythema; apthous lesion on side of tongue	Mucous membrane and tongue	Vesiculobullous lesion, tongue manifestation, red and white lesions, periodontal changes	-	Cutaneous findings (36.1%)
16.	Katz J et al (2020) [27]	Recurrent aphthous stomatitis- 0.64%	Oral mucosa	Vesiculobullous lesion	-	-
17.	Fantozzi PJ et al (2021) [28]	Dry mouth-45.9%; swallowing difficulties,-39.2%; dysgeusia-59.5%	Tongue; oral cavity	Taste alteration, xerostomia	First symptom (xerostomia)-19.6%; dysgeusia (87.9%) Duration (xerostomia) -7 days; dysgeusia 6 days	Fever (90.9), cough (46.8), dyspnea (34.3), diarrhea (4.5), sore throat (3.6), fatigue (3.6), myalgia/arthralgia (2.7), vomiting (2.7)
18.	Favia G et al (2021) [29]	Geographic tongue (n=7); fissured tongue (5); ulcerative lesion (65); blisters (19); hyperplasia of papillae (48); angina bullosa (11); candidiasis (28); ulceronecrotic gingivitis (7) Petechiae (14); oral haemorrhage (1) Taste disorders (90%)	Tongue, oral mucosa, lips	Tongue manifestation, vesiculobullous lesion, red and white lesions, periodontal changes, bleeding disorders, taste alteration	Together with general symptoms (26.2%); Duration: one week (41%) After 1 week of general symptoms (32.6%)	Fever, anosmia, cough, sore throat, congestion, runny nose, nausea or vomiting, muscle and body aches, dermatologic manifestation, pneumonia, dyspnea, hypoxia (spo2 < 90%)
19.	Halepas S et al (2021) [30]	Red and/or swollen lips (48.9%); strawberry tongue (10.6%)	Lips, tongue	Lip lesions, tongue manifestation	-	Fever

20.	Rekhtman S et al (2021) [31]	Rashes on lips and tongue-5.7% and 2.9%; ulcers on lips and tongue	Lips and tongue	Tongue manifestation, vesiculobullous lesion, lip lesions		Generalized rashes and vesiculobullous lesions present
21.	Maraouf N et al (2021) [32]	Periodontitis-258/568	Periodontium	Periodontal changes	-	-
22.	Nuno-Gonzalez A et al [5] (2021)	Oral mucosal changes (11.7%), transient anterior U-shaped lingual papillitis (11.5 %), tongue swelling (6.6%), aphthous stomatitis (6.9%), burning sensation in the mouth (5.3%), m ucositis (3.9%), glos sitis with patchy depapillation (3.9%), white tongue (1.6%), and enanthema (0.5%), taste disturbances	Tongue, oral mucosa	Tongue manifestation, vesiculobullous lesion, burning sensation	-	-
23.	Subramaniam T et al (2021) [33]	Ulcers on oral mucosa (case 1); burning mouth and mucositis on lower labial mucosa (cases 2,5); papillary atrophy (case 3); reddish-white spots on the palate (case 4); ulcers on lower lip (cases 6,7,8); pallor of lip (case 9)	Oral mucosa, palate, lips, tongue	Tongue manifestation, vesiculobullous lesion, burning sensation, red and white lesions, lip lesions	-	Fever, cough, dyspnea, runny nose, chest tightness, loss of smell
24.	Abubakr N et al (2021) [34]	Dental pain (23%), pain in jaw bones or joint (12.0%), halitosis (10.5%), ulcerations (20.4%), and dry mouth (47.6%)	Teeth, jaw bones, oral cavity	Vesiculobullous lesion, xerostomia, pain in teeth and jaw, tmj disturbances	-	Fever, myalgia, dysphagia, and hyposmia, loss of smell, nasal itching
25.	Song J et al (2021) [35]	Loss of taste (20.6%; median score, 6)	Tongue	Taste alteration	First symptom (0.4%) Recovery time-7 days	Nasal obstruction (8.6%), rhinorrhea (10.3%), nasal itching (4.9%), sneezing (11.0%), loss of smell (11.4%)
26.	Bardellini E et al (2021) [36]	Oral pseudomembranous candidiasis (7.4%), geographic tongue (3.7%), coated tongue (7.4%); taste alteration (11.1%)	Tongue, oral mucosa	Red and white lesions, tongue manifestation	-	Fever, cough, rhinorrhoea, breathing difficulty
27.	Gherlone EF et al (2021) [37]	Salivary gland ectasia-38%; dry mouth-30%; dysgeusia-17%; white plaque-28%; oral ulcers-12%	Salivary glands, tongue, oral mucosa, oral cavity	Salivary gland disorders, xerostomia, red and white lesions, vesiculobullous lesions, taste alteration	-	-
28.	El Kady DM et al (2021) [38]	Dry mouth 39.7%; loss of salt sensation-34.5%, loss of sweet sensation-29.3%, altered food taste-	Tongue, salivary glands, gingiva, oral mucosa	Xerostomia, taste alteration, periodontal changes, salivary gland disorders, vesiculobullous	-	-

		25.9%; tongue redness 8.8%; gingival bleeding 7%; salivary glands infection 22.4%; swellings in the salivary gland or cheek 13.8%; pain or swelling below mandible-10.8%; burning mouth sensation-22.4%; ulcers-17.2%		lesions, burning sensation		
29.	Fidan V et al (2021) [39]	Aphthous-like ulcer (36.5), erythema (25.7), lichen planus (16.2); tongue (31.8), oral mucosa (27.0), gingiva (14.9), palate (5.4)	Tongue/oral mucosa/gingiva/palate-39.7%/34.5%/18.9%/6.9%	Vesiculobullous lesions, red and white lesions, periodontal changes	Oral lesions prior covid-19 diagnosis	-
30.	Natto ZS et al (2021) [40]	Loss of taste-43.4%; erythema/desquamated gingivitis and coated tongue (7.3%); ulcers/blisters (6.4%); pain and soreness (2.8%); dry mouth (0.9%)	Tongue; gingiva; oral mucosa, oral cavity	Vesiculobullous lesions, taste alteration, xerostomia	After systemic symptoms	Cough, fever, sore throat, runny nose, muscle pain, headaches, nausea, and diarrhea
31.	Elamrousy WAH et al (2021) [41]	Oral ulcers (92.8%); dry mouth (84%); loss of taste (55%); hemorrhagic ulcers with crust on lips	Lip/tongue/labial mucosa-42.3%/38.5%/34.6%	Vesiculobullous lesions, lip lesions, taste alteration	-	Asthenia (67.7), breath problems (67.7), cough (67.7), fatigue (19.4), abdominal symptoms (12.9)
32.	Bulut DG et al (2021) [42]	Taste loss (53%), halitosis (21%), oropharyngeal wound and pain (18%), pain in the chewing muscles (16%), pain in the temporomandibular joint (17.5%), gum bleeding (17.5%), dry mouth (38%, after recovery 12.0), aphthous ulcer (14.5%), sensitivity and/or pain in teeth (12%), herpes labialis (8.5%), burning in the tongue (7.5%)	Tongue, gingiva, lips, oral cavity	Taste alteration, TMJ disturbances, xerostomia, burning sensation, vesiculobullous lesion, periodontal changes, teeth pain	-	Presence of symptoms (87.5)
33.	Naser Al et al (2021) [43]	Burning sensation (6%), numbness or tingling of the tongue (2%), white coat of the tongue, gingiva, palate (31.6%, 22.4%, 15.6%), loss of taste (79.5%), aphthous ulcers (24.8%), black discoloration of oral cavity, lips and tongue (4.7%, 6.8%), yellow coating on lips (5.3%)	Tongue, palate, lips, oral mucosa, oral cavity	Burning sensation, tongue manifestation, red and white lesions, vesiculobullous lesion, fungal infection, lip lesions	-	-

34.	Muthyam AK et al (2022) [44]	Dry mouth (44%) followed by swallowing difficulty, mouth ulcerations, chewing problems, gum bleeding, and burning sensation, altered taste (72%); fissured tongue, halitosis, and loss of taste-2%	Gums, tongue, oral mucosa, oral cavity	Xerostomia, vesiculobullous lesions, taste alteration, periodontal changes, tongue manifestation, burning sensation	Altered taste lasted more than 1 week-53%	Weakness (8%), cough and cold (4%), and body pain (2%)
35.	Ganesan A et al (2022) [45]	Gustatory disturbance-51.2; dry mouth=28%; erythema, ulcers and depapillation of tongue-15.5% A statistically significant correlation between oral manifestations and disease severity ($p \leq 0.001$).	Tongue, oral mucosa	Xerostomia, tongue manifestation, taste alteration	-	-
36.	El Tantawi M et al (2022) [46]	Dry mouth (11.1% vs 7.5%, $p = 0.009$) and change in taste (11.5% vs 2.7%, $p < 0.001$) were greater in covid-19 person; leukoplakia-4.6%; ulcers & hairy tongue-2.3%;gingival inflammation-13.1%	Oral cavity, tongue, gingiva	Vesiculobullous lesions, xerostomia	-	-
37.	Soares CD et al (2022) [47]	Lesions in the palate/tongue/lips or palate- 57.1%, 29%/ 14.3%.	Tongue, lips, palate	Vesiculobullous lesions	-	Anosmia, fever, and headache.
38.	Tuter G et al (2022) [48]	Dry mouth (44.2%); oral lesions (22.4%); oral mucosa (15.2%); tongue (10.8%).	Tongue, Oral mucosa	Vesiculobullous lesions, xerostomia	-	-
39.	Schwab G et al (2022) [49]	Ageusia – 11.0%; opportunistic oral infections such as pseudomembranous candidiasis and herpes simplex-4.5%	Tongue, oral mucosa	Vesiculobullous lesions, taste alteration, red and white lesions	-	Cough – 72.7%; dyspnoea – 63.0%; fever – 53.9%; anosmia – 14.3%
40.	Chawla J et al (2022) [50]	Dry mouth (38%) ($p=0.03$); Dysgeusia (32%) ($p=0.04$); Vesiculobullous lesion-13%; Oral ulcers-3.7%	Oral cavity, tongue	Vesiculobullous lesions, xerostomia, taste alteration	-	Cough/sore throat/shortness of breath/running nose-30%/20%/7%/11%
41.	Binmadi NO et al (2022) [51]	Distortion of taste-60%; dry mouth-42%, oral ulcerations-11%, gingivitis/petechiae/ candidiasis-6%; necrotizing periodontal disease/vesiculobullous lesions/erythema migrans/geographic tongue-4%	Gingiva, tongue, oral mucosa, oral cavity	Vesiculobullous lesions, xerostomia, taste alteration, periodontal changes, red and white lesions, bleeding disorders, tongue manifestation	Concurrently-47%, after the general symptoms-43%, and before the general symptoms-9%	Fever (95%), headache (65%,), fatigue (65%), cough (63%), myalgia/arthralgia (53%), loss of smell (53%), sore throat (50%), shortness of breath or dyspnea (40%), nausea or vomiting (21%), and diarrhea (15%).

42.	de Paula Eduardo F et al (2022) [52]	Saliva alterations-24.4%; dryness-9.9%; tongue coating-3%; sialorhea-3.3%; petechiae-10.5%; oral bleeding-7.5%	Oral mucosa, tongue	Xerostomia, salivary gland disorders, bleeding disorders, tongue manifestation	-	-
43.	Villarroel-Dorrego M et al (2022) [53]	Hemorrhagic ulcerative lesions-7.3%; erythematous and pseudomembranous forms of candidiasis-12.7%; angular cheilitis-1.5%; total loss of taste-60%; burning mouth-36.4%; dry mouth-27.3%	Tongue, oral mucosa	Xerostomia, bleeding disorders, red and white lesions, vesiculobullous lesions, taste alteration, burning sensation	-	-
44.	Manifar S et al (2022) [54]	Dry mouth-68.6% ($p < 0.001$) Dysgeusia-51.4% ($p < 0.001$) Hypogeusia-49.3%; halitosis-31.4%; metallic taste-29.3%	Tongue, oral cavity	Xerostomia, taste alteration	-	Gastrointestinal symptoms, smell defects, asthma, skin rashes, cough, malaise, myalgia, anorexia, respiratory distress, olfactory dysfunction
45.	Bhuyan R et al (2022) [55]	Burning sensation-2.4%; dry mouth-2.4%; loss of taste-31% ($p<0.001$); mouth ulcer-2.4%. Bleeding gum-2.4%.	Oral cavity, gums, tongue	Xerostomia, taste alteration, burning sensation, vesiculobullous lesion, periodontal changes	-	-
46.	Brandao TB et al (2020) [56]	Multiple aphthous-like ulcers covered with mucopurulent membrane in the Upper and lower lip mucosa and tongue (cases 1,2,4,5); ulcers on tongue and hard palate (case 3); ulcers on tongue and aguesia (cases 6,7, 8)	Lips, tongue, palate	Vesiculobullous ulcers, taste alteration, tongue manifestation	06-10 days	Chest tightness, fever, cough (cases 1,5,7,8); cough, Fever, dyspnea (cases 2,6); Abdominal distension, fever, mild dyspnea (cases 3 and 4)
47.	Dima M et al (2020) [9]	Oral candidiasis	Oral mucosa	Red and white lesions	-	Epistaxis and diaper erythema (all 3 cases); palpebral edema (newborn 2)
48.	Tapia ROC et al (2020) [57]	Bulla on the hard palate (x6mm) (case 1); diffuse purple macule (x12mm) and papule-plaque (x8mm) on the left and right palatal mucosa (case 2); tongue enlarge-ment (case 3); Burning mouth sensation and reddish macules on hard palate (case 4)	Palate, oral mucosa, tongue	Vesiculobullous lesion, red and white lesions, burning sensation, tongue manifestation		Fever, myalgia, dysphagia, and hyposmia
49.	Vaira LA et al (2020) [58]	Hypogeusia (33 cases) Complete ageusia (1 case)	Tongue	Taste alteration		Fever, cough, nasal obstruction, sore throat, hyposmia, anosmia, pneumonia

50.	Presas CMC et al (2020) [59]	Dysgeusia (case 1); multiple ulcers On palate (case 2); pain on tongue, blisters in lip mucosa and Desquamative gingivitis (case 3)	Tongue, lips,	Taste alteration, periodontal changes, vesiculobullous lesions	Along with systemic symptoms	Asthenia; hyposmia, and enlargement of lymph nodes in the neck (cases 1 and 3) Fever and diarrhea (case 2)
51.	Sinadinosand Shelswell (2020) [6]	Pain in palate (case 1); pain and ulcerations in palate (case 2), pain in tongue, blisters of the labial mucosa; desquamative gingivitis (case 3)	Palate, tongue, gums, lips	Tongue manifestation, periodontal changes, vesiculobullous lesions	-	Sore throat (case 1) Pneumonia (case 3)
52.	Rodríguez MD et al (2020) [60]	Dysgeusia, aphthous-like lesions, burning sensation, and tongue depapillation (case 1); burning mouth sensation and unilateral commissural fissures (case 2); dry mouth, lesions on the tongue, palate, and commissure (case 3)	Tongue, palate, oral mucosa	Taste alteration, xerostomia, vesiculobullous lesions, tongue manifestation, burning sensation	Before presentation (case 1); after discharge (case 2); with systemic symptoms (case 3)	Fever, malaise, and anosmia, diarrhea, and pneumonia (cases 1 and 3)
53.	Corchuelo and Ulloa (2020) [61]	Reddish plaques on the lower lip, dark brown pigmentation and aphthous ulcers in the gums, whitish area in tongue	Lower lips, gums, oral mucosa	Red and white lesions, vesiculubullous lesions, tongue manifestation	Mean duration: 8-10 days	-
54.	Dos Santos et al (2020) [10]	Hypogeusia, white plaque, multiple pinpoint yellowish ulcers in the tongue, nodule in lower lip (1cm)	Tongue, lower lip, oral mucosa	Taste alteration, vesiculobullous lesions, tongue manifestation	Mean duration: 14 days	Respiratory symptoms and progressive dyspnea on exertion, Fever and diarrhea.
55.	Zarch and Hosseinzadeh (2020) [62]	Vesicles on lower lip mucosa	Lip mucosa	Vesiculobullous lesions	2 days before systemic symptoms	High fever, Fatigue, and lack of appetite
56.	Hjelmeseth J (2020) [63]	Total ageusia	Tongue	Taste alteration	-	-
57.	Kahraman and Çaşkurlu (2020) [64]	Erythematous surface (hard palate), few petechiae in the midline and numerous pustular enanthema near the soft palate border	Palate	Bleeding disorders, vesiculobullous lesions	Mean duration: 10 days	Sore throat Fever, fatigue, severe dry cough, inability to taste or smell,
58.	Smith AC et al (2020) [65]	Loss of taste	Tongue	Taste alteration	Before general symptoms	Frontal headache, loss of smell, headache, loose stools
59.	Maniaci A et al (2020) [66]	Transient loss of taste	Tongue	Taste alteration	Mean duration: 12 days	Fever, sore throat, runny nose, presence of erythematous skin le-sions on the lower limbs, asthenia
60.	Melley LE et al (2020) [67]	Loss of taste	Tongue	Taste alteration	1 week before systemic presentation	Shortness of breath, Fatigue, and loss of appetite

61.	Riad A et al (2020) [68]	Painful white patches on the dorsal surface of the tongue and palate, mild tongue pain	Tongue, palate, oral mucosa	Tongue manifestation, red and white lesions	2 weeks before diagnosis	Sore throat, generalised myalgia, and Fatigue with intermittent fever
62.	Putra BE et al (2020) [69]	Stomatitis aphthous	Oral mucosa	Vesiculobullous lesions	Day 7	Fever, back pain, myalgia, sore throat, dry cough, rhinorrhea, anosmia
63.	Dalipi ZS et al (2021) [70]	Loss of taste Bullous and erosive erythematous lesions of lips and oral mucosa	Tongue, lips	Taste alteration, vesiculobullous lesions, lip lesions	Loss of taste-2 weeks before diagnosis	Fever, cough, headache, muscle pain, loss of smell, dark red, purpuric, irregular maculopapular lesions on abdomen
64.	Eita AAB et al (2021) [71]	Dysgeusia and greasy tongue coat	Tongue	Taste alteration, tongue manifestation	Before systemic symptoms	Sore throat, fever (38° C), nasal congestion, conjunctivitis, nausea, Abdominal pain, diarrhea, fatigue, severe joint pain.
65.	Cirillo and Colello (2021) [72]	Loss of taste	Tongue	Taste alteration	1 week before presentation	Loss of smell, headache, fatigue, and muscle pain
66.	Nejabi MB et al (2021) [73]	Fissured tongue, white scars and painful erosive ulcer on the Dorsal surface of the tongue	Tongue	Tongue manifestation	After 1 week of general symptoms	Fever, cough, taste alterations, olfactory dysfunction, and chest tightness
67.	Klein H et al (2021) [74]	Loss of taste	Tongue	Taste alteration	From 4th to 6 weeks	Fever, dry cough, chest pain, sore throat, diarrhea, nausea, headache, and back pain.
68.	Ramires MCCH et al (2021) [75]	Crusted ulcers on lip vermilion (both upper and lower lips	Lips	Vesiculobullous lesions	2 weeks after the onset of fever	Flu-like syndrome; evere and progressive dyspnea (spo2 = 88 %)
69.	Hocková B et al (2021) [76]	Oral lesions at the dorsal surface of the tongue (case 1); multiple lesions located on the tongue dorsum and labial mucosa (case 2); lesions on upper and lower lip (case 3)	Tongue and lips	Vesiculobullous lesions	After the diagnosis (all 3 cases)	Headache, fever, dry cough, and dyspnoea
70.	Teixeira IS et al (2021) [77]	Painful vesiculobullous lip lesions	Lips	Vesiculobullous lesions	After 4 days (case 1); after 10 days (case 2); after 11 days (case 3); after 19 days (case 4)	Headache, myalgia, and dyspnea
71.	EmelyanovaN et al (2021) [78]	Unusual tongue appearance and burning sensation, intermittent bleeding of gums, severe dryness in the oral cavity and persistent distortion of taste	Tongue, gums, oral mucosa	Burning sensation, periodontal changes, taste alteration, tongue manifestation, xerostomia	Third day (dysgeusia) and fifth day (xerostomia) after systemic symptoms	Rhinorrhea, coughing and increased body temperature to 38.5°
72.	Fathi Y et al (2021) [79]	Oral pain, ulcerative lesions on oral mucosa, hemorrhagic crusts on lips	Oral mucosa and lips	Vesiculobullous lesions, lip lesions,	3rd day (oral pain)	Fever, abdominal pain, nausea and occasional vomiting
73.	Shenoy P et al (2022) [80]	Ulcer with irregular borders on the dorsum of the tongue surrounded by a scrapable whitish plaque	Tongue	Tongue manifestation, red and white lesions	Systemic symptoms-3 weeks prior	Fever, cough, chest tightness

74.	Palaia G et al (2022) [81]	Extensive erosions involving lips, ulcers on the hard palate, blisters and ulcers on the dorsal surface of the tongue cheek mucosa	Palate, lips, oral mucosa	Vesiculobullous lesions	7 days prior to general symptoms (duration of oral lesions-14 days)	Bilateral cutaneous lesions were also evident on the hands. Low-grade fever
75.	Rafałowicz B et al (2022) [82]	Unilateral aphthous-like lesions on the left side of the hard palate (case 1 & 5); hemorrhagic changes on the palate and cheilitis (case 2); smooth tongue with intensely red-purple mucosa (case 3); angioma type lesion on the right side of the palate (case 4); mycosis of the tongue, extensive lesions on the palate, spontaneous bleeding, cheilitis (case 6)	Hard palate, tongue; lips	Vesiculobullous lesions, red and white lesions, fungal infection, tongue manifestation, bleeding disorders	-	Fever, malaise, taste disorders, anosmia, and pneumonia (case 1); dyspnea, persistent diarrhea, and vomiting (case 2); loss of smell and taste and fever for 9 days (case 4 & 5)

Supplementary table 1: Treatment of oral lesions for COVID-19 patient

Author & year	Treatment given for oral lesions	Resolution time	General treatment for COVID-19	Outcome of COVID-19
Sinadinos and Shelswell (2020) [6]	Valaciclovir and topical antiseptics (chlorhexidine and hyaluronic acid)-cases 1 and 3; topical antiseptic mouthwash (case 2)	10 days (cases 1 and 3), 7 days (case 2)	-	All 3 recovered
Dima M et al (2020) [9]	Nystatin for the oral candidiasis.	15 days 21 days (newborn 3)	Vitamin D, topical cream for erythema (cases 1 and 2); Ampicillin (100 mg/kgc/d), Gentamicin (4 mg/kgc/d), aminophylline (3 _ 0.3mL/d), and Fluconazole iv (6 mg/kgc) (newborn 3)	All 3 cases recovered
Dos santos et al (2020) [10]	Oral nystatin (100,000 IU/mL, 8/8h, for 30 days), chlorhexidine digluconate (0.12%) 1% hydrogen peroxide	44 days	Fluconazole 200mg/100mL, Meropeném-1000mg, 8/8hs, Sulfamethoxazole+Trimetropin-400mg +80mg, 1.5 ampule, 8/8hs for 10 days Enoxaparin sodium - 60mg/day.	Recovered
Favia G et al (2021) [29]	Hyaluronic acid gel and chlorhexidine 2% mouthwash, miconazole nitrate twice a day in patients with cytological diagnosis of candidiasis, tranexamic acid for local hemorrhages	14-21 days	-	Good recovery

Naser Al et al (2021) [43]	Chlorhexidine 0.2% mouthwash (35%), Nystatin (15%), Mycoheal (8%), Anginovag spray (22%) Fluconazole (13%), Kenalog spray (6%), Amphotericin B (1%)	7.7 days	-	98% responded to treatment
Soares CD et al (2022) [47]	Most patients with chronic ulcers were treated with topical corticosteroids and the lesions resolved after 1 to 2 weeks.	2 weeks	-	All recovered
Brandao TB et al (2020) [56]	Daily photobiomodulation therapy (PBMT)-10 days; 0.12% chlorhexidine mouthwash	11-14 days	Intravenous acyclovir-250 mg/m 2-3 times a day for 10 days.	Recovered (06 cases); critical condition (cases 2 & 4)
Tapia ROC et al (2020) [57]	Topical Mometasone furoate 0.1% in solution after oral hygiene and clorhexidine 0.12% mouthwash	14 days	Acetaminophen 500mg every 6 h for 4 days and Fexofenadine 180 mg every 24 h per 10 days (case 1,2); Dexanethasone 8mg (case 2)	Recovered
Presas CMC et al (2020) [59]	Topical Antiseptics, chlorhexidine and hyaluronic acid mouthwash (Cases 1 & 2); prednisolone 30 mg per day (case 3)	10 days	Valaciclovir 500 mg every 8 hr for 10 days (case 1); antibiotics, corticosteroids, and lopinavir 200 mg, ritonavir 50 mg, hydroxychloroquine 200 mg) (case 3)	Recovered
Rodrígue z MD et al (2022) [60]	triamcinolone acetonide 0.05% (case 1); ointment containing neomycin, nystatin, and triamcinolone acetonide and chlorhexidine mouthwash (case 2); Nystatin solution rinses (case 3)	10 days (cases 1 and 2); 15 days (case 3);	-	All 3 recovered
Corchuel o and Ulloa (2020) [61]	Nystatin oral suspension-3 ml (300,000 I.U) every 6 h; Chlorhexidine gluconate (0.12%)	14 days	-	Recovered
Kahrama n and Çaşkurlu (2020) [64]	Antibiotherapy	14 days	Clarithromycin 500 mg b.i.d. immediately after the diagnosis	Recovered
Smith AC et al (2020) [65]	-	21days	Fluticasone, Loratadine, and nasal spray	Recovered
Melley LE et al (2020) [67]	-	15days	Hydroxychloroquine 400 mg, azithromycin 500 mg	Recovered
Riad A et al (2021) [68]	Topical antifungal, nystatin (Micostatin) and antibacterial mouthwash, chlorhexidine 0.2%, twice daily (case 1); topical antifungal *miconazole* (Daktarin Gel) (cases 2 and 3); systemic antifungal *fluconazole* (Flucoral) (case 3)	10 days (case 1); 4 days (case 2); 7 days (case 3)	*Azithromycin* (Zithromax, *levofloxacin* (Uniloxam), *r ivaroxaban* (Xarelto), and *lactoferrin* (Pravotin) (case 1)	All 3 recovered

Putra BE et al (2020) [69]	Oral hygiene regimen and mouthwash	21 days	Azithromycin 500 mg, hydroxychloroquine-400 mg (10 days), oseltamivir-75 mg (10 days), vitamin C-1000 mg (14 days), vitamin D-5000 IU (14 days) On day six, the lesions lessened	Recovered
Dalipi ZS et al (2021) [70]	Antibiotic therapy with penicillin and anticoagulant therapy with Fraxiparine solution for injection 0.4 mL, antiseptic mouthwash (0.2% chlorhexidine solution mouthwash twice per day for 14 days	21 days	Systemic corticosteroids, vitamins (C, B complex), and locally applied tablets (panthenol-calcium with pantothenic acid)	Recovered
Eita AAB (2021) [71]	0.12% chlorhexidine mouth rinse and nystatin oral drops 100.000 I.U/ml 2-3 times daily). Daily vitamin C (1000 mg) and zinc (50 mg)	28 days	*Azithromycin 500 mg/day, paracetamol 500 mg 2 tablets ×3 times daily, zinc (50 mg), and vitamin C (1000 mg) supplements*	Recovered
Nejabi MB et al (2021) [73]	Intravenous Acyclovir 5 mg/kg for 7 days; PMBT-10 days; Chlorhexidine 0.12%, H2O2-1%)	14 days	Azithromycin 500 mg daily for one week and ceftriaxone 1g twice a day for 3 days. antifungal agents (fluconazole 200 mg tablets for 1 week)	Recovered
Ramires MCCH et al (2021) [75]	Photodynamic therapy for 2 days, methylene blue at 0.01 % was applied over all lesions. After 5 min (time pre-irradiation), the laser device Therapy EC® was used at 660 nm. A total of 30 points were distributed throughout the affected areas: 20 points on the upper and 10 on the lower lip.	Healed after 4 days of therapy	-	Recovered
Teixeira IS et al (2021) [77]	For PBMT, a laser device Laser DUO® was used at 660 nm, on contact mode, point by point, with 100 mW, 33 J/cm2, 0.5 J, and 5 s per point. Then, aPDT technique was performed, with methylene blue at 0.01 % applied over all lesions and after 3 min, the same laser parameters were used.	Marked improvement after 72 hrs	*Azithromycin and ceftriaxone. dexamethasone*	Recovered
Fathi Y et al (2021) [79]	Removal of dental plaque and chlorhexidine mouthwash (twice a day). Valacyclovir for 5 days	Resolved after 4 days	Metronidazole, ceftriaxone, meropenem, ribavirin and hydroxychloroquine were administered and supplemental oxygen was given	-
Shenoy P et al (2022) [80]	Tab Fluconazole, Clotrimazole mouth paint, Chlorhexidine 0.12% mouth rinse.		Anticoagulants, corticosteroids and multivitamins. Medications include Inj.Enoxararin, Inj. Pantop, Tab.Shelcal HD, Neb.Budecort, Inj.Predmet 40 mg, Cap.Meganeuron	Succumbed to disease.

Rafałowicz B et al (2022) [82]	Semiconductor laser therapy with the Smart bio stimulation function-five treatments at 3-day intervals (case 1); aliva-stimulating tablets SST (Sinclair Pharmaceuticals), Kserostemin (artificial saliva) (Aflofarm), and mouthwash with chlorhexidine three times a day for a period of 14 days (case 3); antifungal Nystatin (Teva) antibiotic was administered at a dose of 100,000 IU/mL four times a day along with vitamin A + E + F (Gorvita) ointment on the lips (case 6)	192 days (case 1); 2 weeks (case 3); 60 days (case 5)	-	-