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Original Article

Estimating the prevalence of oral manifestations in COVID-19 patients: a systematic review

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ABSTRACT

Objectives: Patients with coronavirus disease 2019 (COVID-19) present with a variety of oral manifestations. Therefore, we conducted a systematic review to estimate the prevalence of oral lesions among COVID-19 patients.

Methods: An extensive literature search of several electronic bibliographic databases (PubMed, Scopus, Science Direct, Litcovid) was conducted to retrieve all articles published in the English language from January 1, 2020 to March 31, 2023 that reported the prevalence of oral manifestations among COVID-19 patients. A meta-analysis of pooled prevalence was performed using Jamovi ver. 2.3 (2022). The I^2 and Q statistics were used to assess heterogeneity between studies, and p-values < 0.01 were considered statistically significant.

Results: In total, 79 studies with data from 13,252 patients were included. The articles were predominantly published in 2020 (n = 33), and Italy was the most common country (n = 14). Most of the affected patients more than 50 years old and women (56.6%). The most common sites of involvement were the tongue (n = 65), followed by the oral mucosa (n = 37) and lips (n = 19). High heterogeneity was found between studies. The most common oral manifestation was taste alteration, followed by xerostomia and ulceration, showing pooled prevalence rates of 48%, 35%, and 21%, respectively.

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

Keywords: COVID-19; Oral manifestations; Oral ulcer; SARS-CoV-2

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Introduction

The novel coronavirus disease 2019 (COVID-19) has rapidly evolved into a global crisis, posing a

significant challenge to public health due to its swift spread and high mortality rate. Initially identified in December 2019 in China's Hubei Province, the disease quickly spread across the globe. By March 2020, the World Health Organization (WHO) had declared it a 'pandemic emergency'. As of April 2023, the outbreak has resulted in over 762,201,169 confirmed cases and 6,893,190 deaths worldwide [1]. The disease's incubation period spans from 1 to 14 days, with the most frequently observed symptoms being fever, cough, shortness of breath or difficulty breathing, and fatigue. Other less common symptoms, such as headache, loss of taste or smell, sore throat, diarrhea, and nausea or vomiting, may also manifest [2]. The severity of these symptoms can vary greatly among individuals, as it is influenced by factors such as the timing of exposure to the virus, the patient's age and gender, and any pre-existing health conditions.

Research has shown that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infiltrates human cells using receptors known as angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (also referred to as transmembrane serine protease or TMPRSS2) [3]. Of these 2, the ACE2 receptor is primarily located in the cells of the lungs, liver, kidneys, and gastrointestinal (GI) tract, as well as the salivary glands and the dorsum of the tongue within the oral cavity [4]. These cells, equipped with the receptors, serve as host cells for the virus. The virus penetrates these cells and triggers an inflammatory response in the affected organs [4].

Previously, COVID-19 was not thought to have oral symptoms, unlike other viral rash. However, the subsequent detection of SARS-CoV-2 in patients' saliva suggested that oral manifestations could indeed be clinical characteristics of the disease [3]. The presence of the ACE2 receptor in specific oral organs, such as the tongue and salivary glands, further supports the potential involvement of the oral cavity in COVID-19 infection [3]. The prevalence of oral manifestations among COVID-19 patients is currently unknown, but several studies have attempted to determine their incidence and prevalence [5–10]. A large-scale study by Nuno-Gonzalez et al. [5] involving 666 patients found oral cavity findings in 25.65% of cases. The most frequently observed oral symptoms, as reported in a case series by Sinadinos and Shelswell [6], were blisters, ulcerations, and desquamative gingivitis. Within the oral cavity, the palate and tongue are the sites most commonly affected by COVID-19, followed by the gums and lips [7]. On the tongue, ulcerations are particularly common, especially on the dorsal surface or sides. However, only 15% of patients develop ulcerations on the ventral surface. Other possible tongue symptoms include multiple pinpoint yellowish ulcers and white plaque [3]. The presence of white plaque on the tongue's dorsal surface is often due to fungal infections, another common oral manifestation of SARS-CoV-2, likely resulting from reduced immunity. Dima et al. [8] reported a case of a neonate with COVID-19 who developed oral cavity candidiasis. These oral symptoms are often painful, with 75% of patients reporting discomfort [7]. In another study, 25% of patients reported taste impairment, 15% experienced burning sensations, and 20% had difficulty swallowing. Taste disorders were observed in 24% of patients (ageusia), 35% (hypogeusia), and 38% (dysgeusia). These taste disorders were more prevalent in women than in men [9].

It is crucial for dentists to understand the oral manifestations of COVID-19, as this knowledge aids in early disease diagnosis and consequently, prevents transmission. This systematic review aims to summarize the findings from existing literature on the oral manifestations of COVID-19, highlighting the role of the dentist in mitigating the severity of this deadly pandemic.

HIGHLIGHTS

- The present systematic review shows a higher prevalence of oral manifestations among COVID-19 patients, specifically taste alterations, followed by xerostomia, ulceration, and red and white lesions.
- COVID-19 patients show various oral manifestations that may help clinicians detect the disease early in its course.
- Identifying the oral signs and symptoms of COVID-19 is crucial for initiating early diagnosis and treatment of this deadly disease; therefore, increasing awareness of these symptoms is importa

Materials and Methods

A systematic assessment and description of the currently reported cases and studies related to oral manifestations associated with SARS-CoV-2 infection was conducted. This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [10].

Eligibility Criteria

We conducted a search for clinical evidence in the form of original, peer-reviewed journal articles. These included observational and cross-sectional studies that investigated

the prevalence of oral disorders in patients with COVID-19. In addition to these, we also incorporated case reports and case series into our systematic review. The data publication range was restricted from January 1, 2020 to June 30, 2022. We further updated our research on March 31, 2023 across these databases. We did not utilize conference papers, book reviews, book chapters, letters to the editor and replies, newspaper and newsletter articles, expert opinions, or theses and dissertations. Any articles not published in English were also excluded.

Data Sources and Search Strategy

We carried out a comprehensive search of various electronic bibliographic databases, including PubMed, Scopus, Science Direct, and Litcovid. We gathered all articles published between January 1, 2020, and March 31, 2023. We then screened observational cross-sectional, case-control and cohort studies, case reports/series that reported on multisystem inflammatory syndrome in children, as well as letters to the editor. The 2 independent reviewers (A.G. and K.S.) conducted an electronic search of all cross-sectional studies, case reports, and case series up until March 31, 2023. They used a combination of relevant keywords, appropriately linked by Boolean operators. (1) COVID-19 OR SARS-CoV-2 OR Coronavirus disease 2019 OR novel coronavirus; (2) AND oral manifestations OR oral involvement OR oral lesions; (3) AND cross-sectional studies OR case reports OR case series.

Selection Process

The inclusion of studies was done in 2 phases. During the first phase, the titles of all studies were initially screened, followed by a review of their abstracts using the established inclusion and exclusion criteria. Two authors (A.G. and K.S.) independently performed this screening. If a title and abstract appeared to meet the criteria, the full article was then read and assessed for eligibility by these same 2 authors (A.G. and K.S.). Any disagreements between the authors were resolved through discussion and consensus, with the involvement of a third author (A.A.) if necessary. Duplicates were removed and irrelevant articles were excluded from the systematic review. We obtained and evaluated the full-text articles of all potentially relevant studies. In the second phase, we screened the references of all the included studies, case reports, and case series once more to identify any additional potentially eligible studies.

Data Collection

Three authors (A.G., K.S., and A.P.) independently extracted data from the eligible studies. In the event of disagreements, a 4th author (A.A.) was included to facilitate consensus through discussion. We included all studies that reported orofacial manifestations in patients with COVID-19. To systematically review these studies, we assessed the included studies based on demographic details such as author, year, country, study type, sample size, gender, age, study duration, medical history, intensive care unit (ICU) admission, and disease severity. In addition, we recorded details related to oral manifestations, including the affected site, onset of orofacial manifestations, general symptoms, any special investigations conducted, treatment of oral lesions, and disease outcome. The flow diagram for article inclusion is depicted in Figure 1.

Assessment of Risk of Bias of the Included Studies

The Joanna Briggs Institute (JBI) Critical Appraisal Tools for use in systematic reviews of cross-sectional studies, case-control studies, case reports, and case series were used to assess the risk of bias and the individual quality of the selected studies [11]. Each type of study was assessed using its respective checklist, with each question offering 3 possible responses: yes, no, or unclear. Two blinded reviewers (A.G. and K.S.) evaluated the risk of bias in each study, using a scoring system agreed upon by all reviewers. Following the assessment, studies were categorized based on their scores: high bias (if the study scored up to 49% "yes"), moderate bias (if the study scored between 50% and 69% "yes"), and low bias (if the study scored more than 70% "yes").

Statistical Analysis

Qualitative data were reorganized by grouping and comparing the information reported in the studies. Conditions affecting the oral and mucosal areas were summarized using schematic diagrams. The primary outcome of interest was the prevalence of oral symptoms in COVID-19 patients. The prevalence of oral lesions was categorized into subgroups such as taste alteration, red and white lesions, vesiculobullous lesions, xerostomia, ulceration, burning sensation, and salivary gland disorders. A meta-analysis of the combined prevalence was then conducted using Jamovi ver. 2.3 (2022; https:// www.jamovi.org). To evaluate heterogeneity between studies, the I^2 and Q statistics were utilized, with p-values less than 0.01 considered statistically significant. The analyses were conducted using a random model. Oral lesions in COVID-19 patients, as reported in case reports and case series, were not included in the meta-analysis.

Results

After conducting the initial search, a total of 275 articles

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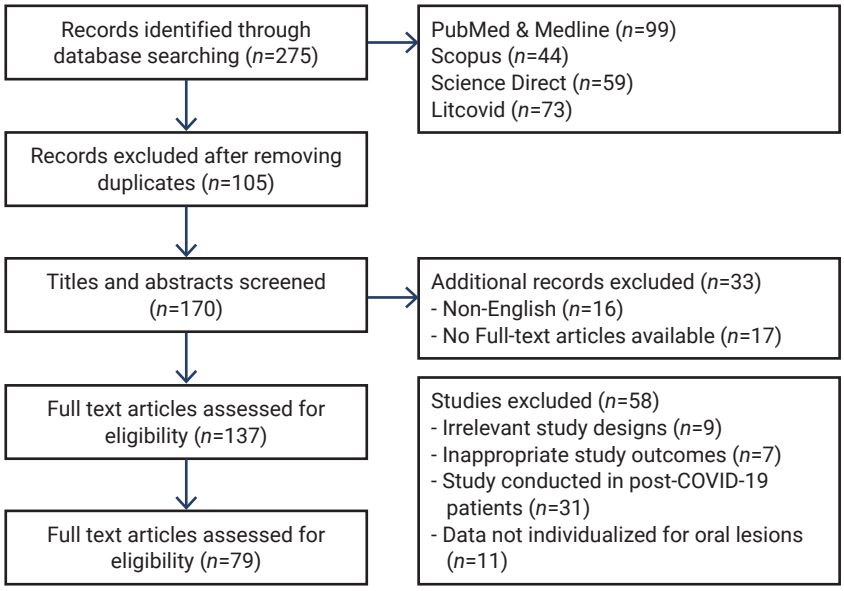

Figure 1. Flow diagram of literature search and selection criteria of the included studies (*n* = 79).

were found. Of these, 79 articles were selected for inclusion in the final analysis [5,6,8,9,12–86].

Characteristics of the Studies

The demographic characteristics of the populations in the studies included in our analysis (*n* = 79) are detailed in Table 1. We extracted data from these 79 studies [5,6,8,9,12–86], which encompassed a total of 13,252 patients. The individual sample sizes within these studies varied, ranging from as few as 14 [47] to as many as 1,172 [35] patients. All of the studies (*n* = 79) were published between the years 2020 [6,8,9,12–27,56–69] and 2023 [83–86]. The majority of these studies (*n* = 33) were published in 2020, followed by 2021 (*n* = 31), 2022 (*n* = 15), and 2023 (*n* = 4).

The 79 articles analyzed presented data from various countries worldwide. Italy accounted for the most articles, with 14 studies [16,19,20,22,23,28,29,36,37,58,66,72,81,86]. This was followed by India with 8 studies [17,33,44,45,50,55,80,83], United States with 7 studies [21,25,30,31,54,62,79], Brazil with 7 studies [9,47,49,52,56,75,77], and both Egypt and Turkey with 5 studies each [34,38,41,68,71] and [26,39,42,48,64], respectively. Iran [5,53,59,60], Iraq [12,43,84,85], and Spain [27,57,65,67] contributed to 4 studies each. Saudi Arabia was represented by 3 studies [40,46,51], while China [15,35] and Israel [13,74] each had 2 studies. Two studies contain data from multiple European countries [18,70]. The remaining countries—Denmark [14], France [24], Qatar [32], Romania [8], the United Kingdom [6], Colombia [61], Norway [63], Indonesia [69], Afghanistan [73], the Czech Republic [76], Ukraine [78], and Poland [82]—each contributed 1 study, respectively.

Most of the 79 studies were cross-sectional studies (*n* = 41) [5,12–26,29–31,33,34,37–46,48–51,53–55,84–86] followed by case reports (*n* = 20) [9,61–75,78–81], case series (*n* = 11) [6,8,56–60,76,77,82,83], retrospective studies (*n* = 6) [27,28,35,36,47,52], and case-control studies (*n* = 1) [32].

The studies contained data from 13,252, of whom 7,509 (56.6%) were females. In most of the studies (*n* = 40), the mean age of the patients was 58.26 ± 11.50 years followed by 41.42 ± 17.32 years (23 studies) and 26.18 ± 18.42 years (12 studies). Three studies did not report the patients' ages [5,34,35] and 1 study was conducted among newborns [8].

Only 34 studies have documented patients' medical history. The majority of these studies documented a history of hypertension (*n* = 26), followed by diabetes (*n* = 20), respiratory diseases and asthma (*n* = 7), cardiovascular disease (*n* = 6), allergies (*n* = 4), and other conditions. Twenty-one studies indicated that patients with COVID-19 were admitted to the hospital. Additionally, 11 studies reported that patients were hospitalized in the ICU, with 5 studies revealing that the patients required ventilation.

Oral signs and symptoms can be broadly categorized into the following: oral ulcerations, redness and burning sensation, xerostomia, red and white lesions, vesiculobullous lesions, morphological changes of the tongue, taste alteration, gingival and periodontal lesions, and salivary gland disorders. Many patients exhibited multiple signs and symptoms affecting various parts of the oral cavity. Therefore, we have assessed each oral manifestation individually. The most prevalent oral manifestation, observed in 23.8% (*n* = 3,157) of patients, was taste alteration (46 studies). This was followed by oral ulceration in 8.1% (*n* = 1,082 patients in 41 studies),

redness and burning sensation in 2.2% (*n*=297 patients in 33 studies), xerostomia in 12.7% (1,694 patients in 24 studies), red and white lesions in 2.4% (326 patients in 18 studies), vesiculobullous lesions in 0.55% (*n*=73 patients in 13 studies), morphological changes of the tongue in 2.7% (*n*=360 patients in 27 studies), gingival and periodontal changes in 3.2% (*n*=430 patients in 12 studies), and salivary gland disorder in 1.07% (*n*=143 patients in 3 studies). In the majority of patients (23.6%), the tongue was the most commonly affected area, followed by the oral mucosa (14.7%), lips (4.9%), gingiva and periodontium (3.2%), palate (1.9%), and salivary glands (1.1%).

Risk of Bias Assessment

JBI critical appraisal checklists were utilized to assess the risk of bias in cross-sectional studies, case-control studies, case reports, and case series. Of the 79 studies evaluated, 50 (63.7%) demonstrated a low risk of bias, while 23 (29.3%) exhibited moderate bias, and a mere 6 studies (7%) showed a high risk of bias (Table 1) [5,6,8,9,12–86]. The detailed computation of the risk of bias, using the JBI Critical Appraisal Tools, is presented in Tables S1–S4 [5,6,8,9,12–86].

Descriptive Characteristics of the Oral Lesions

Taste disorders and tongue manifestation

The prevalence of taste disorders and tongue manifestations was evaluated using data from 46 and 27 studies, respectively. We further subdivided the taste disorders into additional categories. These include complete loss of taste, or ageusia, as reported in 22 studies [12,14,20,23,35,40–42,44,49,53,55,56,58,63,65,67,70,72,74,85], taste alteration or dysfunction, as reported in 19 studies [5,13,16–19,21,22,29,36,38,46,51,54,66,78,84–86], dysgeusia, as reported in 7 studies [24,28,37,50,54,59,60], and amblygeustia, as reported in only one study [15].

Xerostomia

Xerostomia was noted in 22 cross-sectional studies [13,15,22,28,34,37,38,40–42,44–46,48,50–55,84,85] and 2 case reports [60,78].

Vesiculobullous lesions

Thirteen studies, comprising case reports and case series, reported vesiculobullous lesions [6,9,24,26,29,50,57,59,61,62,70,77,81].

Ulceration

Ulceration was reported in 41 studies [5,6,24,27–29,31,33,34,37,39–51,53,55,56,61,64,69,73,75–85].

Table 1. Demographic characteristics of the included studies (*n*=79)

No.	Study	Year of publication	Study location	Study design	Sample size (*n*)	Sex	Mean age (range, y)	Study duration	Medical history	Admission in the ICU	Risk of bias
1	Nuno-Gonzalez et al. [5]	2021	Spain	Cross-sectional	666	-	55.7 (40–70)	April 10–25, 2020	-	History of hospitalization	Low
2	Al-Zaidi and Badr [12]	2020	Iraq	Cross-sectional	65	M, 41.6%; F, 58.4%	41.2 (11–80)	April 5, 2020–May 17, 2020	-	-	Moderate
3	Biadsee et al. [13]	2020	Israel	Cross-sectional	140	M, 58; F, 70	36.5 (18–73)	March 25, 2020–April 15, 2020	-	-	Moderate
4	Bodnia and Katzenstein [14]	2020	Copenhagen, Denmark	Cross-sectional	51	F, 22; M, 28	45 (16–62)	March 2020	-	-	Moderate
5	Chen et al. [15]	2020	China	Cross-sectional	31	M, 15; F, 16	60.6 (18–86)	February 28, 2020–March 4, 2020	-	-	Moderate
6	Dell'Era et al. [16]	2020	Italy	Cross-sectional	355	M, 54%	45 (51–60)	March 10–30, 2020	Cardiovascular disease, allergic (sinusitis)	-	Low
7	Kumar et al. [17]	2021	India	Cross-sectional	141	M, 58.9%; F, 41.1%	15.2 (10–19)	May–August 2020	-	-	Low
8	Lechien et al. [18]	2020	Europe (multi center)	Cross-sectional	417	F, 263; M, 154	36.9 (19–77)	-	Allergic rhinitis, asthma, hypertension, hypothyroidism	Hospitalization of severe cases	Low

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Table 1. Continued

No.	Study	Year of publication	Study location	Study design	Sample size (*n*)	Sex	Mean age (range, y)	Study duration	Medical history	Admission in the ICU	Risk of bias
9	Paderno et al. [19]	2020	Italy	Cross-sectional	508	M, 56%; F, 44% (55±15 y)[a]	55 (40–70)	March 27–April 1, 2020	-	Hospitalization of severe cases	Low
10	Boscolo-Rizzo et al. [20]	2020	Italy	Cross-sectional	202	F, 55.1%; M, 44.9%	56 (20–89)	March 19–22, 2020	-	-	Low
11	Yan et al. [21]	2020	California, USA	Cross-sectional	59 and 203 (COVID-19 +ve and –ve)	M & F, 49.2% (COVID-19 +ve): M, 34%; F, 65% (COVID-19 –ve)	54 (18–80)	March 3–29, 2020	Allergic rhinitis, immunocompromised state, hypertension, DM, cardiac disorders, cancer, CLD, history of head trauma, neurological disease	Hospitalization of severe cases	Low
12	Sinjari et al. [22]	2020	Italy	Cross-sectional	20	-	69.2 (39–81)	May 2020–June 2020	DM, cardiovascular conditions	-	Low
13	Giacomelli et al. [23]	2020	Italy	Cross-sectional	59	M, 40%; F, 60%	60 (40–74)	March 19, 2020	-	-	Moderate
14	Mascitti et al. [24]	2020	France	Cross-sectional	59	M:F, 3:1	57.6 (49–69)	March 31, 2020	-	-	Moderate
15	Salehi et al. [25]	2020	Iran	Cross-sectional	53	M, 43.4%; F, 56.6%	63.1 (27–90)	March 1, 2020–April 30, 2020	Cardiovascular diseases (52.83%), DM (37.7%), chronic kidney disease (20.7%)	-	Low
16	Askin et al. [26]	2020	Turkey	Cross-sectional	210	M, 58.6%; F, 41.4%	57.4 (20–75)	April 2020	Comorbidities	29 in ICU, 129 in wards	Moderate
17	Katz and Yue [27]	2021	USA	Retrospective study	889	F, 509; M, 386	18–34	Registry study	-	-	Moderate
18	Fantozzi et al. [28]	2020	Italy	Retrospective study	326	M, 52.3%; F, 47.7%	57 (48–67)	March 6, 2020–April 30, 2020	Hypertension (*n*=29), chronic pulmonary disease (*n*=11), DM (*n*=10), cardiovascular disease (*n*=9), cancer (*n*=5)	Hospitalized (median, 12.5 d)	High
19	Favia et al. [29]	2021	Bari, Italy	Cross-sectional	123	M:F, 1.3:1	Median, 72	October 2020–December 2020	-	History of hospitalization and ICU	Moderate
20	Halepas et al. [30]	2021	New York, USA	Cross-sectional	47	M, 51.1%; F, 48.9%	9.0 (1.3–20)	March 15–June 1, 2020	-	History of hospitalization, ICU	Moderate

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Table 1. Continued

No.	Study	Year of publication	Study location	Study design	Sample size (*n*)	Sex	Mean age (range, y)	Study duration	Medical history	Admission in the ICU	Risk of bias
21	Rekhtman et al. [31]	2021	New York, USA	Cross-sectional	296	M, 71%; F, 29%	64 (50–77)	May 11, 2020–June 15, 2020	CAD, 23%; congestive heart failure, 14%; asthma, 9%; COPD, 14%; DM, 34%; hypertension, 71%	History of hospitalization	Low
22	Marouf et al. [32]	2021	Qatar	Case control	Case, 40; control, 528	Case: M, 50%; F, 50% Control: M, 54.9%; F, 45.1%	Case, 53.6; control, 41.5	February–July 2020	DM: case, 42.5%; control, 27.8%	Hospitalization and ICU admission	Low
23	Subramaniam et al. [33]	2021	India	Cross-sectional	713	M:F, 6:3	69 (60–81)	May 2020–June 2020	DM, hypertension	-	Moderate
24	Abubakr et al. [34]	2021	Egypt	Cross-sectional	573	F, 408; M, 165	36.19 (30–45)	May 1, 2020–July 1, 2020	-	-	Low
25	Song et al. [35]	2021	China	Retrospective	1172	-	-	December 2019	-	History of hospitalization	Low
26	Bardellini et al. [36]	2021	Italy	Retrospective	27	M:F, 19:8	4.2 y (3 mo–14 y)	March–April 2020	-	-	High
27	Gherlone et al. [37]	2021	Italy	Cross-sectional	122	M, 75.4%; F, 24.6%	62.5 (53.9–74.1)	July 23, 2020–September 7, 2020	CAD, DM, chronic kidney disease, active neoplasia, COPD	History of hospitalization and ICU and ventilation	High
28	El Kady et al. [38]	2021	Egypt	Cross-sectional	58	M, 53.4%; F, 46.6%	18–46	May 15, 2020–June 10, 2020	-	History of hospitalization	High
29	Fidan et al. [39]	2021	Turkey	Cross-sectional	74	M, 66.2%; F, 33.8%	51.6 (28–68)	April–October 2020	-	Hospitalized	High
30	Natto et al. [40]	2021	Saudi Arabia	Cross-sectional	109	M, 67%; F, 33%	39.3 (18–56)	July–October 2020	DM (10.1%), hypertension (7.3%), asthma and arthritis (1.7%)	-	Moderate
31	Elamrousy et al. [41]	2021	Egypt	Cross-sectional	124	M, 74.2%; F, 25.8%	50.32±12.47[a]	September 2, 2020–June 10, 2021	DM (*n*=52), hypertension (*n*=16), cardiac disease (*n*=8), renal disease (*n*=4), liver disease (*n*=4)	Hospitalized	Moderate
32	Bulut et al. [42]	2021	Turkey	Cross-sectional	200	M, 75; F, 125	38 (20–70)	September 2020–March 2021	-	Hospitalized (11.5%)	Low
33	Naser et al. [43]	2021	Iraq	Cross-sectional	338	M, 59%; F, 41%	45	August 2020–March 2021	Respiratory diseases, DM, hypertension, heart disease, urogenital diseases	Hospitalized	Moderate

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Table 1. Continued

No.	Study	Year of publication	Study location	Study design	Sample size (*n*)	Sex	Mean age (range, y)	Study duration	Medical history	Admission in the ICU	Risk of bias
34	Muthyam et al. [44]	2022	India	Cross-sectional	100	M, 51%; F, 49%	More than 35 y, 54%; less than 35 y, 46%	-	Immunocompromised state, multidrug therapy	Hospitalization	Low
35	Ganesan et al. [45]	2022	India	Cross-sectional	500	M, 73.4%; F, 26.6%	53.46±17.50[a]	-	-	-	Low
36	El Tantawi et al. [46]	2022	Multicountry study (Saudi Arabia)	Cross-sectional	434	M, 41.5%; F, 58.5%	18–23	August 2020–January 2021	Cancer, COPD	-	Moderate
37	Soares et al. [47]	2022	Brazil	Retrospective	14	M, 71.5%; F, 38.5%	58 (20–65)	-	-	-	Low
38	Tuter et al. [48]	2022	Turkey	Cross-sectional	204	M, 37.3%; F, 62.7%	53.3 (18–70)	February–March 2021	DM, hypertension, immunosuppression	Hospitalization, ICU	Low
39	Schwab et al. [49]	2022	Brazil	Cross-sectional	154	M, 59.7%; F, 40.3%	54.60 (20–88)	January 13, 2021–May 28, 2021	-	Hospitalization, ICU, ventilation	Moderate
40	Chawla et al. [50]	2022	India	Cross-sectional	217	M, 70%; F, 30%	56 (18–60)	September–December 2020	DM, hypertension, CAD, bronchial asthma	-	High
41	Binmadi et al. [51]	2022	Saudi Arabia	Cross-sectional	195	M, 25%; F, 75%	26 (18–34)	March 2020–March 2022	Immunosuppression, hormonal modulation	Hospitalization, ICU, ventilation	Moderate
42	Eduardo et al. [52]	2022	Brazil	Retrospective	519	M, 68.2%; F, 31.8%	51–80	May 2020–February 2021	-	ICU	Moderate
43	Villarroel-Dorrego et al. [53]	2022	Spain	Cross-sectional	55	M, 54.5%; F, 45.5%	51 (1–89)	-	-	-	Moderate
44	Manifar et al. [54]	2022	Iran	Cross-sectional	140	M, 44.2%; F, 55.8%	53.78 (15–92)	September 1, 2020–October 17, 2020	-	Hospitalization	Moderate
45	Bhuyan et al. [55]	2022	India	Cross-sectional	169 (1st 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)[a]	-	Comorbidities	Hospitalization, ventilator	Moderate
46	Mohammad et al. [84]	2023	Iraq	Cross-sectional	200	M, 81; F, 119	36.69 (16–78)	September–December 2021	-	-	Moderate
47	Al-Magsoosi et al. [85]	2023	Iraq	Cross-sectional	574	M, 196; F, 378	18–78	October 2021–April 2022	-	-	Low
48	Cazzolla et al. [86]	2023	Italy	Cross-sectional	1,155	M, 57%; F, 43%	M, 59±13; F, 56±16[a]	March 15, 2020–April 15, 2021	-	-	Moderate
49	Sinadinos and Shelswell [6]	2020	United Kingdom	Case series	3	M:F, 2:1	56 (45–61)		DM, hypertension (case 2); obesity (case 3)	-	Low
50	Dima et al. [8]	2020	Romania	Case series	3	M:F, 2:1	Newborns	May 2020	Diaper erythema	Neonatology ward	Low

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Table 1. Continued

No.	Study	Year of publication	Study location	Study design	Sample size (*n*)	Sex	Mean age (range, y)	Study duration	Medical history	Admission in the ICU	Risk of bias
51	Brandao et al. [56]	2021	Brazil	Case series	8	M, 5; F, 3	53 (28–83)	-	Hypertension, COPD (case 1); DM, obesity, renal failure, bariatric surgery, fibromyalgia (case 2); obesity, Parkinson disease, hypertension, COPD (case 3); DM, hypertension (case 4)	Hospitalization	Low
52	Cruz Tapia et al. [57]	2020	Latin America	Case series	4	F:M, 3:1	47.2 (41–54)	-	-	Case 2, hospitalized	Low
53	Vaira et al. [58]	2020	Italy	Case series	72	M, 27; F, 45	49.2 (18–67)	March 31, 2020–April 6, 2020	History of head trauma, allergic rhinitis, chronic rhino sinusitis, psychiatric or neurological disorders	-	Low
54	Martin Carreras-Presas et al. [59]	2021	Spain	Case series	3	M:F, 2:1	55 (56–65)	Last week of March–First week of April 2020	DM, hypertension (case 2); obesity, hypertension (case 3)	Case 3, hospitalization	Low
55	Rodriguez et al. [60]	2022	Spain	Case series	3	F:M, 2:1	68 (53–78)	-	-	Case 1, home quarantine; cases 2 & 3, hospitalization	Low
56	Corchuelo and Ulloa [61]	2020	Colombia	Case report	1	F	40	-	-	-	Low
57	Amorim Dos Santos et al. [9]	2020	Brazil	Case report	1	M	67	March 31, 2020	CAD, autosomal dominant polycystic kidney disease, and kidney transplant, immunosuppression, venous thromboembolism	Hospitalization in ICU	Low
58	Eghbali Zarch and Hosseinzadeh [62]	2021	Iran	Case report	1	F	56	October 2020	-	-	Low
59	Hjelmesaeth and Skaare [63]	2020	Norway	Case report	1	F	60	-	-	-	Low
60	Cebeci Kahraman and Caskurlu [64]	2020	Turkey	Case report	1	M	51	March 18, 2020	-	-	Low
61	Smith et al. [65]	2020	USA	Case report	1	M	21	March 19, 2020	-	-	Low
62	Maniaci et al. [66]	2020	Italy	Case report	1	M	15	-	-	-	Low

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Table 1. Continued

No.	Study	Year of publication	Study location	Study design	Sample size (*n*)	Sex	Mean age (range, y)	Study duration	Medical history	Admission in the ICU	Risk of bias
63	Melley et al. [67]	2020	Pennsylvania, USA	Case report	1	F	59	May 2020	-	-	Low
64	Riad et al. [68]	2022	Egypt	Case report	1	F	47	-	Cardiovascular disease, DM	-	Low
65	Putra et al. [69]	2020	Indonesia	Case report	1	M	29	-	Cardiovascular diseases	-	Low
66	Dalipi et al. [70]	2021	Europe	Case report	1	M	17	-	-	-	Low
67	Eita [71]	2021	Egypt	Case report	1	F	31	-	Irritable bowel syndrome, atopy	-	Low
68	Cirillo and Colella [72]	2021	Italy	Case report	1	F	36	March 2020	-	-	Low
69	Nejabi et al. [73]	2021	Afghanistan	Case report	1	M	62	-	-	-	Low
70	Klein et al. [74]	2021	Israel	Case report	1	F (pregnant)	40	-	-	-	Low
71	Ramires et al. [75]	2021	Brazil	Case report	1	F	50	-	Obesity, hypertension, type 2 DM	Hospitalization, ventilation	Low
72	Hockova et al. [76]	2021	Czech Republic	Case series	3	M:F, 3:0	62		Arterial hypertension, hypercholesterolemia, GERD (case 1); arterial hypertension, history of MI, septic shock (case 2)	ICU	Low
73	Teixeira et al. [77]	2021	Brazil	Case series	4	M:F, 1:3	68.75 (57–84)	-	Hypertension, hypothyroidism, rectal tumor (case 2); hypertension, hypothyroidism (case 3); bipolar disorder (case 4)	-	Low
74	Emelyanova et al. [78]	2021	Ukraine	Case report	1	F	38	-	-	-	Low
75	Fathi et al. [79]	2021	Iran	Case report	1	F	22	April 2020	-	Hospitalization (2nd day)	Low
76	Shenoy et al. [80]	2022	India	Case report	1	F	55	-	-	-	Low
77	Palaia et al. [81]	2022	Italy	Case report	1	F	30	-	-	-	Low
78	Rafalowicz et al. [82]	2022	Poland	Case series	6	M, 4; F, 2	58.8 (43–72)	January–June 2021	Hypertension, insulin resistance (case 2)	No	Low
79	Jogdand et al. [83]	2023	India	Case series	2	M, 1; F, 1	50 and 60	June 2020	Diabetes, hypertension (case 1)	No	Low

ICU, intensive care unit; M, male; F, female; DM, diabetes mellitus; CLD, chronic lung disease; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; MI, myocardial infarction; -, not mentioned in article.

[a]Mean ± standard deviation.

Red and white lesions

Eighteen studies reported red and white lesions in COVID-19-positive patients [8,24–26,29,33,36,37,39,43,49,51,53,57,61,68,80,82].

Periodontal involvement

Twelve studies described the involvement of gingiva and periodontium among patients with COVID-19 [6,26,29,32,38,39,42,44,51,55,59,78].

Redness and burning sensation

In total, 33 studies reported patients who complained of redness and burning sensation [5,6,22,26,28,30,31,33,34,38–44,46,48,50–55,57,59,60,69,78,79,81,82,85].

Salivary gland involvement

Salivary gland disorders [37,38,52] were found in 3 studies.

The latency time between the emergence of systemic symptoms and oral lesions ranged from 2 weeks prior to 10 days following the onset of systemic symptoms. In the majority of the studies (n=14), systemic symptoms occurred after the appearance of oral symptoms (Table 2) [5,6,8,9,12–86].

The general treatment protocol, as well as the specific treatment for oral lesions in COVID-19 patients, is outlined in Table S5 [6,8,9,29,43,47,56,57,59–61,64,65,67–71,73,75,77,79,80,82]. Oral lesions typically healed between 7 and 21 days post-emergence. Depending on the severity and cause of the oral lesions, various therapies were prescribed. These included chlorhexidine mouthwash, nystatin, oral fluconazole, topical or systemic corticosteroids, systemic antibiotics, systemic acyclovir, artificial saliva, and photobiomodulation therapy.

Results of the Meta-Analysis

Data from 48 studies were meta-analyzed to determine the prevalence of taste alteration, xerostomia, red and white lesions, vesiculobullous lesions, ulceration, burning sensation, and salivary gland involvement.

Among the prevalence studies, 28 separate studies [12–14,16–20,22–24,28,29,35,36,38,40–44,46,51,53–55,85,86] investigated the occurrence of taste alteration in a total of 3,157 COVID-19 patients. The meta-analysis of these studies revealed a combined prevalence rate of 48% (95% confidence interval [CI], 39%–57%). The heterogeneity of these studies was assessed using Cochran Q test and the I^2 index, indicating a high degree of heterogeneity with an I^2 value of 98.7 (Figure 2).

A total of 327 COVID-19 patients from 14 different studies reported experiencing red and white lesions [5,13,24,25,29,36,37,39,43,48,51–53,84]. These studies revealed a pooled

Table 2. Oral manifestations of the included studies (n=79)

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
1	Nuno-Gonzalez 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%), mucositis (3.9%), glossitis with patchy depapillation (3.9%), white tongue (1.6%), and enanthema (0.5%), taste disturbances	Tongue, oral mucosa	Redness and burning sensation, oral ulceration, red and white lesions, morphological changes of tongue, taste alteration	-	-
2	Sinadinos and Shelswell [6]	2020	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	Oral ulceration, vesiculobullous lesions, redness and burning sensation, gingival and periodontal changes	-	Sore throat (case 1), pneumonia (case 3)
3	Dima et al. [8]	2020	Oral candidiasis	Oral mucosa	Red and white lesions/ fungal	-	Epistaxis and diaper erythema (all 3 cases); palpebral edema (newborn 2)

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https://doi.org/10.24171/j.phrp.2023.0033

Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
4	Amorim Dos Santos et al. [9]	2020	Hypogeusia, white plaque, multiple pinpoint yellowish ulcers in the tongue, nodule in lower lip (1 cm)	Tongue, lower lip	Vesiculobullous lesions, red and white lesions, taste alteration	Mean duration, 14 d	Respiratory symptoms and progressive dyspnea on exertion, fever and diarrhea
5	Al-Zaidi and Badr [12]	2020	Loss of taste (83%)	Tongue	Taste alteration	1 wk before systemic symptoms	Fever (63.08%), cough (60.00%), dyspnea (47.69%), sore throat, diarrhea (32.31%), chest pain (30.77%)
6	Biadsee et al. [13]	2020	Taste alteration (n = 67), dry mouth (n = 72), plaque-like changes in the tongue (n = 9), swelling in the oral cavity (n = 10)	Tongue, oral mucosa	Red and white lesions, taste alteration, xerostomia	Along with systemic symptoms	Cough and runny nose (p = 0.018), olfactory dysfunction
7	Bodnia and Katzenstein [14]	2020	Total loss of taste (70%)	Tongue	Taste alteration	1–3 wk (78%), 3–6 wk (22%)	Fatigue, headache, fever, dry cough, disturbance of the sense of smell
8	Chen et al. [15]	2020	Amblygeustia (47.2%), dry mouth (11.1%)	Tongue, oral mucosa	Taste alteration, xerostomia	Along with systemic symptoms	Submandibular lymph node enlargement (n = 1), cough (n = 21), fever (n = 20), diarrhea (n = 4), chest tightness (n = 13)
9	Dell'Era et al. [16]	2020	Taste disorders (65.5%)	Tongue	Taste alteration	Mean duration, 10 d	Fever (72.1%), cough (47.9%), fatigue (40.3%), dyspnea (21.7%), diarrhea (19.7%)
10	Kumar et al. [17]	2021	Taste, dysfunction (28.4%)	Tongue	Taste alteration	Duration, 2–15 d	Malaise (14.2%), sore throat (19.9%), cough (20.6%), fever (48.2%), diarrhea (5.7%), nasal discharge (3.5%), headache (5.7%)
11	Lechien et al. [18]	2020	Gustatory dysfunction (88.8%)	Tongue	Taste alteration	Mean duration, 9.2 ± 6.2 d	Olfactory dysfunction (85.6%)
12	Paderno et al. [19]	2020	Gustatory dysfunction (group A, 51.9%; group B, 78.9%); partial, 36.8%; total, 60.1%; unable to assess, 3.1%	Tongue	Taste alteration	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, pharyngodynia
13	Boscolo-Rizzo et al. [20]	2020	Loss of taste (n = 113)	Tongue	Taste alteration	Mean duration, 9.5 d	Dry cough, fever, headache, sore throat, chest pain, nausea, abdominal pain
14	Yan et al. [21]	2020	Gustatory impairment (71%) (p < 0.001)	Tongue	Taste alteration	-	Fatigue (81%), fever (70%), anosmia (68%), myalgia or arthralgia (63%), diarrhea (48%), nausea (27%)
15	Sinjari et al. [22]	2020	Impaired taste (25%), burning sensation (15%), difficulty in swallowing (20%), dry mouth (30%) (p = 0.02)	Oral mucosa, tongue	Redness and burning sensation, taste alteration, xerostomia	-	-

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
16	Giacomelli et al. [23]	2020	Dysgeusia (8.5%), ageusia (1.7%)	Tongue	Taste alteration	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%)
17	Mascitti et al. [24]	2020	Oral lichenoid reaction (32.5%), oral enanthema (27.5%), macroglossia (25.0%), cheilitis (12.5%), ageusia (20.5%), extensive ulcerations of the tongue (2.5%)	Lips, tongue, oral mucosa	Oral ulceration, vesiculobullous lesions. taste alteration	-	Macular exanthema (80%), face edema (32%), livedo (13%), urticarial rash (8%), purpura (5%), oral lichenoid lesions (33%), conjunctivitis (18%)
18	Salehi et al. [25]	2020	White plaques on the intraoral mucous layer of oral mucosa	Oral mucosa	Red and white lesions	-	-
19	Askin et al. [26]	2020	Aphthous stomatitis (5.8%), rash and erythema, aphthous lesion on side of tongue	Tongue, oral mucosa	Vesiculobullous lesions, redness and burning sensation	-	Cutaneous findings (36.1%)
20	Katz and Yue [27]	2021	Recurrent aphthous stomatitis (0.64%)	Oral mucosa	Oral ulceration	-	-
21	Fantozzi et al. [28]	2020	Dry mouth (45.9%), swallowing difficulties (39.2%), dysgeusia (59.5%)	Tongue, oral mucosa	Redness and burning sensation, oral ulceration, taste alteration, xerostomia	First symptom (xerostomia) (19.6%); dysgeusia (87.9%), duration (xerostomia), 7 d; dysgeusia 6 d	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%)
22	Favia et al. [29]	2021	Geographic tongue (n = 7), fissured tongue (n = 5), ulcerative lesion (n = 65), blisters (n = 19), hyperplasia of papillae (n = 48), angina bullosa (n = 11), candidiasis (n = 28), ulceronecrotic gingivitis (n = 7), petechiae (n = 14), oral haemorrhage (n = 1), taste disorders (90%)	Tongue, oral mucosa, lips	Red and white lesions, morphological changes of tongue, vesiculobullous lesions, oral ulceration, taste alteration	Together with general symptoms (26.2%); duration, 1 wk (41%); after 1 wk 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 (SpO_2 < 90%)
23	Halepas et al. 2021 [30]	2021	Red and/or swollen lips (48.9%), strawberry tongue (10.6%)	Lips, tongue	Redness and burning sensation, morphological changes of tongue	-	Fever
24	Rekhtman et al. [31]	2021	Rashes on lips and tongue (5.7% and 2.9%), ulcers on lips and tongue	Lips and tongue	Redness and burning sensation, oral ulceration		Generalized rashes
25	Marouf et al. [32]	2021	Periodontitis (258/568)	Periodontium	Gingival and periodontal changes	-	-

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https://doi.org/10.24171/j.phrp.2023.0033

Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
26	Subramaniam et al. [33]	2021	Ulcers on oral mucosa; burning mouth and mucositis on lower labial mucosa, papillary atrophy; reddish-white spots on the palate; ulcers on lower lip; pallor of lip	Oral mucosa palate, lips, tongue	Oral ulceration, petechiae, redness and burning sensation, morphological changes of tongue	-	Fever, cough, dyspnea, runny nose, chest tightness, loss of smell
27	Abubakr et al. [34]	2021	Dental pain (23%), pain in jaw bones or joint (12.0%), halitosis (10.5%), ulcerations (20.4%), dry mouth (47.6%)	Oral mucosa	Oral ulceration, redness and burning sensation, xerostomia	-	Fever, myalgia, dysphagia, and hyposmia, loss of smell, nasal itching
28	Song et al. [35]	2021	Loss of taste (20.6%)	Tongue	Taste alteration	First symptom (0.4%), recovery time, 7 d	Nasal obstruction (8.6%), rhinorrhea (10.3%), nasal itching (4.9%), sneezing (11.0%), loss of smell (11.4%)
29	Bardellini et al. [36]	2021	Oral pseudomembranous candidiasis (7.4%), geographic tongue (3.7%), coated tongue (7.4%), taste alteration (11.1%)	Tongue, oral mucosa	Red and white lesions, morphological changes of tongue, taste alteration	-	Fever, cough, rhinorrhoea, breathing difficulty
30	Gherlone et al. [37]	2021	Salivary gland ectasia (38%), dry mouth (30%), dysgeusia (17%), white plaque (28%), oral ulcers (12%)	Salivary glands, tongue, oral mucosa	Red and white lesions, oral ulceration, xerostomia, salivary gland disorder	-	-
31	El Kady et al. [38]	2021	Dry mouth (39.7%), loss of salt sensation (34.5%), loss of sweet sensation (29.3%), altered food taste (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%)	Tongue, salivary glands, gingiva, oral mucosa	Redness and burning sensation, taste alteration, xerostomia, gingival and periodontal changes, salivary gland disorder	-	-
32	Fidan et al. [39]	2021	Aphthous-like ulcer (36.5%), erythema (25.7%), lichen planus (16.2%), tongue (31.8%), oral mucosa (27.0%), gingiva (18.9%), palate (5.4%)	Tongue (39.7%), oral mucosa (34.5%), gingiva (18.9%), palate (6.9%)	Oral ulceration, redness and burning sensation, red and white lesions	Oral lesions prior COVID-19 diagnosis	-
33	Natto et al. [40]	2021	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 ulceration, redness and burning sensation, taste alteration, xerostomia, gingival changes	After systemic symptoms	Cough, fever, sore throat, runny nose, muscle pain, headaches, nausea, diarrhea

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
34	Elamrousy et al. [41]	2021	Oral ulcers (92.8%), dry mouth (84%), loss of taste (55%), hemorrhagic ulcers with crust on lips	Lip (42.3%), tongue (38.5%), labial mucosa (34.6%)	Oral ulceration, redness and burning sensation, taste alteration, xerostomia	-	Asthenia (67.7%), breath problems (67.7%), cough (67.7%), fatigue (19.4%), abdominal symptoms (12.9%)
35	Bulut et al. [42]	2021	Taste loss (53%), halitosis (21%), oropharyngeal wound and pain (18%), pain in the chewing muscles (16%), 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 ulceration, redness and burning sensation, taste alteration, xerostomia	-	Presence of symptoms (87.5%)
36	Naser et al. [43]	2021	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 ulceration, redness and burning sensation, red and white lesions, taste alteration	-	-
37	Muthyam et al. [44]	2022	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 ulceration, redness and burning sensation, morphological changes of tongue, taste alteration, xerostomia	Altered taste lasted more than 1 wk (53%)	Weakness (8%), cough and cold (4%), body pain (2%)
38	Ganesan et al. [45]	2022	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	Morphological changes of tongue, oral ulceration, taste alteration, xerostomia	-	-
39	El Tantawi et al. [46]	2022	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 redness and burning sensation (13.1%)	Oral mucosa tongue, gingiva	Morphological changes of tongue, oral ulceration, redness and burning sensation, taste alteration, xerostomia, gingival and periodontal changes	-	-

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
40	Soares et al. [47]	2022	Ulcerative lesions in the palate (57.1%), tongue (29%), lips or palate (14.3%)	Tongue, lips, palate	Oral ulceration	-	Anosmia, fever, headache
41	Tuter et al. [48]	2022	Dry mouth (44.2%), oral ulceration (22.4%), oral mucosa (15.2%), tongue (10.8%)	Tongue, oral mucosa	Oral ulceration, redness and burning sensation	-	-
42	Schwab et al. [49]	2022	Ageusia (11.0%); opportunistic oral infections such as pseudomembranous candidiasis and herpes simplex (4.5%)	Tongue	Red and white lesions/ fungal, taste alteration, oral ulceration	-	Cough (72.7%), dyspnoea (63.0%), fever (53.9%), anosmia (14.3%)
43	Chawla et al. [50]	2022	Dry mouth (38%) ($p = 0.03$), dysgeusia (32%) ($p = 0.04$), vesiculobullous lesion (13%), oral ulcers (3.7%)	Oral mucosa tongue	Oral ulceration, redness and burning sensation, vesiculobullous lesions, taste alteration, xerostomia	-	Cough (30%), sore throat (20%), shortness of breath (7%), running nose (11%)
44	Binmadi et al. [51]	2022	Taste disturbance (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 ulceration, redness and burning sensation, vesiculobullous lesions, morphological changes of tongue, red and white lesions, taste alteration, xerostomia	Concurrently (47%), after the general symptoms (43%), 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%), diarrhea (15%)
45	Eduardo et al. [52]	2022	Saliva alterations (24.4%), dryness (9.9%), tongue coating (3%), sialorrhea (3.3%), petechiae (10.5%), oral bleeding (7.5%)	Oral mucosa tongue, salivary glands	Red and white lesions, redness and burning sensation, salivary gland disorder, xerostomia	-	-
46	Villarroel-Dorrego et al. [53]	2022	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, lips, oral mucosa	Oral ulceration, redness and burning sensation, red and white, lesions, xerostomia	-	-
47	Manifar et al. [54]	2022	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 mucosa	Redness and burning sensation, taste alteration, xerostomia	-	Gastrointestinal symptoms, smell defects, asthma, skin rashes, cough, malaise, myalgia, anorexia, respiratory distress, olfactory dysfunction
48	Bhuyan et al. [55]	2022	Burning sensation (2.4%), dry mouth (2.4%), loss of taste (31%) ($p < 0.001$), mouth ulcer (2.4%), bleeding gum (2.4%)	Oral mucosa gums, tongue	Oral ulceration, redness and burning sensation, taste alteration, xerostomia, gingival changes	-	-

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
49	Brandao et al. [56]	2021	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 ageusia (cases 6, 7, 8)	Lips, tongue, palate	Oral ulceration, taste alteration	6–10 d	Chest tightness, fever, cough (cases 1, 5, 7, 8); cough, fever, dyspnea (cases 2, 6); abdominal distension, fever, mild dyspnea (cases 3, 4)
50	Cruz Tapia et al. [57]	2020	Bulla on the hard palate (×6 mm) (case 1); diffuse purple macule (×12 mm) and papule-plaque (×8 mm) on the left and right palatal mucosa (case 2); tongue enlargement (case 3); Burning mouth sensation and reddish macules on hard palate (case 4)	Palate, tongue	Redness and burning sensation, vesiculobullous lesions, morphological changes of tongue		Fever, myalgia, dysphagia, hyposmia
51	Vaira et al. [58]	2020	Hypogeusia (33 cases); complete ageusia (1 case)	Tongue	Taste alteration		Fever, cough, nasal obstruction, sore throat, hyposmia, anosmia, pneumonia
52	Martin Carreras-Presas et al. [59]	2021	Dysgeusia (case 1); multiple ulcers On palate (case 2); pain on tongue, blisters in lip mucosa and Desquamative gingivitis (case 3)	Tongue, lips	Oral ulceration, redness and burning sensation, vesiculobullous lesions, taste alteration, gingival changes	Along with systemic symptoms	Asthenia, hyposmia, enlargement of lymph nodes in the neck (cases 1, 3); fever, diarrhea (case 2)
53	Rodriguez et al. [60]	2022	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	Redness and burning sensation, morphological changes of tongue, taste alteration, xerostomia	Before presentation (case 1); after discharge (case 2); with systemic symptoms (case 3)	Fever, malaise, anosmia, diarrhea, pneumonia (cases 1, 3)
54	Corchuelo and Ulloa [61]	2020	Reddish plaques on the lower lip, dark brown pigmentation and aphthous ulcers in the gums, whitish area in tongue	Lower lips, gums	Oral ulceration, vesiculobullous lesions, red and white lesions	Mean duration, 8–10 d	-
55	Eghbali Zarch and Hosseinzadeh [62]	2021	Vesicles on lower lip mucosa	Lip	Vesiculobullous lesions	2 d before systemic symptoms	High fever, fatigue, lack of appetite
56	Hjelmesaeth and Skaare [63]	2020	Total ageusia	Tongue	Taste alteration	-	-
57	Cebeci Kahraman and Caskurlu [64]	2020	Erythematous surface (hard palate), few petechiae in the midline and numerous pustular enanthema near the soft palate border	Palate	Red and white lesions, oral ulceration	Mean duration, 10 d	Sore throat; fever, fatigue, severe dry cough, inability to taste or smell

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
58	Smith et al. [65]	2020	Loss of taste	Tongue	Taste alteration	Before general symptoms	Frontal headache, loss of smell, headache, loose stools
59	Maniaci et al. [66]	2020	Transient loss of taste	Tongue	Taste alteration	Mean duration, 12 d	Fever, sore throat, runny nose, presence of erythematous skin lesions on the lower limbs, asthenia
60	Melley et al. [67]	2020	Loss of taste	Tongue	Taste alteration	1 wk before systemic presentation	Shortness of breath, fatigue, loss of appetite
61	Riad et al. [68]	2022	Painful white patches on the dorsal surface of the tongue and palate, mild tongue pain	Tongue, palate	Red and white lesions	2 wk before diagnosis	Sore throat, generalized myalgia, fatigue with intermittent fever
62	Putra et al. [69]	2020	Stomatitis aphthous	Oral mucosa	Oral ulceration, redness and burning sensation	Day 7	Fever, back pain, myalgia, sore throat, dry cough, rhinorrhea, anosmia
63	Dalipi et al. [70]	2021	Loss of taste Bullous and erosive erythematous lesions of lips and oral mucosa	Tongue, lips	Vesiculobullous lesions, taste alteration	Loss of taste, 2 wk before diagnosis	Fever, cough, headache, muscle pain, loss of smell, dark red, purpuric, irregular maculopapular lesions on abdomen
64	Eita [71]	2021	Dysgeusia and greasy tongue coat	Tongue	Morphological changes of tongue, taste alteration	Before systemic symptoms	Sore throat, fever (38 °C), nasal congestion, conjunctivitis, nausea; abdominal pain, diarrhea, fatigue, severe joint pain
65	Cirillo and Colella [72]	2021	Loss of taste	Tongue	Taste alteration	1 wk before presentation	Loss of smell, headache, fatigue, muscle pain
66	Nejabi et al. [73]	2021	Fissured tongue, white scars and painful erosive ulcer on the dorsal surface of the tongue	Tongue	Morphological changes of tongue, oral ulceration	After 1 wk of general symptoms	Fever, cough, taste alterations, olfactory dysfunction, chest tightness
67	Klein et al. [74]	2021	Loss of taste	Tongue	Taste alteration	From 4th to 6 wk	Fever, dry cough, chest pain, sore throat, diarrhea, nausea, headache, back pain
68	Ramires et al. [75]	2021	Crusted ulcers on lip vermilion (both upper and lower lips)	Lip	Oral ulceration	2 wk after the onset of fever	Flu-like syndrome: severe and progressive dyspnea (SpO_2 = 88%)
69	Hockova et al. [76]	2021	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, lips	Oral ulceration	After the diagnosis (all 3 cases)	Headache, fever, dry cough, dyspnoea

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
70	Teixeira et al. [77]	2021	Painful vesiculobullous lip lesions	Lips	Vesiculobullous lesions	After 4 d (case 1); after 10 d (case 2); after 11 d (case 3); after 19 d (case 4)	Headache, myalgia, dyspnea
71	Emelyanova et al. [78]	2021	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	Redness and burning sensation, morphological changes of tongue, xerostomia	3rd day (dysgeusia) and 5th day (xerostomia) after systemic symptoms	Rhinorrhea, coughing and increased body temperature to 38.5 °C
72	Fathi et al. [79]	2021	Oral pain, ulcerative lesions on oral mucosa, hemorrhagic crusts on lips	Oral mucosa, lips	Oral ulceration, redness and burning sensation	3rd day (oral pain)	Fever, abdominal pain, nausea, occasional vomiting
73	Shenoy et al. [80]	2022	Ulcer with irregular borders on the dorsum of the tongue surrounded by a scrapable whitish plaque	Tongue	Oral ulceration, red and white lesions	Systemic symptoms, 3 wk prior	Fever, cough, chest tightness
74	Palaia et al. [81]	2022	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	Oral ulceration, vesiculobullous lesions, redness and burning sensation	7 d prior to general symptoms (duration of oral lesions, 14 d)	Bilateral cutaneous lesions were also evident on the hands. Low-grade fever
75	Rafalowiczet al. [82]	2022	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, cheilitis (case 6)	Hard palate, tongue, lips	Oral ulceration, redness and burning sensation, red and white/fungal, morphological changes of tongue	-	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 d (cases 4, 5)
76	Jogdand et al. [83]	2023	Ulcers with yellowish gray pseudo-membrane on oral mucosa and palate	Oral mucosa, palate	Oral ulceration, red and white lesions	-	-
77	Mohammad et al. [84]	2023	Dry mouth (50%), gustatory dysfunction (37%), burning mouth sensation (22.5%), oral pain (17%), aphthous lesions, fissural cheilitis and tongue depapillation (9.5%), candidiasis (7.5%), gingival bleeding (2.5%)	Gingiva, oral mucosa, tongue	Oral ulceration, red and white lesions, morphological changes of tongue, taste alteration, xerostomia, gingival changes	-	Fever (83.5%), weakness (80%), myalgia (73%), headache (70%), cough (65%), loss of smell sensation (54%), loss of taste sensation (48.5%), sore throat (38.5%), nasal congestion (26.5%), runny nose (25%), gastrointestinal symptom (24.5%)

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Table 2. Continued

No.	Study	Year of publication	Presenting symptoms given by the patient	Site	Oral signs and symptoms	Occurrence/duration of oral manifestation	Systemic manifestation
78	Al-Magsoosi et al. [85]	2023	Ageusia (66.8%), dry mouth (59%), gustatory changes (46%), dysphagia (40.5%), burning sensation (20.8%), oral ulceration (14.5%), gingival bleeding (3.3%)	Tongue, oral mucosa, gingiva	Redness and burning sensation, taste alteration, xerostomia	-	-
79	Cazzolla et al. [86]	2023	Taste dysfunction (208/25%)	Tongue	Taste alteration	1 wk before general symptoms	Fever, breathing, asthenia, rhinorrhea, headache, abdominal symptoms, sore throat, chest pain, cough

-, not mentioned in article.

prevalence of these symptoms at 17% (95% CI, 9%–26%), with an I^2 value of 98.2% (Figure 3).

Xerostomia was reported in 22 studies [13,15,22,28,34,37,38,40–42,44–46,48,50–55,84,85] involving 1,694 COVID-19 patients, showing a pooled prevalence of 35% (95% CI, 26%–44%) and I^2 = 98.7% (Figure 4).

Ulceration was reported in 23 studies [5,24,27–29,31,33,34,37,39–48,50,51,53,85] involving 1,086 patients, with a a prevalence of 21% (95% CI, 12%–30%) and I^2 of 99.62% (Figure 5).

The pooled prevalence of a burning sensation was reported to be 12% (95% CI, 6%–18%) with I^2 = 98.3%; this symptom was found in 297 patients in 11 studies [5,22,33,38,42–44,53,55,84,85] (Figure 6).

Vesiculobullous lesions were reported by 73 participants from 5 studies [26,29,36,50,51], with a pooled prevalence of 10% (95% CI, 5%–16%) and an I^2 of 98.5% (Figure 7A).

Salivary gland involvement was reported only in 3 studies [37,38,52] involving 193 patients, showing a pooled prevalence of 32% (95% CI, 22%–41%) and I^2 = 98.7% (Figure 7B).

Funnel plots demonstrated asymmetry, indicating the presence of high publication bias in the studies (Figure 8).

Discussion

COVID-19 has emerged as a global public health issue. Initially, it was believed that the absence of oral mucosa involvement distinguished COVID-19 from other viral infections. However, in April 2020, a case report by Chaux-Bodard et al. [87] demonstrated a link between COVID-19 and oral mucosa. The report detailed a 45-year-old woman who experienced painful inflammation of the tongue's papilla, which eventually healed into an asymptomatic ulcer within 10 days, leaving no scar. This patient also developed a skin lesion on her toe and tested positive for COVID-19 on the eighth day. Since this report, numerous observational studies and case reports have been published, highlighting the involvement of oral mucosa in COVID-19 patients. This systematic review was undertaken to determine the prevalence of oral manifestations in patients with COVID-19.

SARS-CoV-2 infiltrates human cells in the lower respiratory system using receptors known as ACE2 and transmembrane protease serine 2 [3]. Of these 2, the ACE2 receptor is primarily located in the cells of the lung, liver, kidney, GI tract, and even in the cells of the nasal epithelium and oral mucosa [4]. These cells serve as host cells for the virus, which invades these body cells and triggers an inflammatory response in these organs. This response, in turn, leads to early smell and taste dysfunctions during the disease's progression [15]. Therefore, the development of oral lesions can occur directly

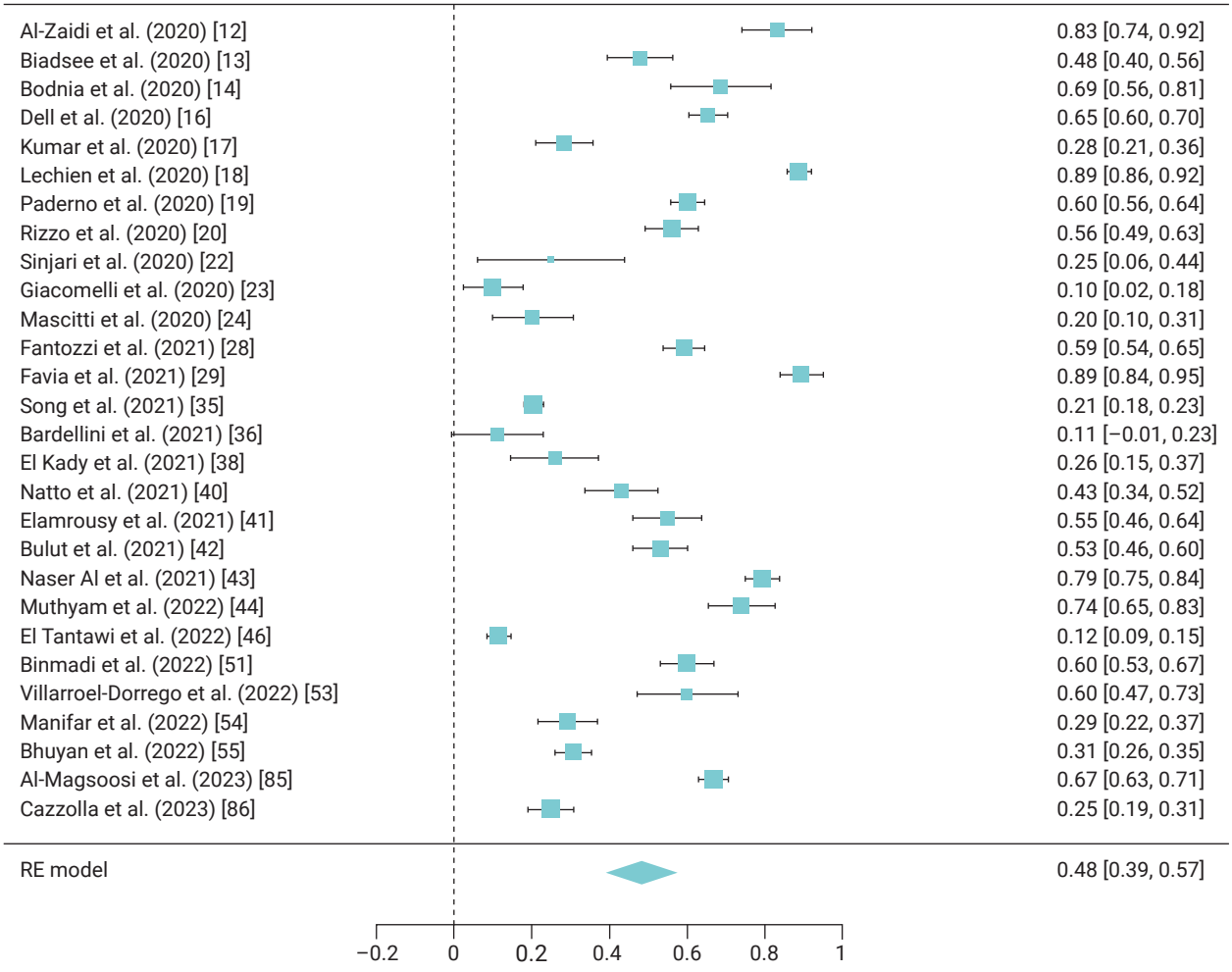

Figure 2. Forest plot showing the pooled prevalence of taste disorders in patients with COVID-19 (28 studies). RE, random effects.

through the effects of the virus replicating in these cells (resulting in SARS-CoV-2-specific lesions) and indirectly as a consequence of potential drug reactions that may occur during the latency period, viral exanthem, due to the physical and psychological stress of COVID-19 or its treatment, or co-infection with other bacterial infections that exacerbate the severity of COVID-19 [59,88]. The involvement of the oral cavity becomes a unique characteristic of COVID-19 [89]. According to Amorim dos Santos et al. [4], the general health deterioration of COVID-19 patients, coupled with extended hospitalization periods and numerous treatment procedures, also increases the likelihood of oral lesions. Chaux-Bodard et al. [87] proposed that oral lesions might emerge as a result of various inflammatory reactions that induce vascular inflammation. Previous reports from Italy and the United Kingdom have noted a temporary association between pediatric inflammatory multisystem syndrome and SARS-COV-2 cases [90]. Certain diseases, such as Kawasaki disease and erythema multiforme, can predispose individuals to oral manifestations. Consequently, we have excluded such conditions from our systematic review.

Regarding oral lesions, the tongue was the most frequently affected area (n=65), followed by the oral mucosa (n=37), and then the lips (n=19). de Sousa and Paradella [7] identified the palate and tongue, followed by the gums and lips, as the areas most commonly affected in COVID-19 patients. The oral manifestations among COVID-19 patients are described below:

Taste Disorders

Numerous studies have indicated that alterations in smell and taste can serve as early signs of COVID-19 infection, playing a crucial role in early diagnosis and decision-

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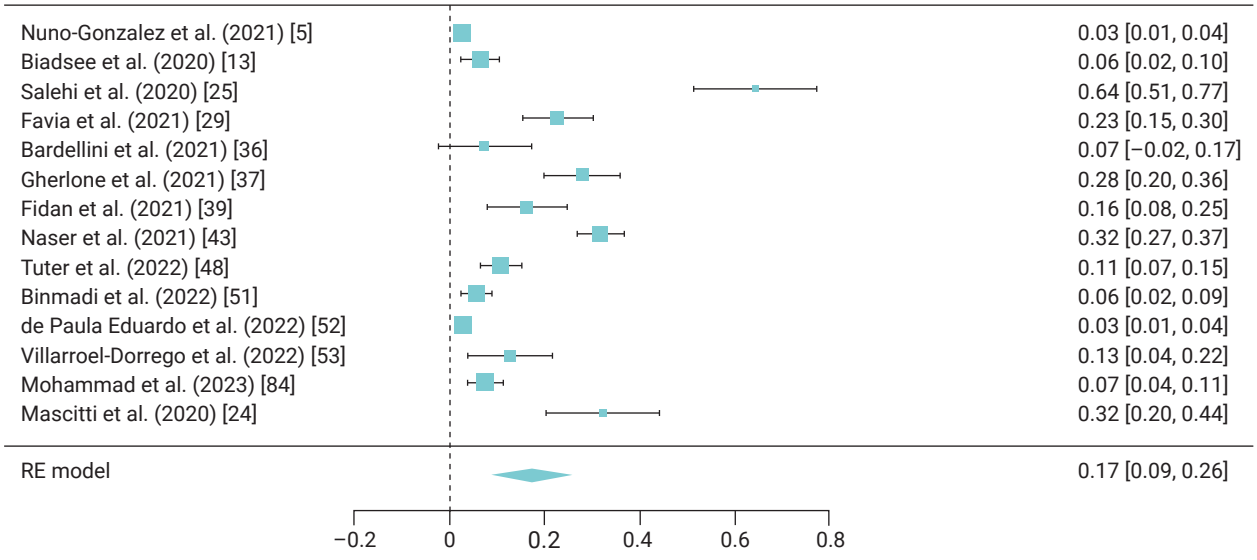

Figure 3. Forest plot showing the pooled prevalence of red and white lesions in patients with COVID-19 (14 studies). RE, random effects.

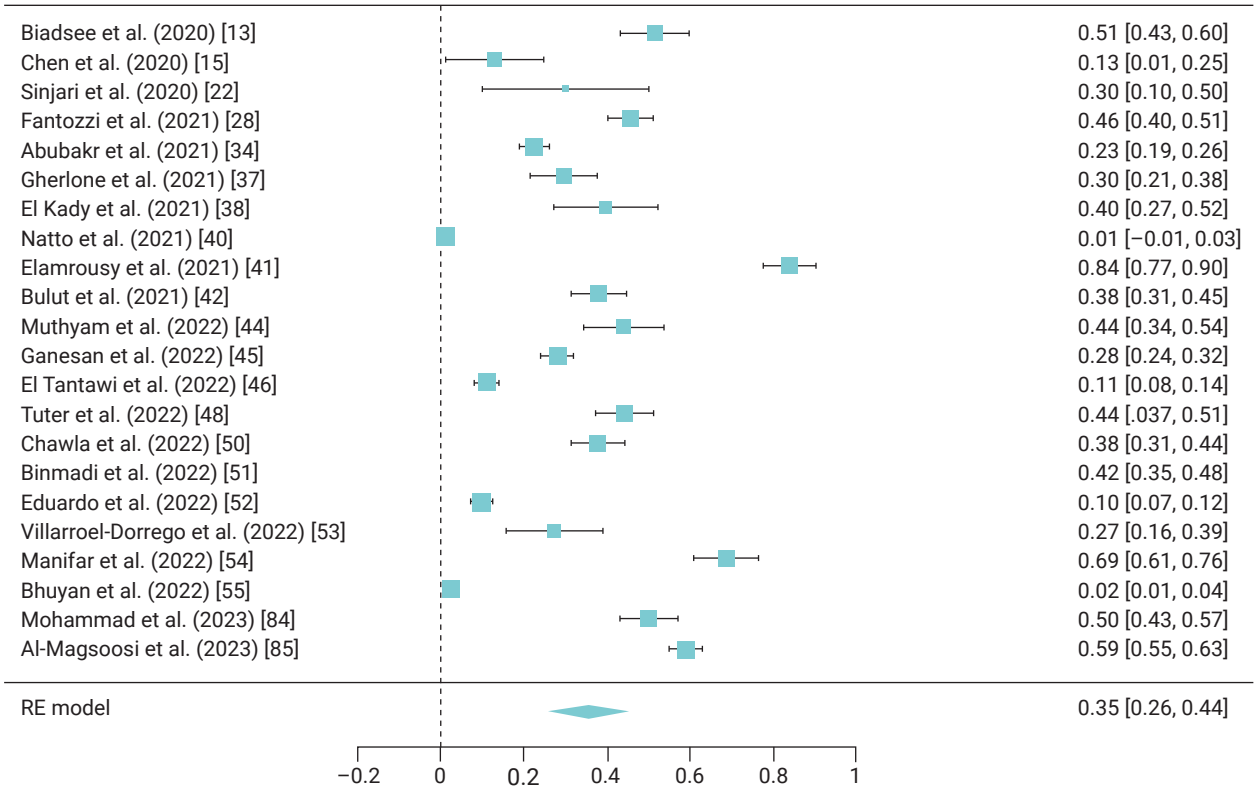

Figure 4. Forest plot showing the pooled prevalence of xerostomia in patients with COVID-19 (22 studies). RE, random effects.

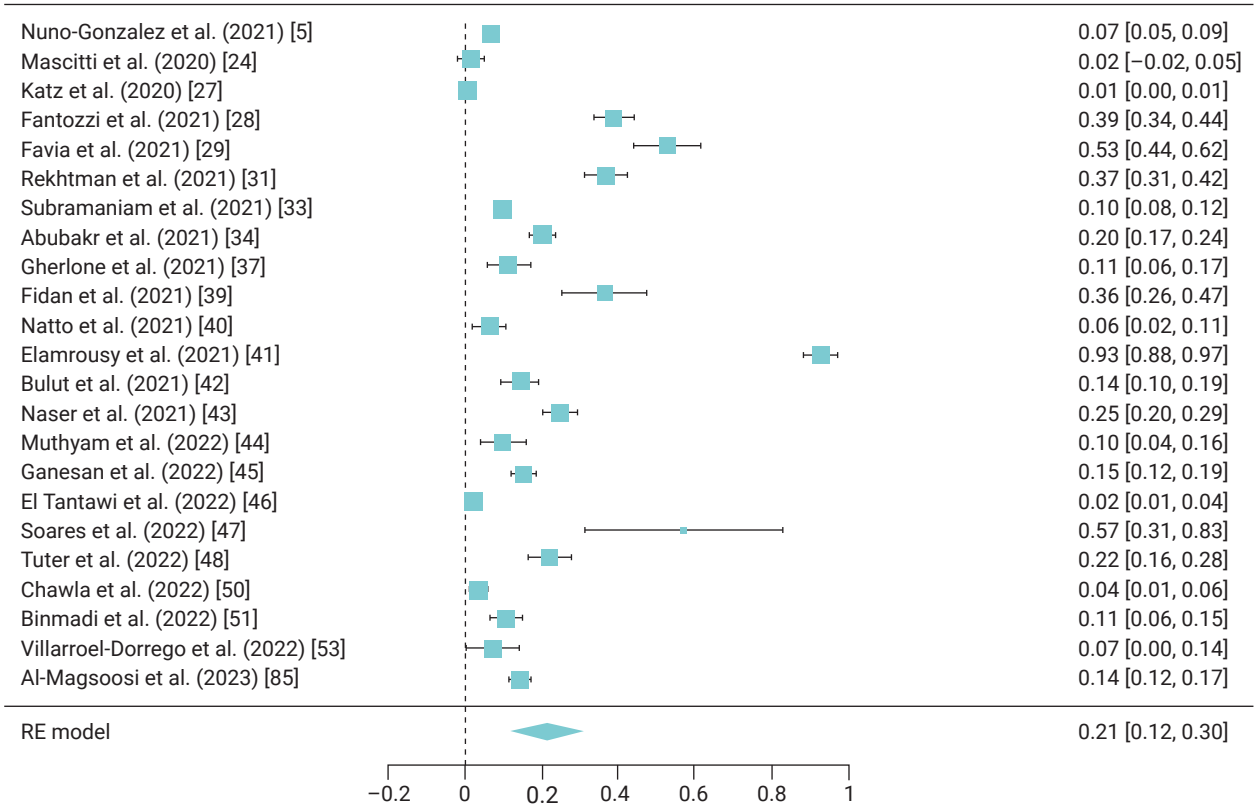

Figure 5. Forest plot showing the pooled prevalence of ulceration in patients with COVID-19 (23 studies). RE, random effects.

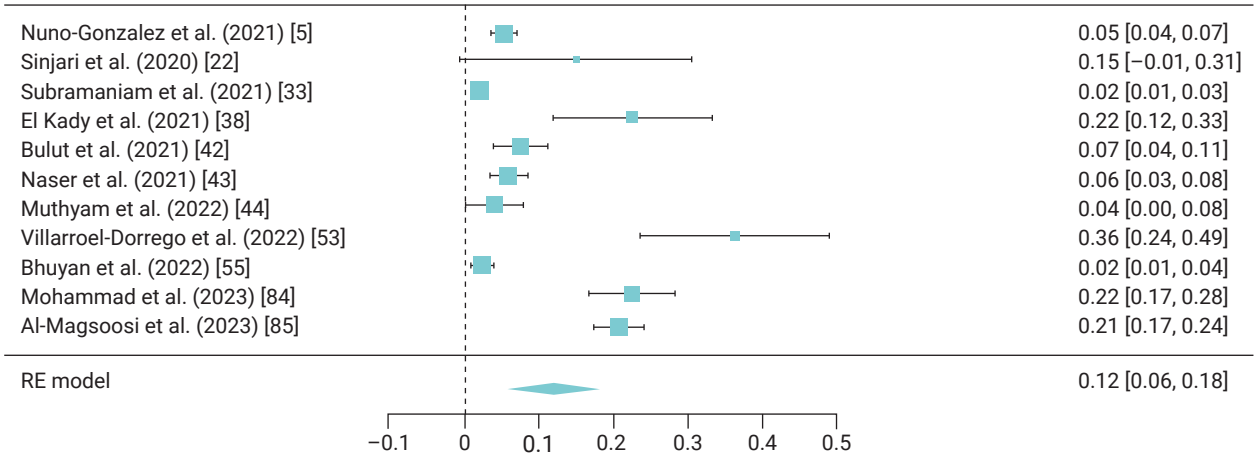

Figure 6. Forest plot showing the pooled prevalence of burning sensation in patients with COVID-19 (11 studies). RE, random effects.

making. While these symptoms are not life-threatening, they can significantly impact a patient's quality of life. Professor C. Hopkins, President of the British Rhinological Society, has noted that the loss of smell or taste may be the sole symptom of COVID-19 [91]. Several public health surveillance organizations, including the European Centre for Disease Prevention and Control, the Centers for Disease Control and Prevention, the WHO [92], and Public Health England, have incorporated the sudden onset of anosmia, ageusia, or dysgeusia into their primary clinical criteria for defining a COVID-19 case [93]. The present systematic review also found that general symptoms typically follow

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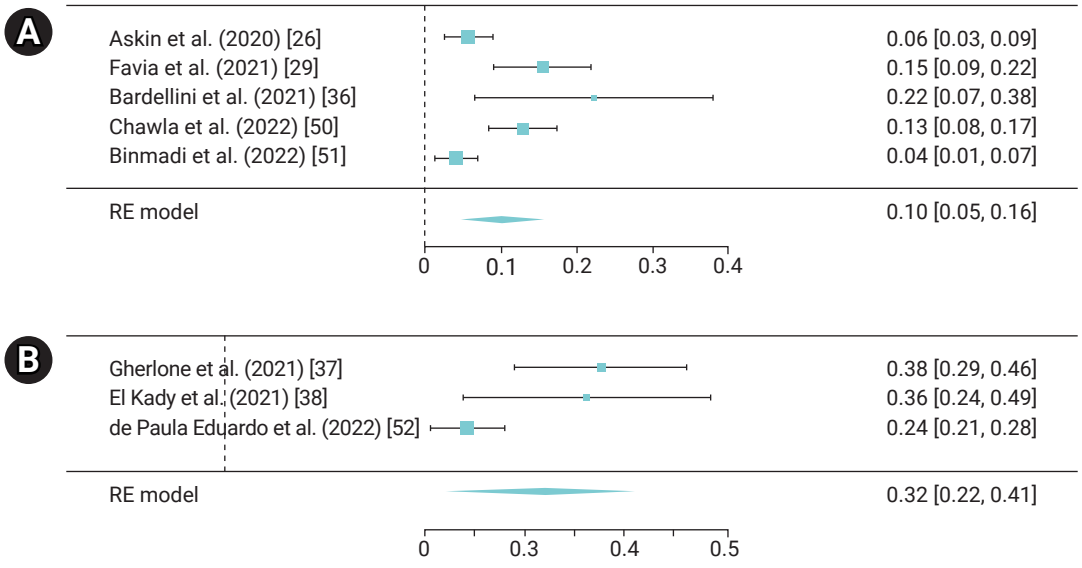

Figure 7. Forest plot showing the pooled prevalence of (A) vesiculobullous lesions (5 studies) and (B) salivary gland involvement (3 studies) in patients with COVID-19. RE, random effects.

oral symptoms, particularly the loss of taste. The likely reason for taste alteration in COVID-19 patients is the higher expression of the ACE2 receptor in the tongue than in the buccal and gingival tissues. This results in damage to the mucosal epithelial cells of the oral cavity [94,95].

In the present systematic review, the pooled prevalence of taste alteration was 48%. A recent review by Scotto et al. [89] indicated that the prevalence of taste disorders varied widely across studies, ranging from 1.0% to 93.0%. In a cross-sectional study by Al-Zaidi and Badr [12], 83.08% of COVID-19 patients experienced taste dysfunction. For 50% of these patients, taste returned within a week, while for 25% it took less than a week, for 18.75% it took within 2 weeks, and for 6.25% it took within 3 weeks. In their living systematic review (LSR), Amorim dos Santos et al. [4] identified taste disorders as the most common oral symptom in this population, with a prevalence of 45%. However, in their subsequent LSR, the prevalence dropped to 38%. They noted that the prevalence of taste disorders among COVID-19 patients varies geographically, from 14% in Africa to 49% in Europe [96]. Yan et al. [21] reported taste loss in 71% of COVID-19-positive subjects, and found a strong association between taste loss and COVID-19 positivity (odds ratio, 10.2; 95% CI, 4.74–22.1). In a study by Biadsee et al. [13], 52% of participants reported changes in taste sensation, with 52 patients noting a change in spicy taste perception, 54 in salty taste, 53 in sour taste, and 61 in sweet taste. Bodnia and Katzenstein [14] found that 70% of patients experienced a total loss of taste, which resolved within 1 to 3 weeks for 78% of patients and within 3 to 6 weeks for 22%. A meta-analysis by Tong et al. [97] revealed that 43.93% of individuals noted changes in taste. Another meta-analysis by Nijakowski et al. [98] estimated the prevalence of taste alterations to be around 54.73% (95% CI, 46.28%– 63.04%).

Three studies in our systematic review, conducted by Favia et al. [29], Bardellini et al. [36], and Binmadi et al. [51], reported geographic tongue. Bardellini et al. [36] carried out a retrospective cohort study on pediatric patients and identified the most common oral lesions as oral pseudomembranous candidiasis (n=2), coated tongue (n=2), taste alteration (n=3), and geographic tongue (n=1). Notably, the occurrence of geographic tongue coincided with a high fever, as reported by the patient's mother. The etiopathogenesis of geographic tongue remains unclear, but some researchers have suggested a link with several non-genetic multifactorial factors, including viral infections [99].

Vesiculobullous Lesions and Ulceration

Thirteen studies, encompassing both case reports and case series [6,9,24,26,29,50,57,59,61,62,70,77,81], documented vesiculobullous lesions. Among these, 5 cross-sectional studies revealed a combined prevalence of 10%.

Ulceration was reported by 23 studies [5,24,27–29,31,33,34,37,39–48,50,51,53,85], involving 1,086 patients with a pooled prevalence of 21%. This is slightly higher than the value reported in the meta-analysis by Aragoneses et al.

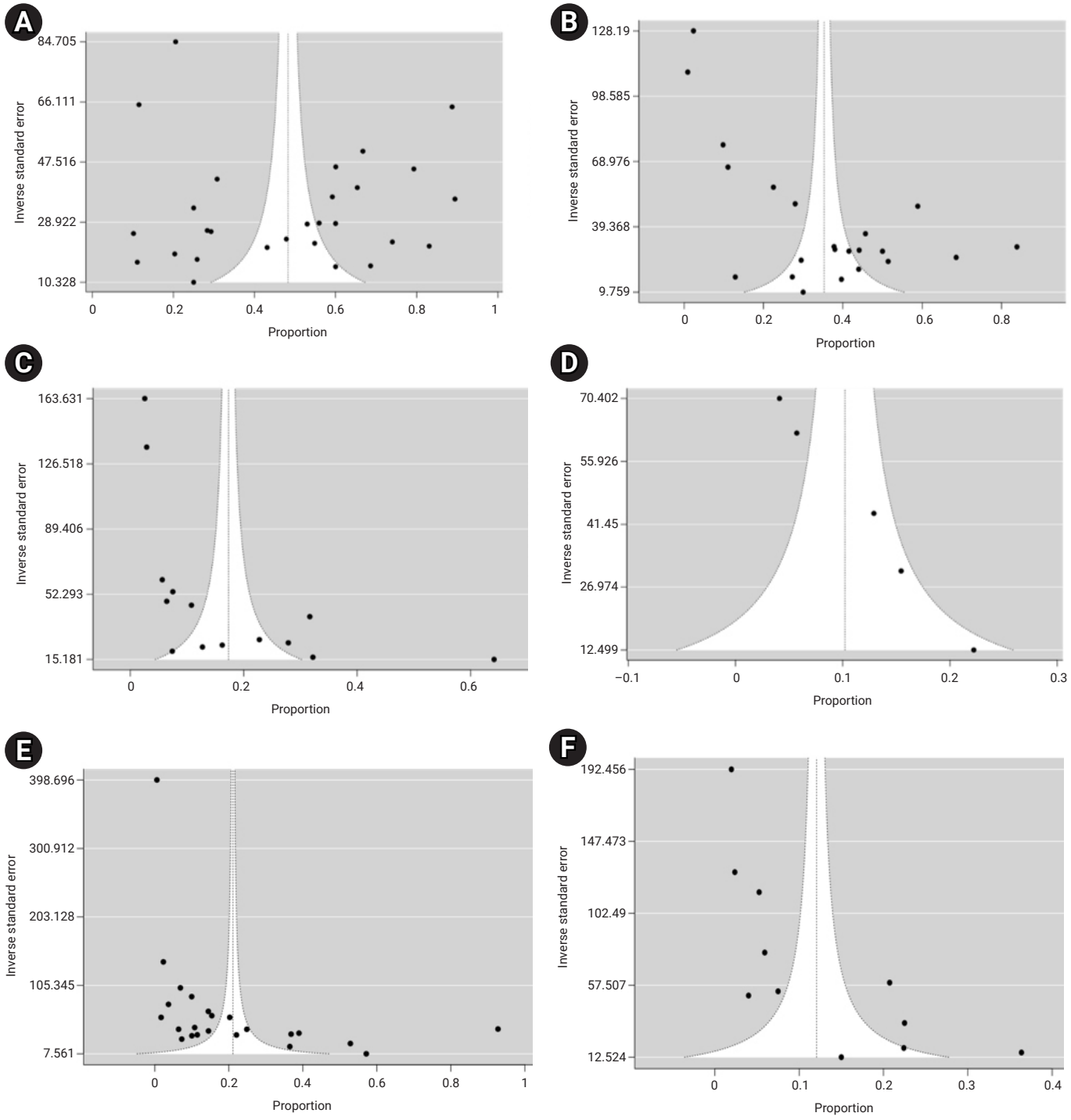

Figure 8. Funnel plot of studies on the prevalence of (A) taste alteration, (B) xerostomia, (C) red and white lesions, (D) vesiculobullous lesions, (E) ulceration, and (F) burning sensation.

[100] (10%). Favia et al. [29] provided a detailed description of the histological aspects of oral SARS-CoV-2-related lesions, identifying ulcers as the most common oral manifestation, in 52.8% of patients. Martin Carreras-Presas et al. [59] reported 3 cases of ulcers, 1 of which was confirmed to be infected with SARS-CoV-2, while the other 2 were suspected cases. These lesions were similar in appearance to herpes simplex infection, but this was not confirmed by biopsy. Halboub

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et al. [101] conducted a review and found that painful oral ulcers were the most common orofacial manifestation in patients with COVID-19. Bullous lesions on the palate and oral mucosa were found by Cruz Tapia et al. [57] and Dalipi et al. [70], respectively. Orilisi et al. [102] conducted a systematic review and reported that oral ulcers, cheilitis, and tongue lesions were more common in patients prior to hospitalization. In contrast, perioral pressure ulcers, macroglossia, blisters, and oral candidiasis were more frequently observed in patients during their hospital stay.

The mechanism behind ulcer formation is thought to involve an elevated level of tumor necrosis factor-α in COVID-19 patients, which can trigger the chemotaxis of neutrophils to the oral mucosa, leading to the development of aphthous-like lesions. Other potential causes for these lesions in COVID-19 patients could be stress and immunosuppression, both secondary effects of the infection [9].

Red and white lesions

Eighteen studies have reported the presence of red and white lesions in patients who tested positive for COVID-19, with a pooled prevalence of 17% [8,24–26,29,33,36,37,39,43,49,51,53,57,61,68,80,82]. The variety of red and white lesions documented in these studies include cheilitis and oral lichenoid reactions [24], white plaques on the inner oral mucous layer [25,37,43,68,80], rashes 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 observed in 22 cross-sectional studies [13,15,22,28,34,37,38,40–42,44–46,48,50–55,84,85] and 2 case reports [60,78]. These studies reported a combined prevalence of 35%, a figure slightly lower than the 44% prevalence (95% CI, 36%–52%) found in a recent meta-analysis by Aragoneses et al. [100]. In research conducted by Biadsee et al. [13], 56% of patients reported experiencing xerostomia, as determined by the question, "Do you feel the need to drink more (dry mouth)?". In the revised version of the LSR by Amorim Dos Santos et al. [96], xerostomia was the most frequently reported oral symptom in COVID-19 patients, whereas tassate disturbances were the primary feature in the original LSR [4]. In a meta-analysis by Nijakowski et al. [98], xerostomia was prevalent in 37.58% (95% CI, 26.35%–49.53%) of COVID-19 patients.

Gingival and periodontal involvement

Twelve studies (15%) [6,26,29,32,38,39,42,44,51,55,59,78] reported the prevalence of gingivitis and periodontitis. The gingival symptoms identified in COVID-19 patients from our systematic review included gingivitis [29], desquamative gingivitis [6,59], ulceronecrotic gingivitis [29], and gingival bleeding [6,38,42,44,55,78]. Two studies reported instances of periodontitis [32] and necrotizing periodontal disease [51].

Other findings

Red and/or swollen lips was observed by Halepas et al. [30] in 48.9% of patients. Other findings related to lip involvement in COVID-19 patients included pale lips [33], reddish plaques on the lower lip [61], nodules on the lower lip [10], and reddish macules [42]. In terms of palatal findings among COVID-19 patients, there were reddish-white spots on the palate [33], palate ulcerations [6,39,56,59,60,81,82], a white coating on the palate [43,68], bullae on both the left and right palatal mucosa [57], an erythematous surface on the hard palate [64], and an angioma-type lesion on the right side of the palate [82].

Limitations

Although we have attempted to summarize the findings of studies that report oral manifestations in COVID-19 patients, a significant limitation of this systematic review is the absence of a temporal dimension. We cannot definitively state that these oral manifestations are directly linked to COVID-19, or if they are indirect manifestations of other factors such as stress, immunosuppression, and/or medications. Another limitation is the absence of a definitive diagnosis, as most of the cases included in the review did not undergo a biopsy to confirm the diagnosis.

Conclusion

Our systematic review showed a relatively high prevalence of oral manifestations, specifically taste alteration (48%), followed by dry mouth (35%), ulceration (21%), and red and white lesions (17%). These patients exhibit a variety of oral symptoms that could aid clinicians in the early detection of the disease. It is crucial to recognize the signs and symptoms of COVID-19 for a prompt diagnosis and an improved prognosis. Dental practitioners can play a significant role not only in preventing the transmission of COVID-19 but also in interrupting the disease's progression. Increasing awareness of these symptoms is vital for the early diagnosis and treatment of this deadly disease.

Supplementary Material

Table S1. Risk of bias assessed using the JBI Critical Appraisal Tools for use in JBI systematic reviews of case reports (n=20);

Table S2. Risk of bias assessed using the JBI Critical Appraisal Tools for use in JBI systematic reviews of case series (n=11); **Table S3.** Risk of bias assessed using the JBI Critical Appraisal Tools for use in JBI systematic reviews of cross-sectional studies/retrospective/prospective studies (n=47); **Table S4.** Risk of bias assessed using the JBI Critical Appraisal Tools for use in JBI systematic reviews of case control study (n=1); **Table S5.** Treatment of oral lesions in COVID-19 patients. Supplementary data are available at https://doi.org/10.24171/j.phrp.2023.0033.

Notes

Ethics Approval
Not applicable.

Conflicts of Interest
The authors have no conflicts of interest to declare.

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None.

Availability of Data
The datasets are not publicly available but are available from the corresponding author upon reasonable request.

Authors' Contributions
Conceptualization: AG, KS, AP; Data curation: AG, AA; Formal analysis: AG, AP; Investigation: AG, KS, AA; Methodology: AG, KS, AA, AP, RC; Project administration: AG, KS; Software: AG, AP; Supervision: AG, AA; Validation: AG, AP; Visualization: AG, RC; Writing–original draft: AG; Writing–review & editing: all authors. All authors read and approved the final manuscript.

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