META-ANALYSIS / *MÉTA-ANALYSE*

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IMPACT ON ORAL HEALTH OF THE POST COVID-19 INFECTIONS: A SYSTEMTIC REVIEW

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Introduction: The COVID-19 pandemic has been associated with a diverse range of oral health implications, including mucosal lesions, periodontitis, and disruptions of the oral microbiota. Since airborne particles primarily transmit COVID-19, understanding its potential impact on oral health is crucial for dental care and infection control.

Objectives: This systematic review aimed to evaluate the effects of post-COVID-19 infections on oral health, highlighting clinical manifestations, periodontal disease associations, and microbiota disturbances.

Methods: Electronic literature searches were conducted between January 2020 and July 2024 by one author across several databases, including PubMed/MEDLINE, Scopus, Cochrane Library, EMBASE, ScienceDirect, Google Scholar, and Web of Science. A total of 3642 publications were screened. Two reviewers analyzed the articles and extracted the data. Of these, 25 studies met the inclusion criteria.

Results: A total of 25 studies were included in this systematic review, addressing oral manifestations, the link between periodontal disease and COVID-19, and broader oral health impacts. Lesions such as ulcers, candidiasis, and taste disorders were reported, with causes attributed to viral effects or secondary inflammation. Evidence suggests a bidirectional relationship between periodontitis and COVID-19, potentially mediated by elevated cytokines (IL-6, TNF-α).

Conclusions: Post-COVID-19 conditions are associated with a range of oral health issues, including opportunistic infections, a potential bidirectional link with periodontitis mediated by inflammation, and altered oral microbiota. However, the evidence is heterogeneous, and the quality of many studies is limited, underscoring the need for more rigorous research to establish causality.

Keywords: Coronavirus, Periodontitis, Oral lesions, Dental aerosols, Dental diseases, Inflammation.

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Conflicts of interest:
The authors declare no conflicts of interest.

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IMPACT DES INFECTIONS POST-COVID-19 SUR LA SANTE BUCCO-DENTAIRE: REVUE SYSTEMATIQUE

Introduction: La pandémie COVID-19 a été associée à diverses conséquences sur la santé bucco-dentaire, telles que des lésions muqueuses, une parodontite et des perturbations de la flore microbienne buccale. COVID-19 se transmet principalement par les particules en suspension dans l'air, il est essentiel de comprendre son impact potentiel sur la santé bucco-dentaire afin d'assurer les soins dentaires et de contrôler l'infection.

Objectifs: Cette revue systématique visait à évaluer l'impact des infections post-COVID-19 sur la santé bucco-dentaire, en mettant l'accent sur les manifestations cliniques, les associations avec les maladies parodontales et les altérations du microbiote oral.

Méthodes: Des recherches documentaires électroniques ont été effectuées par un auteur dans plusieurs bases de données, notamment PubMed/MEDLINE, Scopus, Cochrane Library, EMBASE, ScienceDirect, Google Scholar, and Web of Science. Au total, 3642 publications ont été examinées. Deux évaluateurs indépendants ont analysé les articles et extrait les données. Au total, 25 études répondaient aux critères d'inclusion.

Résultats: Au total, 25 études ont été incluses dans cette revue systématique, portant sur les manifestations bucco-dentaires, les interactions entre la maladie parodontale et la COVID-19, ainsi que sur d'autres impacts bucco-dentaires. Les lésions les plus fréquemment rapportées incluaient des ulcères, des candidoses et des troubles du goût, souvent attribués à l'effet direct du virus ou à des réactions inflammatoires secondaires. Les données disponibles suggèrent par ailleurs une relation bidirectionnelle entre la parodontite et la COVID-19, potentiellement induite par l'élévation de cytokines pro-inflammatoires (IL-6, TNF-α).

Conclusions: Les conditions post-COVID-19 sont associées à un large éventail de manifestations bucco-dentaires, comprenant des infections opportunistes, une possible interaction bidirectionnelle avec la parodontite via l'inflammation, ainsi que des altérations du microbiote oral. Cependant, l'hétérogénéité des études et leurs limites méthodologiques soulignent la nécessité de recherches plus rigoureuses afin de confirmer ces associations et d'établir des relations causales.

Mots-clés: COVID-19, parodontite, lésions buccales, aérosols dentaires, maladies dentaires, inflammation.

Introduction

The transmission of airborne infections in the dental environment is a major health and safety concern for both oral health professionals and patients. Dental procedures often generate aerosols, which are fine particles suspended in the air [1]. These aerosols can contain pathogens, such as viruses, bacteria, and fungi, which can potentially transmit infections [1].

Pathogens in aerosols can include microorganisms responsible for diseases such as influenza, tuberculosis, and more recently, the SARS-CoV-2 virus responsible for COVID-19. Sources of these aerosols in a dental practice include the use of dental turbines, ultrasonic devices, and air polishers, as well as cleaning activities such as tooth brushing and polishing [1].

Due to the nature of dental care, where the mouth is a direct entry point for these infectious agents, the risk of transmission is high if adequate control measures are not put in place [2]. It is therefore essential to adopt strict disinfection protocols, use personal protective equipment (PPE), and improve workspace ventilation to minimize the risk of transmission of airborne infections [2]. A thorough understanding of transmission mechanisms and prevention strategies is crucial to protect both patients and healthcare professionals in dental care.

The objective of this systematic review is to evaluate the effects of post-COVID-19 infections on oral health, covering the period from 2020 to 2024 to present existing studies on the effects of airborne transmission in order to explore the relationship between COVID-19 and oral health.

Materials and methods

This study followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA Statement) and conducted a systematic review and meta-analysis [3]. The registration protocol was performed in Prospero (registration number: CRD42024591808).

A literature search was conducted using electronic databases (MEDLINE/PubMed, Scopus, Web of Science, ScienceDirect, Embase, Cochrane Library, and Google Scholar) for studies that met the inclusion criteria, covering the period from January 2020 to July 2024. The search strategy included a combination of keywords and Medical Subject Headings (MeSH) terms related to airborne infections, oral manifestations, dental aerosols, periodontitis, dental diseases, inflammation and COVID-19. After removing duplicates, titles and abstracts were screened manually. Full-text articles were retrieved for studies deemed eligible.

A total of 3642 publications were identified in all databases. A flow chart that summarizes the study selection process according to the PRISMA Statement is shown in Figure 1, 34 articles meeting the inclusion criteria related to oral health were selected for data extraction. As a result, a total of 25 studies were included in the final review, the references of the selected articles were examined and checked for any citations.

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) is an essential

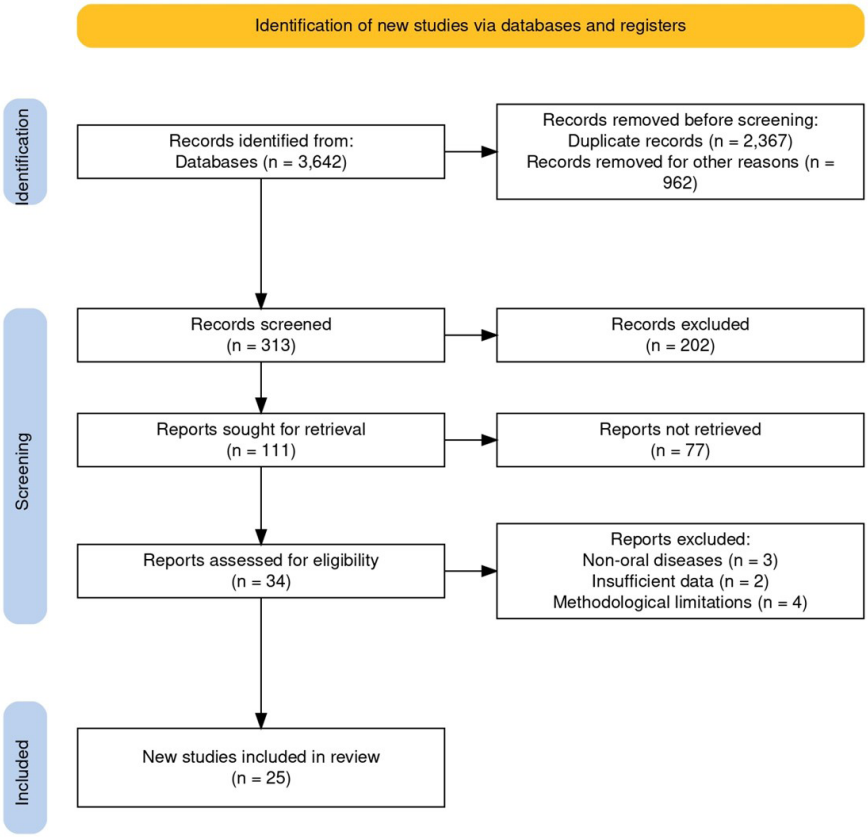

Figure 1. PRISMA Flow Chart of the Study Selection Process (2020–2024)

graphic tool for illustrating the study selection process in a systematic review or meta-analysis [3]. It visualizes the various stages in the selection process, from study identification to final inclusion. The data extracted for the global study are presented in tabular form. The eligibility criteria were as follows:

Eligibility criteria and study selection

Database search protocol

Boolean operators and MeSH keywords were applied in our database search, which was conducted across seven distinct databases. PubMed, Scopus, Web of Science, ScienceDirect, Cochrane Library, Embase, and Google Scholar were the databases that were searched. Keywords and MeSH phrases were combined, the specifics of which are provided in table 2, to create search strings.

Screening and data collection

All records retrieved from the selected databases (MEDLINE/PubMed, Scopus, Web of Science, ScienceDirect, Cochrane Library, Embase, and Google Scholar) for the period 2020–2024 were exported and deduplicated. Titles and abstracts were screened independently by two reviewers based on predefined eligibility criteria. Full texts of potentially relevant studies were assessed for inclusion. Discrepancies were resolved by discussion until consensus was reached. Data were extracted using a standardized form that included information on author, year, country, study design, population characteristics, objectives, main findings, and limitations.

Methodological quality assessment

The following criteria was used to classify the potential risk of bias for each article, as applied in a previous review [4]509 teeth.

- Random sample selection in the population.
- Definition of inclusion/exclusion criteria.
- Report of losses to follow-up (monitoring.
- Validated measurements obtained
- Statistical analysis
- Estimated potential risk of bias

Studies meeting all of the above criteria were classified as having low risk of bias, those that met all but one of the criteria were classified as having a moderate risk of bias, and those that did not meet two or more criteria were classified as presenting a high risk of bias.

Ethical approval was not required for this systematic review as it analyzed publicly available data from previously published studies.

Data extraction

In order to assure consistency and correctness in the obtained data, a standardised form was developed

Table 1. Inclusion and exclusion criteria devised for the review

Criteria	Inclusion	Exclusion
Study design	In vivo studies	Review articles, opinion articles
Type of study	Clinical, observational (cohort, case-control, cross-sectional), and meta-analyses assessing the impact of COVID-19 on oral health.	Studies unrelated to the effects of COVID-19 on oral health (e.g., studies on other airborne infections or general oral health not linked to infection).
Population	Patients diagnosed with COVID-19 or exposed to the virus, with available oral health data. Includes specific age groups (e.g. adults, children, elderly).	Non-human studies or those without relevant oral health data. Studies excluding COVID-19 as an exposure or failing to mention airborne infection as a factor.
Intervention/ Exposure	Confirmed COVID-19 exposure through diagnostic tests, clinical symptoms, or medical history. Includes exposure in dental, ICU, or healthcare settings.	Studies lacking adequate confirmation of COVID-19 infection or focusing solely on airborne infections unrelated to COVID-19.
Outcome	Studies reporting oral symptoms, oral hygiene changes, complications, or dental visit frequency related to COVID-19, with qualitative or quantitative data.	Studies not addressing oral health outcomes or lacking measurable oral health data.
Language	Studies published in English.	Non-English language studies
Publication period	Studies published from 2020 to July 2024 to capture the most recent and relevant data.	Studies published before the pandemic or outside the specified time frame.
Study quality	Studies with sound methodology and acceptable scientific rigor, assessed using tools like the Newcastle-Ottawa Scale.	Studies with significant methodological bias, insufficient scientific quality, or major shortcomings in data collection

Table 2. Search strings utilised across the assessed databases

Database	Search string
PubMed	("COVID-19" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "post-COVID-19") AND ("oral health" OR "oral manifestations" OR "oral lesions" OR "periodontitis" OR "dental diseases" OR "oral microbiota") AND ("airborne transmission OR "airborne infection" OR "droplet transmission")
Scopus	(TITLE-ABS-KEY("COVID-19" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "post-COVID-19")) AND (TITLE-ABS-KEY("oral health" OR "oral manifestations" OR "oral lesions" OR "periodontitis" OR "oral microbiota" OR "dental health")) AND (TITLE-ABS-KEY("airborne transmission" OR "aerosol" OR "airborne infection" OR "droplet transmission"))
Web of Science	TS=("COVID-19" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "post-COVID-19") AND TS=("oral health" OR "oral manifestations" OR "oral lesions" OR "periodontitis" OR "oral microbiota" OR "dental health") AND TS=("airborne transmission" OR "airborne infection" OR "aerosol" OR "droplet transmission")
ScienceDirect	("COVID-19" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "post-COVID-19") AND ("oral health" OR "oral lesions" OR "oral manifestations" OR "periodontitis" OR "oral microbiota" OR "dental health") AND ("airborne transmission" OR "aerosol" OR "airborne infection" OR "droplet transmission")
Cochrane Library	("COVID-19" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "post-COVID-19") AND ("oral health" OR "oral manifestations" OR "oral lesions" OR "periodontitis" OR "oral microbiota" OR "dental health") AND ("airborne transmission" OR "aerosol" OR "droplet transmission" OR "airborne infection")
Embase	('COVID-19' OR 'SARS-CoV-2' OR 'coronavirus disease 2019' OR 'post-COVID-19') AND ('oral health' OR 'oral lesion' OR 'oral manifestation' OR 'periodontitis' OR 'oral microbiota' OR 'dental health') AND ('airborne transmission' OR 'airborne infection' OR 'aerosol' OR 'droplet transmission')
Google Scholar	("COVID-19" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "post-COVID-19") AND ("oral health" OR "oral manifestations" OR "oral lesions" OR "periodontitis" OR "oral microbiota" OR "dental health") AND ("airborne transmission" OR "aerosol" OR "airborne infection" OR "droplet transmission")

and matched this protocol with the research question and review objectives. Next, a methodical plan was developed for data extraction to collect relevant information from the chosen studies. The Microsoft Office Excel 2016 was used to extract the data of interest from the included manuscripts. These were placed on a standardized form. Two trained reviewers separately extracted data from each trial. They then worked together to resolve any differences in their evaluations before entering the data into a spreadsheet for analysis. The data extraction will focus on the outcome criteria, the characteristics of the participants in each study, the characteristics of the digital test used, the characteristics of the comparative test, and the measured results.

Strategy for data synthesis

The data were synthesized qualitatively and consisted of a narrative synthesis of the evidence. The extracted data from the retained studies were:

- Author name,
- Year of publication,
- Country,
- Study design,
- Sample Size and Population Characteristics,
- Simulation software used,
- Evaluation method,
- And results

Any disagreements were resolved by discussion and consensus between the three authors.

Statistical analysis

The literature identified in this review does not meet criteria required for quantitative data or meta-analysis. Furthermore, the heterogeneity of studies (study design, study population, follow-up times, and parameters reported) prevents the plotting of outcomes to feature results. There fore, descriptive methods were mainly used to present the data.

Results

25 studies investigating the impact of the COVID-19 pandemic on the oral environment were included after the final review. Most were conducted in Brazil, followed by India, with additional studies in each of the following countries: Turkey, France... Publication dates range from 2020 to 2024, with research conducted up to July 2024. The study selection process is detailed in the PRISMA flow diagram below, which outlines the number of records identified, screened, assessed for eligibility, and finally included in the review.

In order to structure this review, the included articles were classified into three thematic categories, each corresponding to a specific hypothesis. Hypothesis 1 focuses on the oral manifestations of COVID-19, including lesions, xerostomia, and sensory disturbances such as loss of taste or smell. Hypothesis 2 addresses the potential relationship between periodontal disease and COVID-19, particularly the role of inflammation and cytokine activity in the bidirectional association between these conditions. Hypothesis 3 explores the broader consequences of COVID-19 on oral health, including changes in the oral microbiota, alterations in the salivary immune barrier, and increased bacterial colonization. The following tables provide a summary of the main characteristics and key findings of the studies associated with each hypothesis.

Table 3. Characteristics and Key Findings of Included Studies on Oral Manifestations of COVID-19

Author (Year, Country)	Journal	Objective	Methods	Sample Size	Procedure Cases Study type
Eduardo et al. 2022 (Brazil)	Special Care in Dentistry	Detect type and frequency of oral lesions in COVID-19 patients in ICU	Oral condition and mechanical ventilation data collected from oral medicine records	n = 519	Retrospective study. 472 patients (90.9%) examined by oral medicine staff.
Castilho et al. 2024 (Brazil) a respiratory illness with a global impact on millions, has recently been linked to manifestations affecting various bodily systems, including the oral cavity. Studies highlight oral issues, like ulcers, blisters, and white patches, alongside olfactory and gustatory dysfunction, influencing an individual's quality of life. In this context, our study aimed to assess the frequency of oral lesions, olfactory and gustatory disorders, and xerostomia resulting from COVID-19. An observational study was conducted with 414 patients to evaluate the frequency of oral symptoms resulting from COVID-19. Patients were diagnosed with mild symptoms and evaluated through clinical examination of the oral cavity and a questionnaire to assess functional alterations. The findings showed that 139 out of 414 patients presented clinical manifestations, with oral lesions being the most prevalent (19.1%	Journal of Dentistry	Evaluate frequency of oral lesions, olfactory/gustatory disorders, and xerostomia due to COVID	Clinical examination of oral cavity in mild COVID-19 patients	n = 414	Observational study. 139/414 patients had clinical manifestations.

Prakash et al. 2024 (India)	Journal of Maxillofacial and Oral Surgery	Estimate prevalence of oral manifestations in COVID-19 patients	Visual assessment using mouth mirror and light for erythema, ulcers, vesicles, etc.	n = 472	Observational study. 109/472 patients had clinical manifestations.
Limongelli et al. 2024 (Italy) possibly involving the lungs, brain, kidney, cardiovascular and neuromuscular system, as well the persistency of taste dysfunction. Such symptoms develop during or after infection and continue for more than 12 weeks with pathogenesis related to virus persistency but variable by organs or systems. Materials and Methods: We recently observed six patients recovered from COVID-19 and with negative RT-PCR testing, showing oral mucosa lesions (mainly ulcers	Oral Diseases	Analyze long-term sequelae of SARS-CoV-2 infection focusing on post-COVID syndromes	Mechanism study of symptom persistence >12 weeks post-recovery with multisystemic involvement	n = 6	RT-PCR test and swabbing.
Castro et al. 2024	Contemporary Clinical Dentistry	Observe and treat ulcerative lesions in SARS-CoV-2 patients	Patient admitted to ICU with mechanical ventilation and nasogastric tube due to oral lesions	n = 1	Clinical case. Treatment with low-level laser therapy (LLLT).
Schwab et al. 2022 (Brazil)	Journal of Oral Microbiology	Evaluate oral manifestations during hospitalization for COVID-19	Oral mucosa examined twice weekly until discharge or death	n = 154	Cohort study. Patients grouped into Group 1 and Group 2 based on oral alterations.
Pauli et al. 2021 (Brazil)	Oral Surgery, Oral Medicine, Oral Pathology	Investigate relationship between painful palatal lesion and COVID-19	Cone-beam volume computed tomography and biopsy histology	n = 1	Clinical case study. PCR test.
Subramaniam et al. 2021	Dental Research Journal	Determine if lesions are due to coronavirus or secondary to systemic condition	Short-term observational study of COVID-19 patients with oral signs like herpes, candidiasis, ulcers	n = 713	Observational study.

Cruz Tapia et al. 2020	Specialized Care Dentist	Describe clinicopathological lesions of oral mucosa in confirmed COVID-19 patients	Clinical examination of 4 PCR-confirmed COVID-19 patients with various oral lesions	n = 4	Clinical study. PCR test.

Table 4. Characteristics and Key Findings of Included Studies on the Relationship between Periodontal Disease and COVID-19

Author, Year (Country)	Journal	Objective	Methods	Sample Size	Procedure / Cases / Study Type
Kaygısız Yiğit et al., 2023 (Turkey)	Oral Radiology	Compare pre-COVID-19 and post-COVID-19 dental radiological findings of rRT-PCR-positive individuals and healthy controls.	Included individuals with two panoramic radiographs taken between 2018 and 2022.	n = 102	52 rRT-PCR–positive patients; 50 controls.
Louisa et al., 2024 (Indonesia)	Dental Journal	Show the distribution of periodontal disease severity among COVID-19 long-hauliers and non-COVID-19 patients.	Secondary data from patients at the periodontics clinic, Faculty of Dentistry, Trisakti University Dental Hospital.	n = 40	Observational study; 20 long COVID patients, 20 non-COVID patients.
Gupta et al., 2024	Journal of the Indian Society of Periodontology	Evaluate cytokine levels in saliva of COVID-19-positive patients with and without periodontal disease.	Periodontal examination, saliva sampling, and cytokine assessment via bead-based multiplex assay.	n = 26	17 with periodontal disease; assay using fluorescence-encoded beads with flow cytometry (BD FACS LSRFortessa).
Qin et al., 2023	BMC Oral Health	Identify common molecular mechanisms between periodontitis and COVID-19 for potential therapeutic strategies.	Analyzed two RNA-seq datasets for differentially expressed genes, biological process enrichment, transcription factors (TFs), and immune cell types.	n = 1,616 and 10,201 RT-PCR genes	Relationships between TFs and mRNA determined by Pearson correlation; identified common TF-mRNA network and nine co-upregulated TFs.

Moradi Haghgoo et al., 2023	BMC Oral Health	Study possible interactions between COVID-19 and periodontitis.	Periodontal examination; medical and haematological data from hospital records.	n = 122	Case-control study; 122 patients in final analysis.
Moradi Haghgoo, 2023	BMC Oral Health	Assess association between periodontitis and COVID-19 severity.	Hospitalised patients with COVID-19; controls had mild-to-moderate disease, cases had severe-to-critical disease.	n = 122	Case-control study; periodontal exam plus serum and saliva sampling.
Poyato-Borrego et al., 2023	Medicina Oral, Patología Oral y Cirugía Bucal	Analyze prevalence of apical periodontitis and root canal treatment in COVID-19 patients and correlation with disease severity.	52 patients (30 men, 22 women) with orthopantomograms from the last 2 years.	n = 280	Retrospective study; PCR test.
Costa et al., 2022 (Brazil)	Journal of Periodontology	Evaluate dental and periodontal status of hospitalised COVID-19 patients and association with adverse events.	In-hospital clinical exam, including DMF index, periodontal status, and tooth loss patterns (Eichner index).	n = 128	Preliminary study; Chi-square test.
Marie et al., 2023 (Italy)	The Open Dentistry Journal	Determine effect of long COVID on periodontal severity via pro-inflammatory cytokines IL-1β, IL-6, and TNF-α.	Gingival sulcus fluids collected with paper tips.	n = 20	Case-control pilot study; 10 COVID-19 patients, 10 controls; ELISA test.
Fernandes Matuck et al., 2020 (Brazil)	Journal of Oral Microbiology	Investigate SARS-CoV-2 presence in periodontal tissue.	Minimally invasive post-mortem biopsy in 7 fatal COVID-19 cases using a smartphone-adapted video-endoscope.	n = 7	Post-mortem study; RT-PCR for SARS-CoV-2 RNA and histopathology.

Gardelis et al., 2022 (Switzerland)	Clinical and Experimental Research in Dentistry	Assess whether younger ICU-hospitalised severe COVID-19 patients (≤ 60 years) are more susceptible to severe periodontitis.	Radiographic bone loss (RBL) measured from recent dental radiographs (bitewing, periapical, panoramic).	n = 87	Pilot clinical and radiographic study.
Natto et al., 2022	Oral Microbiology	Evaluate SARS-CoV-2 in periodontal pockets and carious lesions as potential reservoirs.	72 participants in 6 groups: symptomatic/asymptomatic positives with pockets or lesions, positive and negative controls.	n = 72	RT-PCR cross-sectional study; 180 samples tested for E and S genes.

Table 5. Characteristics and Key Findings of Included Studies Examining the Impact of COVID-19 on Oral Health Biomarkers and Microbiota

Author, Year (Country)	Journal	Objective	Methods	Sample Size	Procedure / Cases / Study Type
Jahagirdar et al., 2024	Journal of Oral and Maxillofacial Pathology	Evaluate and compare the role of serum biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), and D-dimers in the severity of COVID-19 infection.	Data collected from 250 subjects; 100 were included according to inclusion criteria. Data were recorded retrospectively from healthcare professionals via Google Forms in Udaipur, Rajasthan.	n = 250	Retrospective, cross-sectional, observational pilot study
Brzychczy-Sroka et al., 2023	Journal of Oral Microbiology	Evaluate the oral microbiota of 60 participants: COVID-19 convalescents with and without antibiotics, and healthy individuals.	Clinical samples (saliva, dorsal swabs, supragingival and subgingival plaque) were collected and used to prepare the metagenomic library for next-generation sequencing (NGS).	n = 60	Next-generation sequencing (NGS) method

Karimzadeh et al., 2023	Journal of Protein Dentistry	Compare bacterial colonisation on removable dentures in patients with COVID-19 before and after diagnosis.	Swabs collected at two different time intervals from denture areas; samples were cultured, and colony smears were Gram-stained.	n = 60	Clinical study; statistical analysis using the Mann-Whitney U test (α = 0.05)
Santos et al., 2022 (Brazil)	Journal of Oral Biosciences	Assess the impact of SARS-CoV-2 on saliva composition.	Participants divided into three groups: (1) asymptomatic volunteers with a negative PCR test for SARS-CoV-2 (control, n = 21); (2) patients with COVID-19 symptoms < 7 days and PCR-confirmed infection (n = 13); (3) recovered patients from group 2, symptom-free for at least 2 months (n = 13).	n = 34	Longitudinal study using real-time PCR for SARS-CoV-2 detection and ELISA to measure salivary TNF-α, IL-6, IL-10, lactoferrin, lysozyme, IgG, IgA, and IgM levels

The main conclusions relating to the result of interest are presented in table form:

Table 6. Key Findings from Studies on COVID-19's Impact on Oral Health

Study	Main Outcome
Eduardo et al. 2022 (Brazil)	242 out of 472 patients (51.3%) had alterations of the oral cavity. Most frequent changes: Mechanical trauma (18.1%) mainly due to intubation; Vascular/clotting disorders (24.1%) including petechiae, ecchymosis, varicose veins, oral bleeding; Saliva alterations (24.4%) with dry mouth and sialorrhea.
Castilho et al. 2024 (Brazil)	Most common oral lesions (19.1%), taste disorders (18.1%), xerostomia (14.2%), olfactory dysfunction (14%). Most frequent lesions: ulcerations (51%), candidiasis (8%), erythema/red plaque (7%). 50 patients (12.1%) died during the study.
Prakash et al. 2024 (India)	103 patients (21%) had oral lesions: 41 (39.8%) with macular palatal enanthema, candidiasis (19, 18.4%), ulcers (4, 3.8%), mucositis (5, 4.8%), angular cheilitis (3, 2.9%), white coating on tongue (25, 24.2%), depilated tongue with glossitis (6, 5.8%).
Limongelli et al. 2024 (Italy)	Epithelial ulceration and inflammation observed, with enlarged vessels, flattened endothelium, no thrombus. Low SARS-CoV-2 positivity in epithelium but virus detected in lymphomonocytes, endothelium, perivascular pericytes.

Castro et al. 2024	Painful viral ulcers found on tongue, palate, labial commissure, oropharynx during oral evaluation.
Schwab et al. 2022 (Brazil)	Oral lesions in group 1 mostly opportunistic infections, not suggestive of SARS-CoV-2; group 2 lesions statistically associated with intubation and prolonged hospitalization ($p < 0.001$).
Pauli et al. 2021 (Brazil)	Histology showed ulcerated lesion with coagulative necrosis, hemorrhage, abundant neutrophils. Few studies linked COVID-19 with mucormycosis; post-mortem study found one case of disseminated mucormycosis.
Subramaniam et al. 2021	Nine patients (1.26%) reported oral discomfort; lesions included herpes simplex ulcers and angular cheilitis; only 9 of 713 COVID-positive patients expressed complaints.
Cruz Tapia et al. 2020	One patient's biopsy showed perivascular reactive lymphocytic infiltrate, capillary thrombosis, hemorrhage; lesions probably associated with COVID-19.
Kaygısız Yiğit et al. 2023 (Turkey)	Significant difference in R-PBL % and types in COVID group; both groups showed significant difference in DMFT index.
Louisa et al. 2024 (Indonesia)	Generalized gingivitis more frequent in non-COVID; generalized periodontitis more frequent in long COVID survivors. No evidence that long COVID increases periodontitis severity.
Gupta et al. 2024	Cytokine levels increased in patients with both COVID-19 and periodontal disease; MIG higher in periodontally healthy COVID-19-positive subjects ($P=0.01$).
Qin et al. 2023	Identified 1616 DEGs in periodontitis and 10,201 in COVID-19; nine shared transcription factors; increased plasma cells in both conditions; RT-PCR confirmed up-regulation of shared TFs in periodontitis.
Moradi Haghgoo et al. 2023	Lower white blood cell count associated with periodontitis severity; periodontitis-COVID interaction linked with increased WBC and decreased platelets.
Moradi Haghgoo 2023	Periodontitis severity correlated with COVID-19 severity ($P < 0.001$); generalized stage III/IV periodontitis increased odds for severe COVID-19 (OR 4.24); IL-6 in saliva/serum associated with severity; hospital stay length associated with periodontitis severity ($P=0.004$).
Poyato-Borrego et al. 2023	Decayed teeth number higher in severe COVID group (3.4 vs 1.4; $p=0.02$); regression showed association of decayed teeth and endodontic status with COVID-19 severity.
Costa et al. 2022 (Brazil)	Periodontitis linked to ICU admission, critical symptoms, death risk (IRR 1.44-2.56); Eichner index classes B and C associated with ICU admission.
Marie et al. 2023 (Italy)	No significant difference in IL-1β, IL-6, TNF-α between COVID patients with gingivitis/periodontitis and controls.
Fernandes Matuck et al. 2020 (Brazil)	SARS-CoV-2 detected in periodontal tissue (5/7 cases); histopathology showed keratinocyte alterations and nuclear pleomorphism.
Gardelis et al. 2022 (Switzerland)	Out of 87 patients, 30 evaluated clinically/radiographically; half classified as Stage III/IV periodontitis; 26.7% Grade C.
Natto et al. 2022	SARS-CoV-2 detected in 41.7% symptomatic positive with periodontal pockets, 16.7% with carious lesions; sensitivity and specificity varied for detection in periodontal pockets and lesions.
Jahagirdar et al. 2024	CRP elevation: minor 1%, moderate 3%, marked 31%, severe 65%; 96% had IL-6 levels >7; significant difference in IL-6 groups 0-7 range.
Brzychczy-Sroka et al. 2023	Poorer oral health in COVID groups; higher Veillonella, Tannerella, Capnocytophaga, Selenomonas; decreased Akkermansia in COVID groups.
Karimzadeh et al. 2023	Streptococcus and Klebsiella pneumoniae more frequent in COVID-19-positive group ($P=0.047$ and $P=0.036$).
Santos et al. 2022 (Brazil)	Lactoferrin and IgA decreased in COVID/post-COVID groups; IgM increased during acute infection compared to post-COVID ($p < 0.05$).

Table 7. Quality assessment of the selected studies/Risk of bias

Author and Year	Random selection in population	Defined inclusion/ exclusion criteria	Reported loss to fol-low-up	Validated measurements	Statistical analysis	Estimated potential risk of bias
Eduardo et al. 2022	Yes	Yes	Not reported	Yes	Yes	Moderate
Castilho et al. 2024	Yes	Yes	Not reported	Yes	Yes	Low
Prakash et al. 2024	No	Yes	No	Yes	No	High
Limongelli et al. 2024	No	Yes	No	Yes	No	High
Castro et al. 2024	No	Yes	No	Yes	No	High
Schwab et al. 2022	Yes	Yes	Yes	Yes	Yes	Low
Pauli et al. 2021	No	Yes	No	Yes	No	High
Subramaniam et al. 2021	Yes	Yes	No	Yes	Yes	Moderate
Cruz Tapia et al. 2020	No	Yes	No	Yes	No	High
Kaygısız Yiğit et al. 2023	Yes	Yes	Yes	Yes	Yes	Low
Louisa et al. 2024	Yes	Yes	Yes	Yes	Yes	Low
Gupta et al. 2024	No	Yes	No	Yes	Yes	Moderate
Qin et al. 2023	Yes	Yes	Yes	Yes	Yes	Low
Moradi Haghgoo et al. 2023	Yes	Yes	Yes	Yes	Yes	Low
Moradi Haghgoo et al. 2023	Yes	Yes	Yes	Yes	Yes	Low
Poyato-Borrego et al. 2023	No	Yes	No	Yes	No	High
Costa et al. 2022	Yes	Yes	Yes	Yes	Yes	Low
Marie et al. 2023	Yes	Yes	Yes	Yes	Yes	Low
Fernandes Matuck et al. 2020	No	Yes	No	Yes	No	Moderate
Gardelis et al. 2022	Yes	Yes	Yes	Yes	Yes	Low
Natto et al. 2022	Yes	Yes	Yes	Yes	Yes	Low
Jahagirdar et al. 2024	No	Yes	No	Yes	No	Moderate
Brzychczy-Sroka et al. 2023	Yes	Yes	No	Yes	Yes	Low
Karimzadeh et al. 2023	Yes	Yes	No	Yes	Yes	Low
Santos et al. 2022	Yes	Yes	Yes	Yes	Yes	Low

In the present review, the quality evaluation showed that 14 studies demonstrated a low risk of bias, 7 studies showed a moderate risk of bias, and 5 studies were classified as having a high risk of bias.

Discussion

Several studies have been published in the literature reporting on several late signs/symptoms frankly attributable, according to the authors, to manifestations of the post-COVID condition, including oral lesions, periodontitis, xerostomia, and alterations in the oral microbiota and biomarkers.

Common manifestations and nature of oral lesions

Multiple studies confirm the presence of oral lesions in patients with COVID-19 [6-13]. For example, Eduardo et al. reported that 16.9% of lesions observed were infectious, with a high prevalence of viral infections, mainly herpesvirus-related (15.7%) [5]as well as to describe the patient´s management in each case. Methods: Information about oral conditions and mechanical ventilation was collected from oral medicine records of COVID-19 patients in an ICU (n = 519. Similarly, Prakash et al. confirmed the presence of such lesions in COVID-19 patients, while Castilho et al. identified common symptoms, including xerostomia (dry mouth) and olfactory/gustatory dysfunctions [6, 7]a respiratory illness with a global impact on millions, has recently been linked to manifestations affecting various bodily systems, including the oral cavity. Studies highlight oral issues, like ulcers, blisters, and white patches, alongside olfactory and gustatory dysfunction, influencing an individual's quality of life. In this context, our study aimed to assess the frequency of oral lesions, olfactory and gustatory disorders, and xerostomia resulting from COVID-19. An observational study was conducted with 414 patients to evaluate the frequency of oral symptoms resulting from COVID-19. Patients were diagnosed with mild symptoms and evaluated through clinical examination of the oral cavity and a questionnaire to assess functional alterations. The findings showed that 139 out of 414 patients presented clinical manifestations, with oral lesions being the most prevalent (19.1%.

Limongelli et al. suggest that SARS-CoV-2 may persist in the oral mucosa after the acute phase of infection, potentially causing lesions [8]possibly involving the lungs, brain, kidney, cardiovascular and neuromuscular system, as well the persistency of taste dysfunction. Such symptoms develop during or after infection and continue for more than 12 weeks with pathogenesis related to virus persistency but variable by organs or systems. Materials and Methods: We recently observed six patients recovered from COVID-19 and with negative RT-PCR testing, showing oral mucosa lesions (mainly ulcers. Similarly, Cruz Tapia et al. argued that the infection could lead to various oral manifestations, possibly as a result of thrombus formation and vasculitis [13].

However, Schwab et al. express scepticism about a direct relationship between oral lesions and SARS-CoV-2. They consider it unlikely that these lesions are a direct manifestation of the virus or a marker of COVID-19 progression [10]. This perspective is also supported by Subramaniam et al., who did not identify any specific or characteristic oral lesions among the 713 COVID-positive patients studied [12].

According to Pauli et al., mucormycosis and other deep fungal infections should be considered as serious complications associated with SARS-CoV-2 infection. This underlines the importance of monitoring for fungal complications, particularly in patients with COVID-19 [11].

Finally, Castro et al. observe that oral lesions in COVID-19 patients usually appear after systemic symptoms, suggesting that these manifestations may be secondary to other pathological processes related to the infection [9].

These studies show that there is an association between COVID-19 and oral lesions, although the exact nature of this relationship remains debated. While some researchers interpret these lesions as direct or indirect manifestations of the infection, others highlight the absence of conclusive evidence for a causal link. The complexity of these oral manifestations therefore calls for further research to clarify their mechanisms and clinical implications.

Impact of COVID-19 on periodontitis

Kaygısız Yiğit et al. confirmed that the COVID-19 pandemic increased the incidence of periodontitis, suggesting that the health crisis could have adversely affected overall oral health [14]. This increase was particularly noticeable in survivors of long COVID, as observed by Louisa et al., although no increase in the severity of periodontitis was noted according to standard classification methods [15]as both long COVID and periodontal disease release similar proinflammatory cytokines such as Acute phase proteins, CRP, TNF-α, IL-1β, IL-2, IL-6, and IFN-γ. Purpose: This study aims to show periodontal-disease severity-frequency distribution in COVID-19 survivors with long COVID and in non-COVID-19 patients. Methods: Patients' secondary data in the Periodontics Clinic Faculty of Dentistry at Trisakti University Dental Hospital (n=40.

A bidirectional relationship exists between periodontitis and COVID-19 [16-20]. Moradi Haghgoo et al. have shown that the severity of periodontitis is associated with the severity of COVID-19, with higher levels of interleukin-6 (IL-6) in saliva and serum, which could explain some of the adverse events [19]. Costa et al. also observed an association between oral health issues, particularly periodontitis, and severe COVID-19 outcomes in hospitalized patients [21].

Gupta et al. proposed that periodontal disease might contribute to the cytokine storm

induced by COVID-19, amplifying the impact of the infection [16]. This point is corroborated by Marie et al., who found that IL-6 and TNF-□ levels were higher in patients with periodontitis and long COVID, suggesting a possible exacerbation of inflammatory responses [22].

Several studies have highlighted the presence of SARS-CoV-2 in oral tissues. Fernandes Matuck et al. [23] demonstrated the presence of the virus in the periodontal tissue of COVID-positive patients. Natto et al. have also detected the virus in periodontal pockets and carious lesions, although the sensitivity of this detection is low compared with other methods [23-25]. This may explain why Gardelis et al. found that half of patients with severe forms of COVID-19 requiring admission to an intensive care unit (ICU) also had severes [24].

Therapeutic and pathogenic implications

Qin et al. explored the interaction between periodontitis and COVID-19 pathogenesis, with particular attention to transcription factor (TF) expression and lymphocytes [17]and periodontitis is a risk factor. Periodontitis and COVID-19 probably have a relationship. Hence, this study aimed to identify the common molecular mechanism that may help to devise potential therapeutic strategies in the future.\nMATERIAL AND METHODS: We analyzed two RNA-seq datasets for differential expressed genes, enrichment of biological processes, transcription factors (TFs. These findings could offer potential targets for the treatment of both conditions.

These studies highlight a close interaction between COVID-19 and periodontitis, where each can influence the severity and progression of the other. Not only does COVID-19 appear to increase the incidence of periodontitis, but periodontitis may also worsen the infection by exacerbating the inflammatory response. The detection of SARS-CoV-2 in periodontal tissues suggests that these areas could serve as reservoirs for the virus, highlighting the importance of rigorous oral health management during the pandemic. These complex interactions require particular attention in the management of patients with COVID-19, especially those with periodontal disease.

Impact of COVID-19 on biomarkers

Jahagirdar et al. identified a notable correlation between COVID-19 infection and fluctuating biomarker levels. This observation suggests that the disease may lead to significant changes in the body's biological responses, possibly by disrupting the immune and inflammatory systems [26]. These biomarkers could serve as potential indicators for assessing the overall health status of COVID-19 patients.

Brzychczy-Sroka et al. found that SARS-CoV-2 infection was not the main factor affecting the composition of the oral microbiota. Instead, the use of antibiotic therapy played a decisive role [27] COVID-19 convalescents without antibiotic therapy (II. These results highlight the significant impact of medical treatments on altering the microbiota rather than the viral infection itself, which could have important implications for the oral care management of patients with COVID-19, particularly with regard to antibiotic prescription.

Bacterial colonisation

Karimzadeh et al. reported that higher rates of bacterial colonisation, particularly by *Streptococcus* and *Klebsiella pneumoniae*, were observed on removable dentures after COVID-19 infection [28]coinfections and even superinfections in the background of SARS-CoV-2 viral infection have been reported. Such bacterial and fungal strains may be colonized in different tissues and organs, including the oral cavity. Whether infection with COVID-19 could increase colonization of different bacterial strains on removable dental prostheses is unclear. Purpose: The purpose of this clinical study was to compare bacterial colonization on removable dental prostheses in patients with COVID-19, before versus after diagnosis. Material and methods: Two sex- and age-matched groups of complete-denture-wearing participants (N=60. This suggests that the infection may make oral surfaces more susceptible to bacterial colonization, thereby increasing the risk of secondary infections. Dentures, in particular, can become reservoirs for these bacteria, requiring special attention in terms of cleaning and disinfection.

Modification of the salivary immune barrier

Santos et al. demonstrated that SARS-CoV-2 modifies the salivary immune barrier. These alterations may compromise the oral cavity's primary defense against pathogens, making it more vulnerable to additional infections. This weakened immune barrier could also account for the heightened bacterial colonization reported by Karimzadeh et al. [28, 29]coinfections and even superinfections in the background of SARS-CoV-2 viral infection have been reported. Such bacterial and fungal strains may be colonized in different tissues and organs, including the oral cavity. Whether infection with COVID-19 could increase colonization of different bacterial strains on removable dental prostheses is unclear. Purpose: The purpose of this clinical study was to compare bacterial colonization on removable dental prostheses in patients with COVID-19, before versus after diagnosis. Material and methods: Two sex- and age-matched groups of complete-denture-wearing participants (N=60.

This review has a number of strengths and limitations. The limitations include the heterogeneity of the studies regardless of primary inclusion and exclusion criteria

for article selection for the present study. Also, differences in how data are reported and measured across studies could hinder accurate comparisons and synthesis of findings. Small sample sizes in several included studies further reduce the statistical power and generalizability of their findings. This heterogeneity suggests a potential benefit from future meta-analysis, which could provide a more precise estimate of the effect size and help reconcile discrepancies among the study findings.

Recommendations and Future Research

Future studies are needed to better understand the impact of COVID-19 on oral health. It is recommended to consider the evaluation of more standardized procedures to improve comparability across studies. Researchers should explore the long-term consequences of COVID-19 on oral health, including potential post-COVID oral complications and their impact on dental treatment planning. Preventive and therapeutic strategies, such as oral care protocols for COVID-19 patients, should be assessed to mitigate risks of oral complications and secondary infections. Furthermore, evaluating the effects of COVID-19 treatments on oral tissues could offer important information for clinical practice.

Conclusions

These studies reveal that COVID-19 infection has multidimensional effects on oral health. Fluctuations in biomarkers, changes in the oral microbiota due to antibiotic therapy, increased bacterial colonisation on dentures, and alteration of the salivary immune barrier are all consequences that can have important clinical implications. These findings underline the need for an integrated approach to managing the oral care of patients with COVID-19, taking into account not only the infection itself but also the treatments administered and the biological changes induced.

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