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Review Article

Oral Manifestations in Patients with COVID-19: A Systematic Review

Manifestaciones orales en pacientes con COVID-19: Una revisión sistemática

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Abstract

Introduction: This secondary study focuses on the question: What are the oral manifestations described in patients with COVID-19?

Objective: The aim of this review is to characterize oral manifestations reported in research on patients with COVID-19.

Methods: A systematic review was conducted focusing on COVID-19 oral manifestations. Research articles involving COVID-19 patients describing at least one oral manifestation were included. The search strategy was executed in databases such as PubMed, Scopus, and Web of Science. Detailed information on oral manifestations during the disease was extracted. The review used the STROBE tool to assess the risk of bias (RoB) and performed a descriptive data analysis.

Results: After analyzing 207 articles and eliminating duplicates, 10 studies were selected, revealing data from 2878 patients. The most common oral manifestations were changes in oral mucosa (21.1%), xerostomia (19.4%), and loss of taste (12.9%). Others, such as ulcers or blisters (5.0%), had lower incidence (< 5%). Less frequent manifestations included glossitis (0.9%), enanthema (0.1%), and difficulty chewing (0.2%), all less than 2% of the total studied patients.

Conclusions: Findings revealed that changes in oral mucosa, xerostomia, and loss of taste were the most frequent manifestations. Ulcers, dental pain, and less common symptoms like glossitis or enanthema occurred in a minority of cases. These results underscore the importance of recognizing a broad range of oral manifestations in COVID-19 patients to enhance early detection and clinical management of the disease.

Keywords: COVID-19/complications; oral manifestations/epidemiology; systematic review as topic; disease progression; xerostomia/etiology; loss of taste/etiology.

Resumen

Introducción: Este trabajo de revisión aborda la cuestión: ¿Cuáles son las manifestaciones orales descritas en pacientes con COVID-19?

Objetivo: El propósito es caracterizar las manifestaciones bucales referidas por investigaciones en pacientes con COVID-19.

Métodos: Se llevó a cabo una revisión sistemática centrada en las manifestaciones bucales del COVID-19. Se incluyeron artículos de investigación que involucraban a pacientes con COVID-19 y describían, al menos, una manifestación bucal. La estrategia de búsqueda se ejecutó en bases de datos como PubMed, Scopus y Web of Science. Se extrajo información detallada acerca de las manifestaciones orales presentes durante la enfermedad. La revisión utilizó la herramienta STROBE para evaluar el riesgo de sesgos y realizó un análisis descriptivo de los datos.

Resultados: Después de analizar 207 artículos y depurar los duplicados se seleccionaron 10 estudios que revelaron los datos de 2878 pacientes. Las manifestaciones bucales más comunes fueron: cambios en la mucosa oral (21,1 %), xerostomía (19,4 %) y pérdida del gusto (12,9 %). Otras, como úlceras o ampollas (5,0 %), presentaron menor incidencia (< 5 %). Las manifestaciones menos frecuentes incluyeron glositis (0,9 %), enantema (0,1 %) y dificultad para masticar (0,2 %), todas con menos del 2 % del total de pacientes estudiados.

Conclusiones: Los hallazgos destacan que los cambios en la mucosa oral, la xerostomía y la pérdida del gusto fueron las manifestaciones más frecuentes. Por otro lado, las úlceras, el dolor dental y síntomas menos comunes, como glositis o enantema, se presentaron en una minoría de casos. Estos resultados resaltan la importancia de reconocer una amplia gama de manifestaciones bucales en pacientes con COVID-19 para mejorar la detección temprana y la gestión clínica de la enfermedad.

Palabras clave: COVID-19; manifestaciones bucales; revisión sistemática; progresión de la enfermedad; xerostomía; pérdida del gusto.

Introduction

The COVID-19 pandemic has had a significant impact on global public health, sparking considerable interest in understanding its clinical manifestations. [1,2,3] Among these manifestations, those related to the oral cavity have emerged as a crucial area of

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study.[1,2,4,5,6] In this context, the undertaking of a systematic review addressing the oral manifestations of COVID-19 stands as a fundamental contribution to better comprehend this disease and its impact on oral health, driven by the research question: What are the oral manifestations described in patients with COVID-19?

Oral manifestations associated with COVID-19 infection have garnered growing interest in the scientific community. Despite the primary focus of research being on respiratory and systemic symptoms, it is crucial to recognize that the oral cavity may serve as a site for early and specific disease manifestations. Therefore, understanding and characterizing these oral manifestations are essential for a comprehensive assessment of the disease and the development of effective diagnostic and treatment strategies.[7,8]

In addressing this topic, a comprehensive insight into oral manifestations associated with SARS-CoV-2 infection is sought to contribute to current scientific knowledge and informed clinical decision-making. The aim is to identify and describe the most common oral manifestations in COVID-19 patients, including lesions in the oral mucosa, taste disturbances, symptoms on the tongue, gums, and other oral structures. Furthermore, the need for broad knowledge of the prevalence of these manifestations, their clinical presentation, their relationship to disease severity, and their potential utility as early diagnostic markers has been emphasized.[4,5,6]

This systematic review is grounded in the necessity to consolidate existing knowledge about the oral manifestations of COVID-19, intending to provide a robust foundation for future research and guide clinical practice and public health policies. By addressing this topic, a significant contribution is anticipated towards a comprehensive understanding of the disease, as well as the identification of potential strategies for prevention, diagnosis, and treatment in the context of oral health.

Considering all the aforementioned points, the objective of this review was to characterize the oral manifestations reported in research on patients with COVID-19.

Methods

A systematic review was conducted from November to May 3, 2022, at the Faculty of Medical Sciences Victoria de Girón of the University of Medical Sciences of Havana, Cuba. The guide employed for the execution of this research was the PRISMA guide.

Inclusion criteria

1. Research articles in any language involving human participants observed or surveyed.
2. Participants testing positive for COVID-19 via Polymerase Chain Reaction (PCR) test.
3. Manifestations described during the period when participants had latent infection.
4. Articles describing at least one oral manifestation in patients during COVID-19 illness.
5. Surveys-based works with or without of an examination to verify oral manifestations.

Exclusion criteria

1. Any type of review articles.
2. Studies with methodologies that did not include PCR-positive patients.
3. Other articles not of the original type and based on human studies.

Search strategy

The search was conducted through PubMed, Scopus, and Web of Science (WOS) databases. MeSH keywords, including “covid”, “oral manifestation”, “oral sign”, and “oral symptom”, with respective wildcards, were used and had to appear in the title of each selected article.

Search formulation

- PubMed (49 results): (covid*[Title]) AND ((oral manifestation*[Title]) OR (oral sign*[Title]) OR (oral symptom*[Title])).
- Scopus (79 results): TITLE ((covid*) AND (oral AND (manifestation* OR sign* OR symptom*))).
- WOS (79 results): TI=((covid$) AND (oral AND (manifestation$ OR sign$ OR symptom$))).

Article selection

An initial filtering of titles and abstracts was conducted, identifying the presence of keywords. Selected studies were managed with EndNote version 21 to identify duplicates. Full texts were reviewed to identify studies meeting selection criteria, involving two independent evaluators and a third in case of discrepancies, using Rayyan as a platform.

Data extraction

Information on author, country, study type, number of subjects, and the percentage of individuals with oral manifestations during COVID-19 latency was collected. Specific manifestations included changes in oral mucosa, lingual papillitis, lingual inflammation, aphthous stomatitis, burning mouth, mucositis, glossitis, white

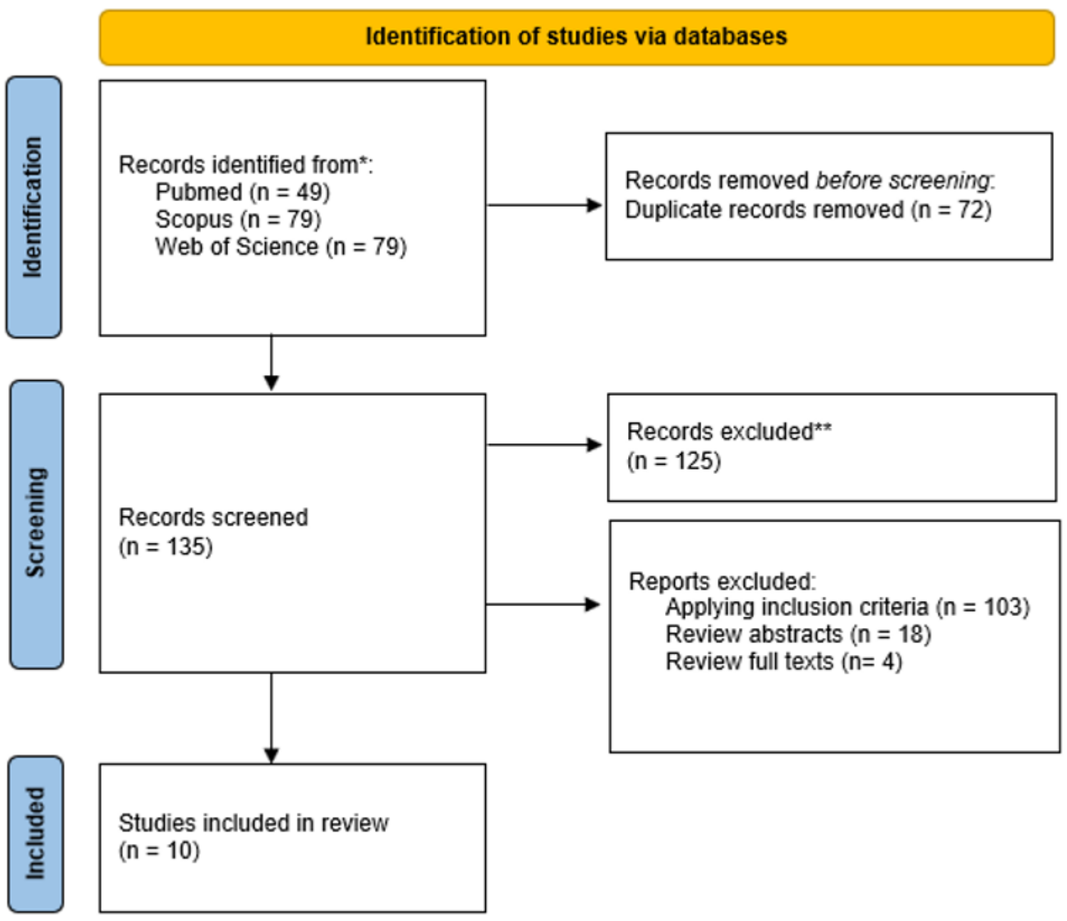
tongue (candidiasis), enanthema, loss of taste, erythematous or desquamative gingivitis, coated tongue, ulcers or blisters, xerostomia, difficulty swallowing, chewing difficulties, gum bleeding, dental pain, temporomandibular joint pain, and halitosis.

Data analysis

Descriptive analysis was performed using IBM SPSS for Windows version 26, reporting minimum and maximum values for quantitative variables, and frequencies for qualitative variables.

Results

The flowchart (fig. 1) illustrates that the initial search yielded a total of 207 articles, which, after duplicate removal, narrowed down to 135. Subsequently, researchers conducted article selection based on titles, abstracts, and full texts, applying inclusion and exclusion criteria, resulting in a final set of 10 articles (table 1) included for data extraction.



Source: Author's property.

Fig. 1 *– Flowchart of the search result. PRISMA flow diagram for new systematic reviews.*

Table 1 *- Distribution of oral manifestations in the included studies and their percentile values relative to the total*

S	SA	COM	LO	IT	AS	BM	M	G	WT(C)	E	TL	E/DG	CT	U/B	X	DS	DC	GB	T	TMJ* pain	H
1[9]	666	78	77	44	46	35	26	26	11	3											
2[10]	109										47	8	8	7							
3[11]	55	43				20			2	1	33			2	15						
4[12]	713													9							
5[6]	217	37				44					78				93						
6[5]	100					4								10	44	16	7	6			
7[13]	573	411												117	273				132	69	60
8[1]	367										188	57			103						
9[14]	58	39	3								20				23			4			
10 [15]	20					3					5				6	4					
T(n)	2878	608	80	44	46	106	26	26	13	4	371	65	8	145	557	20	7	10	132	69	60
Total (%)		21,1	2,8	1,5	1,6	3,7	0,9	0,9	0,5	0,1	12,9	2,3	0,3	5,0	19,4	0,7	0,2	0,3	4,6	2,4	2,1

Legend: S: Study; SA: Sample; COM: Changes in oral mucosa; LO: Lingual papillitis; IT: Inflamed tongue; AS: Aphthous stomatitis; BM: Burning mouth; M: Mucositis; G: Glossitis; WT (C): White tongue (Candida); E: Enanthema; TL: Taste loss; E/D G: Erythema/desquamative gingivitis; CT: Coated tongue; U/B: Ulcers/blisters; X: Xerostomia; DS: Difficulty swallowing; DC: Difficulty chewing; GB: Gingival bleeding; T: Toothache; *Temporomandibular joint (TMJ); H: Halitosis; T (n): Total.

Source: Author's property.

From these studies, data were collected from 2878 participant patients. Among the most prevalent oral manifestations, notable figures include changes in oral mucosa (21.1%), xerostomia (19.4%), loss of taste (12.9%), ulcers or blisters (5.0%), dental pain (4.6%), burning mouth syndrome (3.7%), lingual papillitis (2.8%), temporomandibular joint pain (2.4%), and halitosis (2.1%) (table 1).

Other oral manifestations presented an incidence lower than 2% of the total, including inflamed tongue (1.5%), aphthous stomatitis (1.6%), mucositis (0.9%), glossitis (0.9%), white tongue (0.5%), enanthema (0.1%), coated tongue (0.3%), difficulty swallowing (0.7%), difficulty chewing (0.2%), and gingival bleeding (0.3%) (table 1).

The studies included in this review were published in a variety of journals between 2020 and 2022. The study by Villarroel-Dorrego and others covered the largest age range, including participants from 1 to 89 years old. However, some studies lacked specific details on the ages and genders of the participants (table 2).

Table 2 *- Characteristics of the ten included primary studies*

Authors	Title	Year	Journal	Research classification	Age Range	Sample	Female	
							#	%
Nuño González and others[9]	Are Oral Mucosal Changes a Sign of COVID-19? A Cross-Sectional Study at a Field Hospital	2021	Actas Dermosifiliogr (Engl Ed)	Cross-Sectional	Not declared	666	N/D	
Natto and others[10]	Characteristics of Oral Manifestations in Symptomatic Non-Hospitalized COVID-19 Patients: A Cross-Sectional Study on a Sample of the Saudi Population	2021	Int J Gen Med	Cross-sectional	Not declared	109	N/D	
Villarroel-Dorrego and others[11]	Oral Findings in Patients With COVID-19	2022	Actas Dermosifiliogr	Cross-sectional	1- 89	55	25	45.5
Subramaniam and others[12]	Oral manifestations among COVID-19: An observational study of 713 patients	2021	Dent Res J (Isfahan)	Observational	12- 80	713	297	41.7
Chawla and others[6]	Oral manifestations associated with COVID-19 disease: An observational cross-sectional study	2022	J Oral Biol Craniofac Res	Cross-sectional	18- 60	217	62	28.6
Muthyam and others[5]	Oral manifestations in COVID-19 patients: An observational study	2022	J Family Med Prim Care	Cross-sectional	Defined by > or < than 35 years old	100	49	49%
Abubakr and others[13]	Oral manifestations in mild-to-moderate cases of COVID-19 viral infection in the adult population	2021	Dent Med Probl	Survey	19- 50	573	408	71.2
Ganesan and others[1]	Oral Manifestations of COVID-19 Infection: An Analytical Cross-Sectional Study	2022	J Maxillofac Oral Surg	Analytical Cross-Sectional	53,46 ± 17,50	367	133	36.2
El Kady and others[14]	Oral manifestations of COVID-19 patients: An online survey of the Egyptian population	2021	Clin Exp Dent Res	Survey	18- 46	58	27	46.6
Sinjari and others[15]	SARS-CoV-2 and Oral Manifestation: An Observational, Human Study	2020	J Clin Med	Survey	Not declared	20	N/D	

Legend: N/D- Not declared.

Source: Author's property.

Discussion

To ensure the validity of this review, it was crucial that patients included in the studies reported positive results for COVID-19, which would help reduce associative bias with the described manifestations. Although this research did not focus on making statistical associations, other researchers are encouraged to thoroughly explore this possible relationship. Examples, such as the study by Aragoneses and colleagues,[16] suggesting a certain association between COVID-19 and xerostomia, find support in our investigation, where it was observed

that this manifestation was one of the most frequent.

The prevalence of oral manifestations in patients with COVID-19 revealed in this study largely aligns with previous findings, highlighting the frequency of changes in oral mucosa, xerostomia, and loss of taste as the most common symptoms.[4,16,17,18,19,20,21] Comparable research has also identified changes in oral mucosa and xerostomia as prominent manifestations. For instance, a study by Halboub and others[9] showed a prevalence for changes in oral mucosa and xerostomia in COVID-19 patients close to our findings. Furthermore, the loss of taste has been consistently reported as a significant manifestation in multiple studies,[1,4,11,19,22,23,24] coinciding with the results of this investigation.

Despite these similarities, subtle differences have been observed in other studies. For example, while our analysis showed a low incidence of ulcers or blisters, some previous studies have reported an even lower frequency.[17,25] Moreover, the prevalence of less common symptoms such as dental pain and burning mouth syndrome in our sample may vary compared to other studies that have recorded slightly higher or lower rates for these specific symptoms.[26,27,28]

These discrepancies can be attributed to differences in the study population, inclusion/exclusion criteria, assessment methods, and the variability in the clinical presentation of COVID-19 in different geographic regions and time periods.

Previous research suggests the tongue, labial mucosa, and palate are the primary sites for oral lesions.[29] However, data from the current review indicate variations, with the tongue and palate showing differing patterns of lesion localization. Participant ages in the reviewed studies ranged from infants to the elderly. Older adults and individuals with severe COVID-19 presented with a higher incidence of more extensive and pronounced oral lesions.[30,31,32]

Collectively, our results align with the general trend in existing scientific literature,[33,34,35] reinforcing the importance of recognizing these oral manifestations as relevant clinical signs in patients with COVID-19, emphasizing the need for a comprehensive and standardized assessment of these symptoms for better clinical management of the disease.

Conclusions

The conclusions indicate that, after analyzing data from 2878 individuals in 10 studies, the most frequent oral manifestations in patients with COVID-19 were changes in oral mucosa, xerostomia, and loss of taste. On the other hand, ulcers, dental pain, and less common symptoms such as glossitis or enanthema were presented in a smaller proportion. These findings underscore the importance of recognizing various oral manifestations in COVID-19 patients, emphasizing the need for early detection and more effective clinical management of the disease.

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Conflict of interests

Authors declare no to have any conflict of interests.

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