Taste and smell as chemosensory dysfunctions in COVID-19 infection

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Abstract: Purpose: To review the literature on the presence of two clinical manifestations in patients presenting COVID-19 (SARS-CoV-2) infection: loss of taste (ageusia) and loss of smell (anosmia). **Methods:** PubMed and EMBASE were searched and studies were selected starting from November, 2019 until April 2020; also, the references of the selected articles were evaluated for methodological quality. **Results:** Of the 19 studies analyzed, five were included to evaluate the presence of ageusia and/or anosmia as symptoms in patients who were tested and resulted positive for the SARS-CoV-2 virus. In a total of 10,818 patients, 8,823 presented ageusia (81.6%; range 5.6%-88%) and 8,088 presented anosmia (74.8%; range 5.1-85.6%). Only one study recorded both symptoms with a percentage of 18.6%. (*Am J Dent* 2020;33:135-137).

Clinical significance: This systematic review demonstrated significant presence of ageusia and anosmia in the patients with COVID-19 infection. These symptoms may be considered as the first manifestation of the infection.

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Introduction

Since December 2019, a cluster of pneumonia infections appeared in Wuhan, China. The number of infected people in the pandemic known as COVID-19, for which the SARS-CoV-2 virus is responsible, continues to increase quickly all over the world.[1] After a median incubation period of 3 days, the main clinical symptoms of the infection were described to be fever, cough and fatigue, with some of these patients also developing conjunctivitis as a consequence of the virus spreading to the ocular surface. Patients with increased acute respiratory distress syndrome (ARDS) develop the symptoms in 9 days. Patients with comorbidities, such as hypertension, diabetes and obesity, are more likely to get infected. Clinical observations show that alteration in taste (ageusia) and smell (anosmia) could potentially be related to the COVID-19 infection at early onset.[2] Two studies[3,4] showed a significant increase in new onset of anosmia compared to before COVID-19 appearance. However, it is impossible to determine if these alterations of taste and smell are certainly COVID-19 related or just related to more common recognition of post-viral taste and smell; the frequency that those symptoms may occur has not been determined. The identification of taste and smell loss as an early clinical sign of COVID-19 infection can be vital, because if demonstrated, it could then be possible to isolate the infected patients before they become asymptomatic carriers spreading the disease.

Materials and Methods

Focused question - This review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.[5] The main question to answer was: "can ageusia and anosmia be considered as common clinical manifestations in all or in most of the patients presenting COVID-19?"

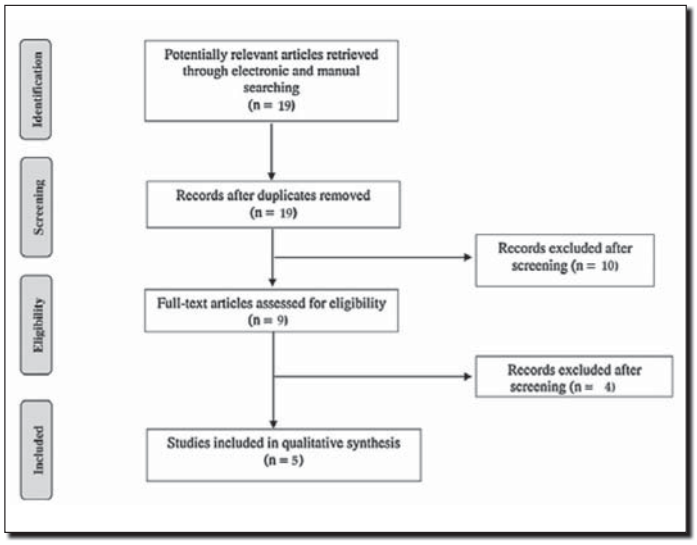

Figure. Study selection process and results of the literature search (PRISMA flow diagram).

Selection criteria - The titles for potential articles of interest were evaluated (Figure). For the studies to be included, they had to fulfill the following criteria:

1. Population: The study sample had to be of patients affected by the COVID-19 infection;
2. Clinical manifestations: Manifestations of the infection were recorded and the number of patients or percentage of patients presenting ageusia and/or anosmia were recorded;
3. Study design: Only studies written in English were included in the review.

Studies on animals, letters to editors, review articles, and unpublished abstracts were excluded.

Search strategy - The research was made using electronic data-bases including MEDLINE and EMBASE, considering articles from November 2019 until April 2020. The literature search

Table. General description of the included studies.

Investigators	Country	Number of patients included	Patients with ageusia N (%)	Patients with anosmia N (%)	Patients with both ageusia & anosmia N (%)
Mao et al.[6]	China	214	12 (5.6%)	11 (5.1%)	
Giacomelli et al.[3]	Italy	59	6 (10.2%)	3 (5.1%)	11 (18.6%)
Yan et al.[7]	United States	59	42 (71%)	40 (65%)	
Lechien et al.[4]	France	417	367 (88%)	357 (85.6%)	
Bagheri et al.[8]	Iran	10,069	8,396 (83.4%)	7,677 (76.4%)	

was conducted using the combinations of the following Medical Subject Heading (MeSH) and text words: (COVID-19 OR SARS-COV-2 OR COVID) AND (taste OR smell) AND (ageusia OR anosmia OR loss).

Screening methods and data abstraction - After the title and abstracts of the studies were screened, the inclusion criteria were analyzed and evaluated. Data were extracted from the included studies following these parameters: author/country, number of patients included and/or number of patients and/or percentage of patients presenting taste and/or smell symptoms.

Results

Study selection - After the initial search based on title and abstract, 19 studies were selected. No duplicates were found. Examining the abstracts, 10 articles were excluded because they were not relevant to the objective of the review. Of the nine full-text studies that were selected, four were eliminated because they did not follow the inclusion criteria. Therefore, only five studies[3,4,6-8] were included. All included studies were conducted in health care centers or university hospitals. The Table shows a diagram of the study selection process and results of the literature search according to the PRISMA guidelines.[5]

General characteristics of included studies - The origins of the included studies were China, Italy, United States, France and Iran.[3,4,6-8] In these studies, the number of patients presenting alteration or absence of taste (ageusia) and smell (anosmia) was recorded. Except for one study,[8] all other studies presented less than 500 patients. Only one study[3] reported the presence of patients with both alterations of taste and smell; in all the other studies just one of those alterations was considered or recorded; even if analyzing the symptoms, it seems possible that more patients presented both conditions[3,7,8] (Table). A meta-analysis of the studies was not performed in this review due to the methodological heterogeneity, such as study groups, age of the patients and level of the infection. Thus, the outcomes are reported as a narrative review.

Main outcomes of the studies - In all the analyzed studies, the presence of ageusia and/or anosmia in patients COVID-19 positive was reported. A total of 10,818 patients was analyzed, of which 8,823 presented ageusia (81.6%; range 5.6%-88%) and 8,088 presented anosmia (74.8%; range 5.1%-85.6%). Only one study[3] reported the presence of both conditions in the sample examined (11 out of 59 patients; 18.6%).

Discussion

This systematic review evaluated the clinical manifestations of taste and smell alterations as common symptoms of infection of the COVID-19 SARS-CoV-2 virus. Anosmia was reported as a manifestation in severe acute respiratory syndrome (SARS) and other coronavirus infections,[9,10] but in only a few cases. Being able to identify those symptoms as COVID-19-related could help in the early diagnosis of the infection. With the rapid progression of this pandemic, obtaining accurate information in a short time on the symptoms and progression of those symptoms can make the difference between life and death. In this review, it seems clear that ageusia and anosmia are present in COVID-19 infected patients in a significant percentage (81.6% and 74.8% for ageusia and anosmia, respectively). Also, in those patients, the conditions did not present nasal obstruction or other rhinitis symptoms. This could be important to perform a correct differential diagnosis in subjects at risk. In many patients, ageusia and anosmia often represent the only symptoms or the earliest symptoms, so it is important to perform an olfactory and gustatory test. This is also recommended for COVID-19 positive patients, to qualitatively estimate the severity of the sensory alteration. Moreover, in one study,[3] the differences of chemosensory dysfunction in patients presenting COVID-19 with patients without COVID-19 reported ageusia and anosmia in 68% and 71%, respectively of patients presenting COVID-19, instead of 16% and 17% of patients without COVID-19 ($P< 0.001$). While ageusia and anosmia were strongly associated with the COVID-19 infection, sore throat was more frequently found in patients who were negative to the COVID-19 infection. In the patients presenting anosmia, suspected to be caused by COVID-19, 74% completely healed from the alteration of smell with the elimination of the viral infection, demonstrating beyond any reasonable doubt that the COVID-19 infection is a trigger for those conditions. Therefore, ageusia and anosmia can be used as clinical symptoms to make a diagnosis of the infection or at least to suspect it.

Another aspect evaluated by one study[4] was the number of cigarettes smoked by the patients; there were non-smoker patients (361 patients, 86.6% of the total sample); mild smoker patients (1-10 cigarettes daily, 40 out of 417, 9.6%); moderate smoker patients (11-20 cigarettes daily, 16 out of 417, 3.8%) with no heavy smoker patients (> 20 cigarettes daily). So, although almost all the patients were non-smokers or light smokers, the problems related to chemosensory dysfunctions was reported being very common, since 367 patients (88%) had ageusia and 357 patients (85.6%) had anosmia, values similar with all the analyzed studies. The present review did not include the evaluation of smoking as a risk factor due to the small number of smokers included in the studies.

A limitation of this review was the unavailability of the ages of the patients included and the fact that in only one study[3] the presence of both ageusia and anosmia was recorded. More studies, with a larger number of patients pre-

senting both ageusia and anosmia diseases, is recommended. However, based on the results of the studies included in this review, it is possible that the COVID-19 infection may cause ageusia and/or anosmia; therefore, those conditions could be used as criteria to diagnose the infection.

This systematic review demonstrated the presence of ageusia and anosmia in multiple cases of patients presenting COVID-19 infection, making the presence of those symptoms important to suspect the possibility of the patient being infected by the SARS-CoV-2 virus, as reported in other studies.[11-14] Therefore, it could be recommended to include these symptoms and related outcomes to those conditions in the protocol for the management of COVID-19 infected patients during dental emergencies[15-17], as a preventive measure to stop the spread of the infection. During the telephone triage, the patients should be asked if they have experienced a sudden onset of an altered sense of taste or smell in the 2 weeks before performing the Sino-nasal Outcome Test 22 (SNOT-22)[18]. If the patients have experienced loss of taste and/or smell, they could be referred for COVID-19 testing.

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