ORIGINAL ARTICLE



Should anosmia and dysgeusia be a concern for oral and maxillofacial surgeons during the COVID-19 pandemic?

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Abstract

Purpose Dysgeusia and anosmia have been liked to COVID-19 infection. The aim of this study is to study the prevalence of dysgeusia and anosmia in COVID-19 patients treated at the University of Florida Health Center and establish the odds of having an olfactory and gustatory disorder with a confirmed COVID-19 infection.

Methods This is a retrospective cross-sectional study utilizing the University of Florida Health Center patients' registry i2b2 platform to search for ICD 10 diagnoses of COVID-19 infection and taste and smell disturbances. We assessed the odds ratio for patients with dysgeusia and anosmia having a laboratory-confirmed COVID-19 infection using a logistic regression model adjusting for gender, race, age, and comorbidity conditions. P < 0.05 was deemed significant.

Results Out of 889 individuals that tested positive for COVID-19, 12.88% were diagnosed with taste and smell disturbances. The odds ratio for COVID-19 for people with dysgeusia and anosmia was 39.107. After adjusting for sex, age, and race, it was 41.9, 37, and 34.2, respectively.

Conclusion Taste and smell disturbances in COVID-19 are not anecdotal. It is paramount that oral and maxillofacial surgeons include taste and smell disturbances in the history and physical examination as these symptoms are suspicious of active COVID-19 infection. Patients presenting with an olfactory and gustatory disorder should undergo further evaluations for COVID-19 infection and oral and maxillofacial surgeons should enhance the personal protective equipment used when treating these patients to prevent further spread of the infection and protect other healthcare members.

Keywords COVID-19 · Dysgeusia · Anosmia · Taste disturbance · Smell Disturbance

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Introduction

The outbreak of novel coronavirus (COVID-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infected disease began in Wuhan, Hubei Province, China, in December 2019 [1]. Two months later, In February 2020, the World Health Organization named the disease as a novel coronavirus COVID-19. Since then, the disease has spread globally and become a pandemic with an urgent threat to global health and a massive impact on economic stability [2].

Human to human transmission of SARS-CoV-2 has been confirmed [3], through the infected fluid droplets secreted by infected individuals' respiratory system.

Studies showed that physicians could be at risk of COVID-19 infection [4, 5]. Oral and maxillofacial surgeons, especially, are at increased risk of COVID-19 infection. This profession requires close contact with the patients during physical examinations, especially given the high risk of

encountering aerosolized viral particles while using instruments to examine and treat the oral cavity.

Therefore, it is crucial to identify high predictive signs and symptoms, where it could be used as a diagnostic tool for COVID-19 and diagnose the disease earlier, especially in asymptomatic patients with only dysgeusia and anosmia, thus, cutting off the route of transmission and protecting the physicians.

The most common clinical findings of confirmed cases of COVID-19 are those associated with lower respiratory tract infection, including fever, cough, shortness of breath, and abnormal chest CT. Other common symptoms include myalgia, tiredness, stomach pain, nausea, diarrhea, and vomiting. Recent studies have also shown that COVID-19 patients may develop neurologic symptoms, which may range from major events like impaired consciousness, acute cerebrovascular diseases, skeletal muscle injury, or minor effects like dysgeusia and anosmia [6–8].

Multiple reports have been published about the prevalence of dysgeusia and anosmia among COVID-19 patients since the pandemic started [9–23]. The incidence of loss of smell in COVID-19 patients varied widely among these studies, ranging from 33.9% to 68% [16]. In some cases, anosmia was the only symptom of COVID 19 [24].

The aim of this study is to study the true prevalence of dysgeusia and anosmia in COVID-19 patients and determine if this association should be a concern for oral and maxillofacial surgeons during the pandemic as it could be a clue for the diagnosis of COVID-19?

If the results shows a significant association between dysgeusia and anosmia in COVID-19, then oral and maxillofacial surgeons should be informed and educated about the importance of including taste and smell disturbances in the history and physical examination as dysgeusia and anosmia could be a clue for the diagnosis of COVID-19.

Material and methods

In this retrospective cross-sectional study, we used the University of Florida (UF) Health Office of the Chief Data Officer i2b2 platform and the UF Integrated Data Repository (IDR) which is a large-scale database used to collect, store, and report on information from across UF Health's clinical and research enterprises. Patients' protected health information has been de-identified. For this reason, this study was exempt from approval by the IRB. Data were collected from June 2015 to April 2020. The study population was obtained from the outpatient and inpatient episodes of care at UF Health Centers across Florida. The subjects were selected utilizing the tenth edition of the International Classification of Diseases (ICD-10) and they had a diagnosis of COVID-19 (ICD 10-R43) and Disturbances of Smell and Taste (ICD 10-R43). The total patient population visiting the different departments and the IDR provided their age and sex distribution. The prevalence ratios were used to compare rates between groups. Health Office of the Chief Data Officer provided the analytic data set, and the odds ratio (OR) for the association was calculated by logistic regression using SAS statistical software. The 95% confidence interval (CI) and *P*-value for each OR were tabulated. *p* < 0.05 was deemed significant.

Results

A total hospital population of 987,849 attended the different UF Health centers across Florida in the period from June 2015 to September 2020 was included in this study. Of these, 1324 cases had taste and smell disturbances. A total of 889 individuals tested positive for COVID-19.

In this subset, 12.88% tested positive for COVID-19 were also diagnosed with loss of taste and smell by their physicians.

Table 1 demonstrates the patient's characteristics and demographics between the three groups in our study: (1) control, (2) all COVID-19 patients, and (3) patients with loss of smell and taste, and COVID-19. Out of the 889 confirmed COVID-19 patients, 114 patients had taste and smell disturbances, of which 59 were female and 55 males. Within the COVID-19 group, 45% were White population, and 25.6% were African American, while in the group of patients with both COVID-19 and taste and smell disturbances, 60% were White, and 17.7% were African American. Based on the age, 39.9% from the COVID-19 were at the age group 18–34 years while 68.8% of the patients with both COVID-19 and taste and smell disturbances lies within the age group 18-34 years.

The odds ratio for having COVID-19 for people with taste and smell was 39.107 before adjustments. After adjusting for sex and age, and race, it was 41.9, 37, and 34.2, respectively.

The OR for taste and smell disturbances after adjustment for comorbidities, diabetes, respiratory diseases, cardiovascular, and obesity was 31.4, 13.4, 24.6, and 24.0, respectively (Table 2).

Discussion

The aim of this study is to study the prevalence of dysgeusia and anosmia in COVID-19 patients and to establish the odds of having an olfactory and gustatory disorder with a confirmed COVID-19 infection.

In this study, we found that the odds ratio for having COVID-19 in people with taste and smell disturbances was 39.107, which is a significantly higher number compared

Table 1 Patients characteristics and demographic between control, COVID-19, and loss of smell and taste in COVID-19 patient groups

	COVID-19 with taste and smell disturbances	COVID-19 patients	Hospital Population	
Total population	114	889	987,849	
Female	59	509	532,391	
Male	55	386	455,458	
Female/male	1.07	1.32	1.16	
African American, %	17.7%	25.6%	11.3%	
Asian, %	0	2.8%	1.9%	
White	60%	45%	50%	
Ages 0–9	0	1.9%	9.2%	
Ages 10-17	2	2.47%	6.7%	
Ages 18-34	68.8	39.9%	21.5%	
Ages 35–44	20%	11.1%	9.6%	
45–54	4.2	1.2%	10.8%	
55-64	3	11.2%	15.6%	
65–74	1	12.3%	14.6%	
74–85	1	6.5%	8.5%	

to a study by Menni et al. [13] which reported OR of 6.59 for anosmia and ageusia and by Yan et. al. [14] which reported 10.9 for anosmia and 11.9 for ageusia.

Table 2 Odds ratio with and without adjustments for age, sex, race, and comorbidities

	Odds ratio	95% Wald limits	95% Wald confidence limits	
Taste vs. non-taste ¹	39.107	27.367	55.885	< 0.0001
Taste vs. non-taste ¹	41.852	30.411	57.598	< 0.0001
Male vs female	0.847	0.735	0.976	0.022
Taste vs. non- taste ²	37.239	26.035	53.265	< 0.0001
Age 18–34 vs 0–17	6.565	4.658	9.251	< 0.0001
Age > 34 vs 0–17	3.156	2.249	4.427	0.0343
Taste vs. non-taste ³	34.48	24.323	48.881	< 0.0001
Race Black vs. White	2.683	2.28	3.157	< 0.0001
Race other vs. White	1.13	0.965	1.323	< 0.0001
Taste vs. non-taste ⁴	13.744	9.582	19.714	< 0.0001
Respiratory vs. non-respiratory	8.358	7.268	9.611	< 0.0001
Taste vs. non-taste ⁵	20.947	14.58	30.094	< 0.0001
Endocrine vs. non-endocrine	3.865	3.38	4.419	< 0.0001
Taste vs. non-taste ⁶	24.043	16.7	34.615	< 0.0001
Obese vs. non-obese	5.31	4.564	6.177	< 0.0001
Taste vs. non-taste ⁷	31.407	21.872	45.099	< 0.0001
Diabetes vs. non-diabetes	3.051	2.51	3.707	< 0.0001
Taste vs. non-taste ⁸	24.636	17.144	35.404	< 0.0001
Circulatory vs. non-circulatory	2.951	2.571	3.388	< 0.0001
Taste vs. non-taste9	39.451	27.569	56.454	< 0.0001
Smoke vs. never	0.954	0.804	1.131	0.5872

Model marked with * is a raw model evaluate the association between COVID-19 status with taste and smell without adjusting for any covariate

Models 1, 2, 3, 4, 5, 6, 7, 8, and 9 have been adjusted for gender, race, age, respiratory disease, endocrine, obesity, diabetes, circulatory disease, and smoking one at a time

When adjusted for race, we found that the odds ratio of having COVID-19 for people with loss of taste and smell was 34.2 of the odds for people without taste and smell. Among this subcategory, we found that African Americans had the highest odds (OR: 2.683) of having COVID-19. Also, when we compared the African American ethnicity between the hospital population group and the COVID-19 patient group, we found a significant difference between the two groups, 11.3% among the hospital population group while 25.6% among the COVID-19 patient group. Our explanation for this finding is mainly due to the low socioeconomic status and difficulty accessing care among this patient population. Very few reports have looked into different race groups and the incidence of taste and smell disturbances among COVID-19 patients (Table 3). A study conducted by 12 European hospitals showed the number of COVID-19 patients being predominantly of European race (93%), followed by South American (2.7%), Sub-Saharan African (2.2%), and African Americans (1.4%). However, they did not correlate the association between race and loss of taste and smell in COVID-19 patients [17].

After adjusting the odds ratio for age, we found the odds for having COVID-19 for people with loss of taste and smell was 37 times the odds for people without loss of taste and smell.

Interestingly, most affected individuals were in the age group between 18-34 years (OR: 8.748). This finding is similar to a study conducted by Lee et al. [19]. This could indicate that this segment of the population, for some reason, is more susceptible to the neurotoxic effect of the virus on the chemoreceptors. When OR was adjusted for gender, we found no significant difference between males and females. This is in contrast to a study by Lee et al. [19], which showed that among COVID-19

First authors	Country	Diagnosis methods	Sample size	Prevalence of OS and GS	Mean age	Female proportion	Most common associated comorbidities	Race
Dell' Era V [9]	Italy	Questionnaire/ self-reported	355	70%	49 OS 51 GS	48.5% OS 47.4% GS	CVS (31%) in OS group CVS and res- piratory 30% each in the GS group	Unknown
Vaira LA [10]	Italy	Objective	72	73.6%	49.9*	62.5% *	Pneumonia 30%*	Unknown
Lechien J [17]	European countries	Questionnaire/ self-reported	417	85% OS 88.8% GS	36.9*	63.1% *	Allergic rhinitis 15.7% *	European 93%*
Ling Mao [18]	China	Objective	214	5.1% OS 5.6% GS	52.2*	60.3%*	CVS 23.8%*	Unknown
Giacomelli A [11]	Italy	Questionnaire/ self-reported	59	34%	56	52.6	Unknown	Unknown
Bagheri [12]	Iran	Questionnaire/ self-reported	10,069^	48.2%	32.5	71%	Unknown	Unknown
Menni [13]	UK	Questionnaire/ self-reported	579	59.4%	40.79±11.84*	69%*	Unknown	Unknown
Yan [14]	USA	Questionnaire/ self-reported	59	67.8% OS 71.2% GS	17.6*	49.2%*	Allergic rhinitis 33.9% *	Unknown
Spinato [15]	UK	Questionnaire/ self-reported	202	65%	56*	52%*	Unknown	Unknown
Giuseppe Mer- cante [26]	Italy	Questionnaire/ self-reported	204	56.9%	52.6±14.4 *	More prevalent in female	CVS 24%*	Unknown
Yonghyn Lee [19]	Korea	Questionnaire/ self-reported	3191	15.3%	Median 36.5	68.9%	CVS	Unknown
Shima Moein [20]	Iran	UPSIT assisted by a trained examiner	60	35%	46.5*	33.3%*	13% diabetes*	Unknown
Levinson [21]	Israel	Questionnaire/ self-reported	42	35% OS 33% GS	34*	45%*	24% cardio- vascular*	Unknown
Daniel H. Coelho [23]	USA	Questionnaire/ self-reported	220^	Unknown	Unknown	78.2%	Allergic rhinitis 34%	White 82%
Evan R. Reiter [22]	USA	Questionnaire/ self-reported	549^	Unknown	Unknown	76.7%	Unknown	White 78.7%

Table 3 Summary of the literature on the association between dysgeusia and anosmia in COVID-19 patients

OS, olfactory symptoms; *GS*, gustatory symptoms; *CVS*, cardiovascular system; University of Pennsylvania Smell Identification Test *Among all COVID-19 patients

^Sample size was not confirmed by laboratory testing

patients, the prevalence of loss of taste and/or smell was more common in females than in males. The susceptibility of females to develop olfactory and gustatory dysfunctions could explain the differences in the inflammatory reaction process between the two genders [25]. Among all COVID-19 patients, multiple studies (Table 3) have shown that the prevalence of COVID-19 was more common in females than in males [17, 18, 26].

The association between COVID-19 and other similar comorbidities was reported by multiple studies [9, 10, 14, 17–21, 26].

In our studies, after adjustment for smell and taste disturbances, the comorbidities respiratory diseases and obesity had a significant OR for COVID-19 of 8.1 and 5.3, respectively.

These risk factors and others are known comorbidities responsible for the high death rate in COVID-19 [27, 28].

As the pandemic started in December 2019, both patients and clinicians ignored taste and smell disturbances until some studies indicated a strong association between taste and smell disturbances and COVID-19. The prevalence of loss of smell and loss of taste in COVID-19 patients varied widely among these studies, with prevalence ranging from 33.9% to 68% [11, 13, 14, 16].

However, a significant limitation associated with these reports is that either all of them were either self-reported by the patients or a survey filled out by the patients over the phone or online.

Only few reports, have diagnosed dysgeusia and anosmia based on physical examination, unlike the majority of the studies, which included dysgeusia and anosmia in their studies based on self-reported by the patients or a survey filled out by the patients over the phone or online (Table 3). Moreover, some studies have not even tested the patients to confirm the diagnosis of COVID-19 they assumed that those patients were COVID-19 positive based on the symptoms [12].

Some studies have reported that taste and smell disturbances were the only symptoms of COVID-19 [29, 30]; in these cases, patients do not have the classic sign and symptoms of COVID-19, e.g., lower respiratory tract infection, including fever, cough, and shortness. As a result, there might have been a delay in the diagnosis, as both patients and clinicians were not aware of these symptoms as part of COVID-19. Also, those patients will spread the diseases faster as they are socializing with other healthy people and an increased in the rate of transmission of COVID-19 occurred.

The exact pathophysiology of developing taste and smell disturbances with COVID-19 infection is still unclear.

Changes in smell and taste caused by virus infections like parainfluenza, rhinovirus, some coronavirus, and Epstein-Barr virus are well established in the literature. Rhinorrhea has always been associated with those viruses [31, 32]. However, anosmia in COVID-19 patients is not associated with rhinorrhea, making it different from the other causative agents.

Studies have shown that 2019-nCoV can attach to the human angiotensin-converting enzyme 2 (ACE-2), which is the same entry receptor for SARS-CoV [6]. Hamming et al. have demonstrated in their study that the ACE-2 receptors are expressed in multiple organs includes the basal epidermal layer of the oral and nasal mucosa and the nervous system [33, 34]. This could explain that this virus would cause taste and smell disturbances either by local damage of oral or nasal mucosa or by the neurotoxic effect to these nerve endings. Multiple reports have shown that coronaviruses are known to be neurotropic and neuroinvasive [18, 32, 35, 36]. Another study by Netland et al. demonstrated that SARS-CoV might lead to rapid transneuronal spread by entering the brain through the olfactory bulb [37].

Based on the observation that SARS-CoV-2 does not appear to cause clinically significant nasal congestion or rhinorrhea nor significant oral inflammation, it seems reasonable to hypothesize that the direct or neurotropic effect of the virus on the olfactory and taste receptors can lead to developing anosmia and dysgeusia. This assumption is in accordance with a study published by Xydakis et al. [38], which assumed that the virus is site-specific for the olfactory system.

Oral and maxillofacial surgeons, especially, are at increased risk of COVID-19 infection. This profession requires close contact with the patients during physical examinations, especially given the high risk of encountering aerosolized viral particles while using instruments to examine and treat the oral cavity. Based on our findings, there is an association between taste and smell disturbances and COVID-19. Therefore, we recommend that any specialists focused on the head and neck region (oral and maxillofacial surgeon, dentists, ophthalmologist, otolaryngologists, and head-neck surgeons) to include olfactory and gustatory assessment in their physical examination. Patients with sudden symptoms of taste and smell disturbances should be suspected to have COVID-19.

Further investigation for COVID-19 should be performed to avoid delaying the diagnosis of COVID19 and thus contributing to an epidemic. In conclusion, In the present study, we have found a significant association between taste and smell disturbances and COVID-19 infection. The odds ratio for having COVID-19 for people with taste and smell was 39.1 before adjustments. Our study findings support the addition of anosmia and dysgeusia to the list of screening tools for COVID-19 infection. Oral and maxillofacial surgeons should be suspicious of COVID-19 infection when seeing patients experiencing smell and taste disturbances and should enhance their personnel protective equipment when treating them during the COVID-19 pandemic.

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Declarations

Ethical approval The was IRB exempted as it did not include personal health information (PHI).

Informed consent Not applicable.

Conflict of interest There is conflict of interest.

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