

Original Article

A Cross-Sectional Study of Self-Reported Olfactory and Gustatory Changes in COVID-19 and its Impact on Quality of Life in Taif, Saudi Arabia

Wissam Almandili¹, Abdullah Alfaifi¹, Sultan Daghas¹, Rashed Althobaiti¹, Abdullah Almalki¹, Talal Alnajjar¹, Tamer Abdelrahman^{2,3*}

¹ College of Medicine, Taif University, Taif, Saudi Arabia.

² Surgery Department, Faculty of Medicine, Taif University, Saudi Arabia.

³ Surgery Department, Benha Teaching Hospital, General Organization of Teaching Hospital and Institutes, Benha, Egypt.

Correspondence should be addressed to Tamer Abdelrahman Surgery Department, College of Medicine, Taif University, Saudi Arabia. Email: drtamer17@gmail.com

Received: 9 October 2021, Revised: 23 November 2021, Accepted: 24 November 2021, Published: 26 November 2021

Copyright © 2021 Almandili et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Chemosensory changes in COVID-19 infected individuals have gained substantial attention in recent times. The persistence of olfactory and gustatory problems may negatively impact the quality of life and daily life activities. The study aimed to assess the olfactory and gustatory changes among COVID-19 patients in Taif city, Saudi Arabia..

Methods: A cross-sectional study was done using a pretested questionnaire among COVID-19 infected individuals. A mixture of snowball and convenience was used to collect the responses. The questionnaire recorded participants' baseline characteristics, COVID-19 associated clinical findings, characteristics of clinical olfactory dysfunctions (OD) and gustatory dysfunction (GD), and a short version Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) that measured the effect of gustatory and olfactory changes on the patient's quality of life.

Results: The prevalence of olfactory dysfunction and Gustatory dysfunction was found to be 55.7% and 46.3%, respectively, and about 44.7% of the participants had experienced both OD and GD. The percentage of OD and GD were found to be comparatively higher among those who had experienced general symptoms of COVID-19 than those who were asymptomatic ($p < 0.001$). The patients who had experienced anosmia had demonstrated a poor quality of life compared to those who had Hyposmia ($p = 0.044$).

Conclusion: The high prevalence of OD and GD among COVID-19 infected individuals has an impact on the quality of life. The long-standing or permanent OD and GD symptoms are of big concern, and this should alert physicians about the substantial risk that this individual faces.

Keywords: SARS-CoV-2, COVID-19, Olfactory, Gustatory, Anosmia, Hyposmia, Dysgeusia.

Introduction

According to the World Health Organization reports, as of September 2021, there have been more than 228 million confirmed cases of COVID-19, including 4.7 million deaths and in Saudi Arabia there have been 546,612 confirmed cases of COVID-19 with 8,667 deaths, with a total of 40,959,293 vaccine doses have been administered (1). The key symptoms that may suggest COVID-19 infection include cough, difficulty breathing or shortness of breath, high body temperature, chills, muscle ache, joint pain, sore throat, and loss of smell or taste (2). Many countries worldwide have taken preventive measures such as raising awareness to frequently sanitize hands, advising those with minor symptoms to self-isolate, and introducing travel restrictions and social distancing.

Evidence suggests that COVID-19 frequently impairs the sense of smell and taste, which may precede general symptoms such as cough and shortness of breath (3). Olfactory dysfunction (OD) is characterized as abnormal or diminished capacity to smell while sniffing (orthonasal olfaction) or eating (retronasal olfaction) (4). Similarly, Gustatory dysfunction (GD) is the impairment of salty, sweet, bitter, and sour taste and these taste changes could be a critical diagnostic factor in COVID-19 positive patients (5). Reports from different countries show that OD and GD are commonly associated with COVID-19, and a majority of these patients experience impairment of smell and taste interchangeably (6-8). Many viruses have been known to cause OD as rhinovirus, parainfluenza and Epstein-Barr virus by an inflammatory reaction of the nasal mucosa and the development of rhinorrhea (9,10). Screening for loss of taste or smell could be an effective strategy among COVID-19 infected asymptomatic patients to prevent transmission of the infection. Thus, it is suggested that during the current pandemic, individuals with new-onset of OD and GD with or without other general symptoms of COVID-19 should quarantine themselves before SARS-CoV-2 testing.

Evidence shows most of the COVID-19 patients who experience olfactory and gustatory dysfunction do not require hospitalization and are treated in the outpatient units in the hospitals. It is thus important to assess the recovery of smell and taste dysfunction and also its impact on the quality of life in COVID-19 infected, although it is not a life-threatening problem. However, due to a lack of follow-up with COVID-19 infected patients, it is difficult to know the persistence of OD and GD. In Saudi Arabia, no studies have assessed the prevalence of OD and GD

and their impact on the quality of life. This study aims to investigate the olfactory and gustatory changes among COVID-19 patients in Taif city, Saudi Arabia.

Methodology

A cross-sectional study was conducted from December 2020 to March 2021 using a self-administered pretested questionnaire. The questionnaire was initially sent to 720 patients using online platforms (WhatsApp, Twitter, and email), and 568 patients gave consent to participate in the survey. The inclusion criteria for this study were individuals who had COVID-19 irrespective of gender and who were residents of Taif during the survey period. Patients who already had olfactory or gustatory dysfunction prior to the infection were excluded. Therefore, the final sample size was 544 participants who satisfied the eligibility criteria. A mixture of convenience and snowball sampling was done for recruiting the participants for the study.

The questionnaire was divided into three parts. The first part included participants' characteristics including socio-demographic, body mass index, smoking status, and other co-morbidities. The second part had items that recorded COVID-19 associated clinical findings, characteristics of clinical ODs, characteristics of clinical GDs. The third part included a short version Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) that had seven items to measure the effect of gustatory and olfactory changes on the patient's quality of life. Each item is rated on a scale of 0-3, with higher scores reflecting better olfactory-specific Quality of Life (QoL). The total score ranges from 0 (severe impact on QoL) to 21 (no impact on QoL) (11).

All the responses were entered and tabulated in Microsoft Excel, and data cleaning was done. It was subjected to statistical analysis by an independent biostatistician, and Statistical Package for Social Sciences, Version 23 (SPSS Inc., Chicago, IL, USA) was used for the data analysis. Categorical variables were presented as numbers and percentages. Continuous variables were measured using mean and standard deviation. Student's T-test was used to compare the continuous variables (sQOD-NS scores) between different groups. Pearson chi-square test was used to find an association between categorical variables. A p-value less than 0.05 was considered statistically significant.

Results:

The analysis included responses from 544 COVID-19 infected individuals who satisfied the eligibility criteria. The sociodemographic characteristics showed that 53.3% were females, 38.8% belonged to the 18-25 years age group, 50.4% had body mass index (BMI) more than 25 (overweight and obese), and 37.5% were students. In addition, it was reported by 31.6% that they suffered from some comorbidities, and it was found that hypertension was the most common comorbidity (**Table 1**).

Table 1: Baseline characteristics of the participants			
		Frequency (n)	%
Gender	Male	254	46.7
	Female	290	53.3
Age	< 18 years	17	3.1
	18-25 years	211	38.8
	26-35 years	142	26.1
	36 – 45 years	119	21.9
	46 – 54 years	37	6.8
	55 years or older	18	3.3
Body Mass Index	Underweight	50	9.2
	Normal	220	40.4
	Overweight	150	27.6
	Obese	124	22.8
Job sector	Government sector	137	25.2
	Private sector or business	48	8.8
	Health sector	41	7.5
	Education sector or Teacher	12	2.2
	Student	204	37.5
	Unemployed or housewife	83	15.3
	Retired	19	3.5
Comorbidities	No	372	68.4
	Yes	172	31.6
Types of comorbidities (n=172)	Diabetes	30	17.4
	Hypertension	43	25.0
	Cardiovascular disease	23	13.4
	Cancer	9	5.2
	Renal diseases	32	18.6
	Respiratory disease	45	26.2
	Others	32	18.6
Tested positive smear	No	287	52.8
	Yes	257	47.2

n = numbers

The most commonly reported symptoms were headache (46.1%), high temperature (45.8%), muscle pain (44.3%) and joint pain (36.6%). When we assessed the severity of symptoms in these COVID-19 infected individuals, it was reported by 218 (40.1%) that they had mild symptoms, 97 (17.8%) had moderate symptoms, 72 (13.2%) were asymptomatic, and only 11 (2%) reported severe symptoms. The prevalence of OD and GD was found to be 55.7% and 46.3% respectively, whereas patients who had experienced both dysfunctions were found to be 44.7%. The reported otolaryngological symptoms were rhinorrhea (24.6%), nasal obstruction (22.3%), dyspnea (20.6%), laryngitis/sore throat (20.1%), sneezing (18%) and ear pain (6.6%).

The OD was found to be comparatively more among 36-45 years ($p=0.023$), whereas GD didn't show any statistical significance with the age of the patients ($p=0.127$). Female patients showed a significantly higher prevalence of OD (61.4%) and GD (59.9%) than male patients ($p<0.05$). The percentage of OD and GD were found to be comparatively higher among those who had experienced general symptoms of COVID-19 than those who were asymptomatic ($p<0.001$) (**Table 2**).

The assessment of OD showed that 55.7% had experienced it, where 43.0% had anosmia, and 12.7% had Hyposmia. Among these patients who had OD, 49.5% had it at the same time with the symptoms of COVID-19, whereas 40.3% had developed it after the general symptoms of COVID-19. It was reported by 36.6% of participants that they didn't use any treatment for OD. About 91.7% of the participants who had OD got recovered, where 53.3% had completely recovered from OD, and 38.3% had not completely recovered from the dysfunction. It was reported by patients who had OD recovery, 25.1% had recovered it after 15 days from the day of recovery from general symptoms of COVID-19 (**Table 3**).

The assessment of GD among these patients showed that 46.3% had experienced it. Out of them, 24.4% had it at the same time with general symptoms of COVID-19, whereas 18% had it after general symptoms of COVID-19 had subsided. When we assessed the treatment used for GD, 15.5% reported that they used Gustatory training such as eating garlic, ginger, etc., while 52.8% didn't use any treatment. The recovery of GD showed that 58.7% had a complete recovery from it, and 5.6% reported no recovery. About 25.2% of the participants reported that it took 5-8 days from the day of recovery of general symptoms of COVID-19 to recover from OD, and 21.8% reported that it took more than 15 days (**Table 4**).

Table 2: Relationship of Olfactory and Gustatory dysfunction with age, gender and severity of general COVID-19 symptoms

Variables			OD		P value	OD		P value
			No	Yes		No	Yes	
Age	< 18	N	6	11	0.023*	6	11	0.127
		%	2.5%	3.6%		2.1%	4.4%	
	18-25	N	97	114		117	94	
		%	40.2%	37.6%		40.1%	37.3%	
	26-35	N	65	77		69	73	
		%	27.0%	25.4%		23.6%	29.0%	
	36-45	N	40	79		63	56	
		%	16.6%	26.1%		21.6%	22.2%	
	46-54	N	24	13		26	11	
		%	10.0%	4.3%		8.9%	4.4%	
	55 or more	N	9	9		11	7	
		%	3.7%	3.0%		3.8%	2.8%	
Gender	Female	N	104	186	139	151	0.004*	
		%	43.2%	61.4%	47.6%	59.9%		
	Male	N	137	117	153	101		
		%	56.8%	38.6%	52.4%	40.1%		
Severity of general COVID-19 symptoms	Asymptomatic	N	57	15	59	13	<0.001*	
		%	23.7%	5.0%	20.2%	5.2%		
	Medium	N	24	73	27	70		
		%	10.0%	24.1%	9.2%	27.8%		
	Mild	N	32	186	70	148		
		%	13.3%	61.4%	24.0%	58.7%		
	Severe	N	2	9	3	8		
		%	0.8%	3.0%	1.0%	3.2%		
	I do not know	N	126	20	133	13		
		%	52.3%	6.6%	45.5%	5.2%		

* P-value<0.05 is considered statistically significant, OD: Olfactory dysfunction, GD: Gustatory dysfunction, N=numbers

Table 3: Olfactory dysfunction and associated findings

		Frequency (n)	%
Olfactory dysfunction	None	241	44.3
	Anosmia	234	43.0
	Hyposmia	69	12.7
Onset of olfactory dysfunction	Before general symptoms of COVID-19	31	10.2
	At the same time as general symptoms of COVID-19	150	49.5
	After general symptoms of COVID-19	122	40.3

		Frequency (n)	%
Treatment used for olfactory dysfunction	Nasal saline irrigations	31	10.2
	Vitamins	18	5.9
	Decongestants	35	11.6
	Olfactory training	69	22.8
	No treatment	111	36.6
	Traditional method	39	12.9
Outcome of olfactory symptoms	Complete Recovery	160	53.3
	Partial Recovery	115	38.3
	No Recovery	25	8.3
Recovery time of OD (after general symptoms of COVID-19 have subsided) (n=275)	1-4 days	35	12.7
	5-8 days	58	21.1
	9-14 days	73	26.5
	>=15 days	69	25.1
	Don't remember	40	14.5

OD: Olfactory dysfunction, n=numbers

Table 4: Gustatory dysfunction and associated findings

		Frequency (n)	%
Gustatory dysfunction	Didn't experience gustatory dysfunction	292	53.7
	Before general symptoms of COVID-19	21	3.9
	At the same time as general symptoms of COVID-19	133	24.4
	After general symptoms of COVID-19	98	18.0
Characteristics of clinical Taste disorders	Dysgeusia,	45	23.3%
	Ageusia,	145	75.1%
	Salty taste recognition	50	25.9%
	Sweet taste recognition	48	24.9%
	Bitter taste recognition	43	22.3%
Received treatment for Gustatory dysfunction (n=252)	Acidic taste recognition	43	22.3%
	Oral corticosteroids	3	1.2
	Vitamins	58	23
	Gustatory training (eating garlic, Ginger etc.)	39	15.5
	Traditional treatment	18	7.1
	Nothing	133	52.8
Outcome of gustatory symptoms	Other methods	1	0.4
	Complete Recovery (n=252)	148	58.7
	No Recovery	90	35.7
Recovery time of GD (After general symptoms of COVID-19 have subsided) (n=238)	14	5.6	
	1-4 days	30	12.6
	5-8 days	60	25.2
	9-14 days	56	23.5
	More than 15 days	52	21.8
Don't know/ remember	32	13.4	

GD: Gustatory dysfunction, n=numbers

The quality of life among patients who had OD is summarized in **Table 5**. The analysis showed that patients who had experienced anosmia had demonstrated a poor QoL compared to those who had Hyposmia ($p=0.044$).

Table 5: Comparison of Self-reported Loss of Smell in patients who had olfactory dysfunction (n= 303)

Variables	Inadequate score	Adequate Score	
Changes in the sense of smell isolate me socially	1.75 ±1.20	2.06 ±1.12	0.095
Smell problems have a negative impact on my daily social activities	1.23 ±1.11	1.63 ±1.00	0.19
Smell problems make me more emotional	1.58 ±1.16	2.02 ±1.14	0.013*
Because of my smell problems, I eat less food outside	1.28 ±1.20	1.48 ±1.26	0.278
Due to smell problems I have eaten less than before (anorexia)	1.23 ±1.18	1.37 ±1.20	0.448
Because of my olfactory problems, I should do more to relax	1.41 ±1.19	1.31 ±1.15	0.595
I am afraid I will never be able to get used to smell problems	1.21 ±1.26	1.51 ±1.14	0.122
Total sQOD-NS	9.65 ±6.00	11.51 ±5.67	0.044*
Age (years); mean±SD	24.2±2.2	24.2±2.2	26.1±4.9

* P -value<0.05 is considered statistically significant, sQOD-NS: Olfactory Disorders-Negative Statements

Discussion:

The study findings showed that the prevalence of OD and GD was found to be 55.7% and 46.3%, respectively. Anosmia was found to be more common than hyposmia in OD, whereas ageusia was found to be more common than dysgeusia. A systematic review by Boscutti et al. has reported the prevalence of OD to be 62% with an extreme variability between studies (0-98%), and the prevalence of GD was found to be 59%, which also showed a large inter-study variability (0-89%) (12). There are mainly three types of ODs, conductive or transport impairment, central olfactory dysfunction, and sensorineural impairment (13-15). Evidence suggests that loss of smell in COVID-19 could be due to neurotrophic targeting of olfactory neurons and infection of non-neural olfactory epithelial cells. Thus, the direct involvement with the peripheral or central nervous system is a possible mechanism of OD (16,17). Still, it is not clear whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) attacks the sensory cells or the Olfactory bulb or which olfactory mucosa cells are targeted. However, studies show that chemosensory function has improved over time in COVID-19 patients (18-20). Reports showed that both OD and GD are closely related in patients infected with SARS-CoV-2 infection. The majority of the patients who developed OD had recovered within days to weeks after recovery from COVID-19. In our study, 8.3% had not recovered from OD, and it is still

unclear how this permanent dysfunction is caused. It has been reported that transient loss of smell and taste is common in patients experiencing upper respiratory tract viral infections (21). Our study findings showed that patients who were symptomatic with general COVID-19 symptoms had comparatively more loss of smell and taste than asymptomatic patients. Patients who do not improve olfactory dysfunction could develop the post-viral olfactory disorder (PVOD) secondary to sensorineural insult. Loss of taste is likely to be secondary to the loss of smell, as evidence shows that there is no direct or indirect damage to associated neurons or taste buds in COVID-19 infection (22). This is consistent with our findings, which showed a lesser rate of GD as compared to OD.

Many treatment modalities have been explored specifically for post-viral OD. However, olfactory training therapy is the one that has proved to be beneficial. (15,23). In our study, the most commonly used treatment was found to be olfactory training. The evaluation of particular therapeutics for COVID-19-related to loss of smell is currently being investigated. According to anecdotal evidence, a considerable proportion of olfactory-impaired people experience a lower QoL and show decreased ability to do activities of daily living (ADLs) (24). Findings from the current study show that QoL was comparatively less in patients with COVID-19 related OD. This is in agreement with another study by Elkholy et al., which showed that more than three-fourths of the patients reported a general

decline in QoL where the most commonly reported adverse effects were poor awareness of personal hygiene and less interest in food and drinks (25). It may be argued that individuals with a smell impairment may face restrictions in terms of enjoying food and beverages, socializing, personalities, and perceiving warning signs related to the ability to smell (26). This is supported by the findings of Frasnelli and Hummel, which reported that anosmia patients experienced a lower quality of life compared to hyposmia patients (27).

In our study, the most reported negative side effects that impacted QOL were “Due to smell problems I have eaten less than before” and “I am afraid I will never be able to get used to smell problems.” Although many of these olfactory struggles were not disclosed by all patients, these problems could negatively impact a person’s level of independence, leading to occupational deprivation. This is especially true for people involved in food preparations, such as housewives, mothers, chefs, etc. Our findings showed that both OD and GD were significantly higher among females, younger people, and those who had mild general symptoms of COVID-19. This is in agreement with findings reported by Sayin et al. and Martin-Sanz et al. (28,29). The current study findings show that COVID-19 patients with OD face challenges in daily life and work and the enjoyment of food and drink, social life, and interpersonal relationships.

Some of the limitations should be considered before generalizing the findings. The study used a self-administered questionnaire, and this may have resulted in recall bias. Secondly, participants may have under or over the reported loss of smell and taste-associated factors. Studies show that patients’ self-reports of OD may underestimate the true prevalence of these problems (30,31). In addition, the study might have been subjected to confounding errors, where some of the factors that influence the olfactory and gustatory dysfunctions might have been not assessed for relationship.

Conclusion:

The findings of this study showed that the majority of the COVID-19 patients in this study have experienced the loss of smell and taste, where a few of them had shown no recovery from them. There were significant reductions in quality of life where patients who reported complete loss of smell had comparatively demonstrated diminished quality of life than others. Although therapeutic options for olfactory deficits remain limited in COVID-19 patients,

physicians, especially otolaryngologists, should use a combination of problem-focused as well as anxiety-focused strategies to treat these olfactory and gustatory impairments in COVID-19 patients.

Acknowledgments:

The authors would like to thank and acknowledge all who participate in the survey.

Declaration:

Statement:

The authors declare no conflict of interest.

Funding:

None

Ethical Consideration:

The research was approved by Research Ethics Committee of Taif University (approval letter number 42-0066 and date 13/12/2020). The confidentiality of participants was preserved by not including their names or any details that may identify them.

Data Availability:

The survey used in this paper is attached as a supplementary material.

References:

1. World Health Organization (WHO). WHO Coronavirus (COVID-19) Dashboard. Available at <https://covid19.who.int>. Accessed September 20, 2021.
2. Symptoms of coronavirus. US Centers for Disease Control and Prevention website. Available at <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>. Accessed September 20, 2021
3. Karapetyan LS, Svistushkin VM. Olfactory dysfunction and COVID-19-current state of the problem. *Vestnik Otorinolaringologii*. 2020 Jan 1;85(6):100-4.
4. Whitcroft KL, Hummel T. Olfactory dysfunction in COVID-19: diagnosis and management. *Jama*. 2020 Jun 23;323(24):2512-4.
5. Harikrishnan P. Gustatory Dysfunction as an Early Symptom in COVID-19 Screening. *The Journal of Craniofacial Surgery*. 2020;31(6):e656-e658. 10.1097%2FSCS.0000000000006797

6. Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clinical Infectious Diseases*. 2020;71(15):889-90. 10.1093/cid/ciaa330
7. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *European Archives of Oto-Rhino-Laryngology*. 2020;277(8):2251-61. 10.1007/s00405-020-05965-1
8. Tong JY, Wong A, Zhu D, Fastenberg JH, Tham T. The prevalence of olfactory and gustatory dysfunction in COVID-19 patients: a systematic review and meta-analysis. *Otolaryngology–Head and Neck Surgery*. 2020;163(1):3-11. 10.1177/0194599820926473
9. Suzuki M, Saito K, Min WP, Vladau C, Toida K, Itoh H, et al. Identification of viruses in patients with postviral olfactory dysfunction. *The Laryngoscope*. 2007;117(2):272-7. 10.1097/01.mlg.0000249922.37381.1e
10. Van Riel D, Verdijk R, Kuiken T. The olfactory nerve: a shortcut for influenza and other viral diseases into the central nervous system. *The Journal of pathology*. 2015;235(2):277-87. 10.1002/path.4461
11. Mattos JL, Edwards C, Schlosser RJ, Hyer M, Mace JC, Smith TL, et al. A brief version of the questionnaire of olfactory disorders in patients with chronic rhinosinusitis. *International Forum of Allergy & Rhinology*. 2019;9(10):1144-50. 10.1002/alr.22392
12. Boscutti A, Delvecchio G, Pignoni A, Cereda G, Ciappolino V, Bellani M, et al. Olfactory and gustatory dysfunctions in SARS-CoV-2 infection: A systematic review. *Brain, Behavior, & Immunity - Health*. 2021;15:100268. 10.1016/j.bbih.2021.100268
13. Imamura F, Hasegawa-Ishii S. Environmental toxicants-induced immune responses in the olfactory mucosa. *Frontiers in immunology*. 2016;7:475. 10.3389/fimmu.2016.00475
14. Schwartz JS, Tajudeen BA, Kennedy DW. Chapter 18 - Diseases of the nasal cavity. In: Doty RL, editor. *Handbook of Clinical Neurology*. 164: Elsevier; 2019. p. 285-302. 10.1016/B978-0-444-63855-7.00018-6
15. Miwa T, Ikeda K, Ishibashi T, Kobayashi M, Kondo K, Matsuwaki Y, et al. Clinical practice guidelines for the management of olfactory dysfunction — Secondary publication. *Auris Nasus Larynx*. 2019;46(5):653-62. 10.1016/j.anl.2019.04.002
16. Rocke J, Hopkins C, Philpott C, Kumar N. Is loss of sense of smell a diagnostic marker in COVID-19: a systematic review and meta-analysis. *Clinical Otolaryngology*. 2020;45(6):914-22. 10.1111/coa.13620
17. Brann David H, Tsukahara T, Weinreb C, Lipovsek M, Van den Berge K, Gong B, et al. Non-neuronal expression of SARS-CoV-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19-associated anosmia. *Science advances*. 2020;6(31):eabc5801. 10.1126/sciadv.abc5801
18. Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J, Rodríguez-Jorge F, Natera-Villalba E, Gómez-Corral J, et al. Acute-onset smell and taste disorders in the context of COVID-19: a pilot multicentre polymerase chain reaction based case–control study. *European Journal of Neurology*. 2020;27(9):1738-41. 10.1111/ene.14273
19. Vaira LA, Deiana G, Fois AG, Pirina P, Madeddu G, De Vito A, et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single-center experience on 72 cases. *Head & Neck*. 2020;42(6):1252-8. 10.1002/hed.26204
20. Wee LE, Chan YFZ, Teo NWY, Cherng BPZ, Thien SY, Wong HM, et al. The role of self-reported olfactory and gustatory dysfunction as a screening criterion for suspected COVID-19. *European Archives of Oto-Rhino-Laryngology*. 2020;277(8):2389-90. 10.1007/s00405-020-05999-5
21. Soler ZM, Patel ZM, Turner JH, Holbrook EH. A primer on viral-associated olfactory loss in the era of COVID-19. *International Forum of Allergy & Rhinology*. 2020;10(7):814-20. 10.1002/alr.22578.
22. Moein ST, Hashemian SM, Mansourafshar B, Khorram-Tousi A, Tabarsi P, Doty RL. Smell dysfunction: a biomarker for COVID-19. *International Forum of Allergy & Rhinology*. 2020;10(8):944-50. 10.1002/alr.22587
23. Kattar N, Do TM, Unis GD, Mignerone MR, Thomas AJ, McCoul ED. Olfactory Training for Postviral Olfactory Dysfunction: Systematic Review and Meta-analysis. *Otolaryngology–Head and Neck Surgery*. 2020;164(2):244-54. 10.1177/0194599820943550
24. Miwa T, Furukawa M, Tsukatani T, Costanzo RM, DiNardo LJ, Reiter ER. Impact of Olfactory Impairment on Quality of Life and Disability. *Archives of Otolaryngology–Head & Neck Surgery*. 2001;127(5):497-503. 10.1001/archotol.127.5.497
25. Elkholi SMA, Abdelwahab MK, Abdelhafeez M. Impact of the smell loss on the quality of life and adopted coping strategies in COVID-19 patients. *European Archives of Oto-Rhino-Laryngology*. 2021;278(9):3307-14. 10.1007/s00405-020-06575-7

26. Smeets MA, Veldhuizen MG, Galle S, Gouweloos J, de Haan AM, Vernooij J, Visscher F, Kroeze JH. Sense of smell disorder and health-related quality of life. *Rehabilitation psychology*. 2009 Nov;54(4):404. 10.1037/a0017502
27. Frasnelli J, Hummel T. Olfactory dysfunction and daily life. *European Archives of Oto-Rhino-Laryngology and Head & Neck*. 2005;262(3):231-5. 10.1007/s00405-004-0796-y
28. Sayin İ, Yaşar KK, Yazici ZM. Taste and Smell Impairment in COVID-19: An AAO-HNS Anosmia Reporting Tool-Based Comparative Study. *Otolaryngology–Head and Neck Surgery*. 2020;163(3):473-9. 10.1177/0194599820931820
29. Martin-Sanz E, Riestra J, Yebra L, Larran A, Mancino F, Yanes-Diaz J, et al. Prospective Study in 355 Patients With Suspected COVID-19 Infection: Value of Cough, Subjective Hyposmia, and Hypogeusia. *The Laryngoscope*. 2020;130(11):2674-9. 10.1002/lary.28999
30. Desiato VM, Levy DA, Byun YJ, Nguyen SA, Soler ZM, Schlosser RJ. The Prevalence of Olfactory Dysfunction in the General Population: A Systematic Review and Meta-analysis. *American Journal of Rhinology & Allergy*. 2020;35(2):195-205. 10.1177/1945892420946254
31. Nordin S, Monsch AU, Murphy C. Unawareness of Smell Loss in Normal Aging and Alzheimer’s Disease: Discrepancy between Self-Reported and Diagnosed Smell Sensitivity. *The Journals of Gerontology: Series B*. 1995;50B(4):P187-P92. 10.1093/geronb/50B.4.P187