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Literature Review

Smell and Taste Disorders in COVID-19: A Literature Review

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Abstract

Background: There is increasing evidence that the sudden olfactory dysfunctions (OD) and gustatory dysfunctions (GD) especially in the absence of nasal obstruction, rhinorrhea, or any upper respiratory symptoms, are common early symptoms of COVID-19. The objective of this review was to identify regional and worldwide prevalence of OD and GD in patients with COVID-19.

Methods: A search of the literature using keyword combinations was performed on the 1st of July 2020 among 4 major databases: PubMed, ScienceDirect, Web of Science, and Scopus. Preprints databases (Medrxiv, Biorxiv) were also searched for unpublished manuscripts. Only primary studies that reported on prevalence of OD/GD and written in English were selected. Data synthesis was narrative. Following the review, websites of relevant professional bodies were searched for guidelines and recommendations. Risk of bias was assessed with a 10-item tool.

Results: Twenty-nine articles reported OG or GD symptoms in 15830 patients. Studies have demonstrated great heterogeneity in the reported prevalence of anosmia as a COVID-19 symptom, from 5.1% to 98%. Caucasians have a higher prevalence than East Asians.

Discussion: Preliminary evidence suggests that differences in host or virus genotypes dominating different geographical regions may explain such heterogeneity in the reported prevalence of OD/GD among COVID-19 patients. However, there was no standardized method of detecting anosmia, limiting any strong conclusions. In regions with higher prevalence, OD/GD can be useful as a sensitive biomarker of COVID-19 that may help prioritization of COVID-19 testing and promote self-isolation which would reduce exposure to contagious but otherwise asymptomatic individuals who are much more difficult to identify.

Keywords: COVID-19; Taste Disorders; Olfaction Disorders; Prevalence; Anosmia

Introduction

The senses of smell and taste are frequently associated in the public's mind with the intense enjoyment of a large spectrum of pleasant odors or flavors. In biological and evolutionary terms, these two chemosensory functions are essential not only for enjoying a good quality of life but for life preservation too. Many life-threatening situations can be avoided by identifying harmful, mostly unpleasant, odors and flavors, such as becoming aware of a gas leak or recognizing rotten food.

Since early infancy, learning human brains gradually became hard-wired to the sense of smell or taste with many linked memories and reflexes secured by a highly complex neural network, including the temporal lobe, a large part of the limbic lobe, the amygdala, and the insula [1]. Studies have also shown that prolonged loss of smell or taste can result in intense psychological signs of depersonalization [2]. Thus, the loss of any of these two chemosensory functions should not be considered only as a sensory symptom but also as a complex, psycho-sensorial syndrome.

There is a large spectrum of disorders concerning these two crucial chemosensory functions. Smell or Olfactory Disorders (OD) can range from just decrease in the sense of smell (hyposmia) to complete loss of smell (anosmia). In Taste or Gustatory Disorders (GD), a similar pattern is seen with hypogeusia, a reduced ability to taste sweet, sour, bitter, salty, and savory (umami), and ageusia, the inability to detect any taste. Dysosmia and dysgeusia are the alteration or distortion of the sense of smell or taste respectively, such as when there is a persistent foul, salty, rancid, or metallic taste sensation. Dysgeusia may also be related to alteration in the perception of taste due to loss of the sense of olfaction [3].

The leading cause of temporary olfactory or gustatory disorders (OD/GD) of varying degrees and duration is viral Upper Respiratory Tract Infections (URTIs) [4]. Up to 70% of OD/GD are caused by the influenza virus, parainfluenza, rhinovirus, respiratory syncytial virus, and adenovirus [5]. Due to growing scientific evidence, the new SARS-CoV-2 is now also a member of this list.

In December 2019 in the city of Wuhan, Hubei province in China, a new sequence of human-RNA-coronavirus was first identified. The virus was coined the 2nd severe acute respiratory syndrome coronavirus (SARS-CoV-2) and the disease it causes was coined the Coronavirus disease 2019 (COVID-19) [6]. Owing to its extremely high contagious nature with easy human-to-human transmission, COVID-19 started spreading furiously around the world [7]. In March 2020 the World Health Organization (WHO) declared COVID-19 outbreak a pandemic disease [8,9]. From its outbreak in China in December 2019 to the 17th of October 2020, 39,023,292 confirmed cases of COVID-19, including 1,099,586 deaths, had been reported to WHO [10].

COVID-19 common general symptoms include fever, dry cough, sputum production, headache, arthralgia, myalgia, diarrhea, fatigue, and dyspnea similar to the common general symptoms of infections caused by influenza viruses, rhinoviruses, parainfluenza viruses, adenoviruses, respiratory syncytial viruses or enteroviruses [10]. In its severest form, COVID-19 can result in pneumonia and lead to severe acute respiratory distress syndrome (ARDS) and even death [7]. Mild otolaryngological COVID-19 symptoms are also recognized, such as pharyngodynia, rhinorrhea, nasal congestion, and smell and taste disorders. The British Rhinology Society underlined how a significant number of COVID-19 patients reported anosmia, ageusia and dysgeusia [11-13]. On 23rd March 2020, the *New* York Times published an important article by Roni Caryn Rabin describing the escalating evidence that smell loss is a potential early manifestation of COVID-19 [14].

Evidence surrounding the presentation of patients with COVID-19 indicates that one of the earliest signs is the loss of sense of smell or taste. Although such a symptom can be detrimental to the quality of life of an individual, ironically, this can prove beneficial to the public with potential for early detection and isolation, thus limiting the spread of the disease. This review gathers and discuss the current scientific knowledge relating to the prevalence of loss of smell and taste in the context of the COVID-19 pandemic.

Methods

Eligibility criteria

Studies were included in the review if they reported rates or prevalence of olfactory or gustatory dysfunctions in patients with SARS-CoV-2. Other eligibility criteria included: primary studies (abstracts, original papers, reports, letters to the editor, and clinical trials), and English language. Articles were excluded if they covered inappropriate topics irrelevant to the main objective of the study, or discussed COVID-19 symptoms in general without specific reference to olfactory or gustatory dysfunctions.

Search strategy

A literature search was conducted among 4 major databases (PubMed, ScienceDirect, Web of Science and Scopus) on the 1st of July 2020 to retrieve published articles. The preprints databases Medrxiv and Biorxiv were also searched for unpublished manuscripts. Following the review, the websites of relevant professional bodies were manually searched for guidelines and recommendations, namely the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), The British Rhinology Society, the ENT UK (British Association of Otorhinolaryngology-Head, and Neck Surgery (BAO-HNS), the French Association of Rhinology (AFR) and of the French Society of Otorhinolaryngology (SFORL), US Centers for Disease Control and Prevention and the World Health Organization. A review protocol was not prepared and the review was not registered. No external funding was required.

The following keyword search strategy on titles and abstracts was adopted: ((COVID-19) OR (SARS-CoV-2) OR (2019-nCoV) OR (Coronavirus)) AND ((Smell) OR (Taste) OR (Olfactory) OR

(Gustatory) OR (Anosmia) OR (Hyposmia) OR (Ageusia) OR (Dysgeusia)) OR (Chemosensory)).

Selection process and data extraction

After duplicates removal, the titles and abstracts of retrieved documents were screened. The full texts of potentially eligible studies were reviewed for final inclusion according to the eligibility criteria. Data extracted include information of study characteristics, country of origin, study design, number of patients with anosmia, number of patients with dysgeusia, method of identification of OD/GD, and method of diagnosis of COVID-19 infection.

Outcomes

The outcomes were: a) rates of olfactory disorders in patients diagnosed with SARS-CoV-2; b) rates of gustatory disorders in patients diagnosed with SARS-CoV-2.

Risk of bias assessment

The risk of study bias assessment tool [43] contains ten items covering both external and internal validity, and a summary assessment item evaluating the overall risk of bias. Each individual item was evaluated as either low (0) or high (1) risk of bias (studies with insufficient information for any item were also denoted as high risk of bias for that item).

Synthesis

A narrative synthesis was performed to synthesize the findings of the different studies. This was decided because there is great heterogeneity in the population characteristics, methods of assessment for olfactory or gustatory disorders, and diagnosis of COVID-19. The rates of each olfactory or gustatory disorder were presented as reported from each included study. If this was not available, the prevalence rates were calculated by dividing the number of COVID-19 cases with anosmia/dysgeusia by the total number of COVID-19 cases (with and without anosmia/dysgeusia), and was expressed as a percentage (%).

Results

A total of 499 unique records were screened, of which 463 articles were excluded. Full-text screening of the remaining 36 articles resulted in the removal of 7 articles. Among the 29 articles that were included for the review, 4 articles were from Germany [16-19], 1 from Canada [20], 1 from china [21], 3 from France [22-24], 1 from Greece [25], 1 from Iceland [26], 1 from Iran [27], 1 from Israel [28], 3 from Italy [13,29,30], 2 from Singapore [31,32], 1 from South Korea [33], 2 from Spain [34,35], 1 from Turkey [36], 1 from UK [37], 4 from USA [38-41], 1 Multicenter European Study (12 centers) [12], 1 Multicenter international Study (China, France, and Germany) [42]. Though being a literature review, the details of the selection process was still based and demonstrated on a 4 step PRISMA flow chart diagram (Figure 1) (PRISMA: Preferred Reporting Items for Systematic Reviews And Meta-Analyses) [15].

Figure 1: The details of the selection process shown in a PRISMA diagram.

Table 1 lists a summary of each of the 29 chosen studies including Country, prevalence of OD (sorted in ascending order), number of PCR confirmed COVID-19 patients, Study type, patient identification/data acquisition tools used, prevalence of GD (if reported), and finally overall summary risk of bias as per Hoy., *et al*. [43].

The summary of the ROB assessment was reported in table 1, and the individual item assessments are shown in table. The majority of studies had moderate risk of bias, primarily because of the non-random sampling process, unclear definition of the loss of sense of smell/taste (partial or complete), and the lack of validated assessment of smell or taste dysfunction.

	Study	Country	COVID Sample	Study type	Patient identification/data acquisition tools	OD	GD	ROB
1	Mao., *et al*. (2020) [21].	China	214	Retrospective observational case series	Clinical records	5.1%	5.6%	H
2	Gudbjartsson., *et al*. (2020) [26]	Iceland	1044	Epidemiological	Phone survey	11.5%		M
3	Lee., *et al*. 2020 [33]	South Korea	3191	Cross sectional	Phone survey	15.3%		M
4	Chua., *et al*. 2020 [32]	Singapore	31	Case-control		22.6%		M
5	Wee., *et al*.2020 [31]	Singapore	154	Case-control		22.7%		M
6	Beltrán-Corbellini., *et al*. (2020) [34]	Spain	79	Case control	Questionnaire survey	31.7%	35.4%	M
7	Giacomelli., *et al*. (2020) [13]	Italy	59	Cross sectional	Interview and questionnaire survey	33.9%	10.2%	M
8	Levinson., *et al*. (2020) [28]	Israel	42	Cross sectional		35.7%	33.3%	M
9	Hornuss D,., *et al*. (2020) [18]	Germany	45	Cross-sectional controlled	Olfactory test (Sniffin' Stick12)	40%		L
10	Qiu., *et al*. (2020) [42]	Multicenter international (China, France, and Germany).	Total 394 [China 239, France 116, Germany 39].	Multicenter case series	Questionnaire of Olfactory Disorders (France and Germany) and objective testing (China)	Overall = 41% (China 32%, France 49%, Germany 69%).		M
11	Bénézit., *et al*. (2020) [22]	France	68	Case control	Self-report via telephone survey and questionnaire	45%	62%	M
12	Klopfenstein., *et al*. (2020) [23]	France	114	Retrospective observational case series	self-reported	47%		M
13	Sakalli., *et al*. (2020) [36]	Turkey	172	Cross sectional	Questionnaire survey	51.2%	47.1%	M
14	Carignan., *et al*. (2020) [20]	Canada	134	Case-control study	Telephone interview with a standardized questionnaire	51.5%	63.40%	L
15	Abalo-Lojo., *et al*. (2020) [35]	Spain	131	Cross sectional	Self-report	58.8%	56.5%	M
16	Zayet., *et al*. (2020) [24]	France	95	Case control	Questionnaire of Olfactory Disorder	63.2%	65.3%	M
17	Spinato., *et al*. (2020) [30]	Italy	202	Cross sectional	Questionnaire survey	64.4%		M
18	Haehner., *et al*. (2020) [17]	Germany	34	Cross-sectional controlled		64.7%		M

19	Menni., *et al*. 2020 [37]	UK	6452 +co-vid-19	Online app Community survey For general population	self-reported via free smartphone app "The symptom tracker"	65%		M
20	Yan., *et al*. 2020 [40]	USA	128	observational case series		66.7%	62.7%	M
21	Schmithausen., *et al* (2020) [16]	Germany	41	Cross sectional	Questionnaire survey	68%		M
22	Yan., *et al*. (2020) [39]	USA	59	Cross sectional	Questionnaire survey	68%	71%	M
23	Vaira., *et al*. (2020) [29]	Italy	72	observational case series		73%		M
24	Kaye., *et al*. (2020) [38]	USA	237	Cross sectional	physician-submitted (The AAOHNS COVID-19 Anosmia Reporting Tool)	73%		M
25	Luers., *et al*.2020 [19]	Germany	72	Cross sectional	Questionnaire survey	74%	69%	M
26	Tsivgoulis., *et al*. (2020) [25]	Greece	22	Case control	Quick Smell Identification Test	77.3%		M
27	Lechien., *et al*. (2020) [12]	Multicenter European Study (12 centers)	417	Cross sectional	Questionnaire survey (Questionnaire of Olfactory Disorders-Negative Statements)	85.6%	82%	M
28	Moein., *et al*. (2020) [27]	Iran	60	Case control	Clinical examination – UPSIT test	98%	23.3%	L
29	Wagner., *et al*. (2020) [41]	USA	2317 PCR+ve vs 74,850 PCR-ve	Case control	AI, Augmented curation of clinical notes from a massive EHR system	27-fold more in PCR+ vs PCR-ve		M

Table 1: Summary of identified studies.

OD: Olfactory Disfunction; GD: Gustatory Disfunction; UPSIT :University of Pennsylvania Smell Identification Test; AI: Artificial Inelegance; EHR: electronic health record; ROB: Risk of bias summary as per Hoy., *et al*. [57]; H: High ROB; M: Moderate ROB; L: Low ROB. Table sorted in ascending order of OD prevalence.

There is great heterogeneity in the reported prevalence of OD as a COVID-19 symptom (5.1% to 98%) (Table 1). A study of 237 patients in the United States showed that 73% of cases reported anosmia prior to the diagnosis of COVID-19, and anosmia was the leading symptom in 26.6% of cases [38]. Patients were identified through the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) COVID-19 Anosmia Reporting Tool [3,44] that allows physicians to report cases.

These results are similar to the ones reported by the "COVID Symptom Study" that used a smartphone app developed by researchers at King's College London, UK, to track the self-reported symptoms of Covid-19 in the UK and USA. Among the 15,638 UK app users who had an RT-PCR SARS-CoV-2 test, 64.76 % of 6,452 UK users who tested positive reported losing the sense of smell or taste, and 56.73 % reported new persistent cough, 34.34% reported fever, and 29.8% reported fatigue. Among the 2,763 US app users who had an RT-PCR SARS-CoV-2 test, 67.49% of 726

users who tested positive reported losing the sense of smell or taste, 44.77 % reported new persistent cough, 27.74% reported fever, and 23.42% reported fatigue, suggesting that losing the sense of smell or taste may be an even a stronger predictor of coronavirus infection than fever, new persistent cough or fatigue [37]. In a much smaller study, German clinicians at the University Hospital in Bonn surveyed 41 confirmed COVID-19 cases and found a prevalence of anosmia or dysgeusia of up to 68% [16].

Using the University of Pennsylvania Smell Identification Test (UPSIT), a well-validated 40-odorant test, on 60 confirmed COVID-19 inpatients in Iran, Moein., *et al*. found that only 1 patient was normosmic, 15/60 were anosmic, 20/60 severely hyposmic, 16/60 exhibited moderate hyposmia and 8/60 exhibited mild hyposmia. Interestingly, although 59 out of 60 (98%) of patients exhibited some degree of smell dysfunction based on the UPSIT, only 29% of patients self-reported loss of smell [27]. Another non-peer-reviewed Iranian study reported a surge in the outbreak of olfactory dysfunction in Iran that is highly correlated with COVID-19 positivity (correlation coefficient = 0.87, pe < 0.001) and found that in just 4 weeks from the start of the COVID-19 epidemic in Iran, among 10,069 self-reported anosmia/hyposmia cases, 76.2% described a new sudden onset of anosmia [45].

In Mayo Clinic, Wagner., *et al*. [41] used artificial intelligence to identify and analyze the clinical features of SARS-CoV-2 infection from 15.8 million clinical notes of 77,167 patients subjected to COVID-19 PCR diagnostic testing. During the week prior to PCR testing, the prevalence of anosmia/ageusia among COVID-19-positive patients (2,317) was 27.1-fold than that of anosmia/ageusia among COVID-19-negative patients (74,850). COVID-19-positive patients reported that anosmia/ageusia was one of the earliest symptoms of COVID-19 [41].

Results from studies in south east Asia (Table 1) appear to indicate the prevalence of OD/GD in that population is less pronounced. In South Korea, a phone survey of 3191 confirmed COVID-19 cases reported a 15.3% prevalence of anosmia/ageusia [33]. Another non-peer-reviewed study by Mao., *et al*., from China retrospectively surveyed the medical records of a total of 214 hospitalized confirmed COVID-19 cases, and found only 5.1% of cases reported hyposmia and 5.6% reported hypogeusia, a non-significant finding (p = 0.338) [21]. In Singapore, Wee., *et al*. [31] reported anosmia in 22.7% of their 154 confirmed COVID-19 cases and Chua., *et al* reported anosmia in 22.6% of their 31 confirmed COVID-19 cases [32].

In an international multicenter case series study by Qui., *et al*. the prevalence of olfactory and/or gustatory disorders among a total of 394 PCR-confirmed COVID-19 patients from China, France, and Germany was 32%, 69%, and 49%, respectively [42].

Discussion

This literature review was conducted to identify the worldwide prevalence of OD/GD in patients with COIVD-19. One major finding is the extreme range of reported rates. The heterogeneity in the reported prevalence of anosmia in COVID-19 patients appear to be explained by four possibilities: (1) population differences (ethnicity); (2) sample differences (age, severity of COVID-19); (3) different mutations of SARS-CoV-2 affecting different regions; (4) different OD/GD diagnostic methods.

There is evidence that Asian patients are less vulnerable to OD/GD manifestations than other ethnic groups, and that anosmia/ageusia might be a symptom in milder cases of the disease, rather than critically ill patients who required hospitalization and formed the majority of patients included in low prevalence studies. Von Bartheld., *et al*. [46] examined the effects of age, ethnicity, and disease severity on the prevalence of anosmia/hypogeusia among COVID-19 patients with a meta-analysis (preprint, not yet peer-reviewed). They found the effect of age to be non-significance, but anosmia/hypogeusia was found to decrease significantly with disease severity and the effect of ethnicity proved to be the most significant of all, where Caucasians had a 3-6 times higher prevalence of anosmia/hypogeusia than East Asians [46]. A likely explanation for such a possibility is an ethnicity-specific genetic difference affecting the virus-binding entry proteins in the olfactory epithelium and taste buds. If this proved to be true, it may lead to a variety of genetic-based studies which may explain many variations in the course of COVID-19 and may thus have a major impact on our understanding of infectivity, diagnosis, and management of the COVID-19.

There is also evidence that different world regions are affected by different mutations of the SARS-CoV-2, which may have different pathogenicities [47]. An interesting study by Forster., *et al*. reported

the existence of three central significant SARS-Cov-2 genotypes (A, B and C), with different geographical distributions. The B genotype is the most prevalent in East Asia, whereas significant proportions of Americans and Europeans are infected with the A and C genotypes [48]. Thus, it is reasonable to speculate that, if such a difference really exists, it may be the reason behind any proven geographical or ethnic discrepancies in the pathogenicity of SARS-Cov-2, explaining the higher prevalence of olfactory disorders among Americans and Europeans compared to Asians.

The last yet very significant explanation is the different methods used to identify patients suffering from olfactory or gustatory disorders. It is clear that unless patients are consciously and directly asked or examined for anosmia/ageusia, many of them wouldn't seek medical attention, wouldn't report and may not even become aware of these manifestations. Reviewing the study with the least prevalence of anosmia (5.1%) [21], the results were based only on data from medical records in which gustatory or olfactory complaints may have been neglected. In contrast, studies reporting much higher prevalence used different tools or questionnaires directly assessing smell and taste.

In addition, some tools may overestimate the prevalence of these chemosensory disorders. Lechien., *et al*. [12] in their multicenter European study, claimed an 85.6-82% prevalence of olfactory or gustatory disorders among COVID-19 patients respectively. However, Passali and Bentivoglio criticized such a high prevalence and described it as "inflated" mainly due to the data collecting tool used. They stated that the "Questionnaire of Olfactory Disorders-Negative Statements" used by Lechien., *et al*. assesses the psychological impairment due to olfactory dysfunction rather than the olfactory impairment itself. Thus, the annoyance, social anxiety, and eating questions included in this Questionnaire may be influenced by the isolation and hospitalization of COIVD-19 patients, which may represent strong confounding factors [49].

The effect of the diagnostic method on prevalence rates is best demonstrated in the Iranian study of Moein., *et al*. where only 29% of their COVID 19 inpatients self-reported smell dysfunction, but when assessed with the UPSIT test it was found that 25% were anosmic, 33% were severely microsmic, 27% exhibited moderate microsmia and 13% were microsmic in other words 98% exhibiting various degrees of smell dysfunction and only 2% were normosmic [27]. Thus, standardization of the procedures and tools to assess and score anosmia among COVID-19 cases is essential to compare the prevalence among different studies and populations.

Olfactory dysfunction has been recognized by many professional organizations as an early symptom of COVID-19 and included OD in their COVID-19 diagnostic guidelines. On March 22nd, 2020, The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) officially recommended on its site [50] to add anosmia and dysgeusia to the list of screening test for possible COVID-19 infection [51].

The British Rhinology Society and the ENT UK (British Association of Otorhinolaryngology - Head and Neck Surgery - BAO-HNS) has stated that the sudden loss of sense of smell and taste are "significant symptoms" recognizing the fact that these may be seen even in the absence of other symptoms, and that they could identify otherwise hidden carriers of this highly contagious disease [8,52,53].

Guidelines of clinical practice of the French Association of Rhinology(AFR) and of the French Society of Otorhinolaryngology (SFORL) also recognized the sudden loss of smell without nasal obstruction, as an important symptom of COVID-19 [54].

On May 18th, 2020 A joint statement was shared by the UK Chief Medical Officers, outlining the addition of a loss of taste and smell (anosmia) to the UK's official list of COVID-19 symptoms [55]. This is in line with the US Centers for Disease Control and Prevention [56] and the World Health Organization [57] who have also added these symptoms to their official guidance.

Based on the current literature, it is strongly recommended that those who suffer from a sudden onset of olfactory and gustatory dysfunction, even in the absence of any respiratory symptoms, to presume they are infected and self-isolate in order to minimize risk to others in case they are asymptomatic but contagious. Furthermore, in view of public health difficulties in performing a timely reverse-transcription PCR, professional testing to evaluate olfactory and gustatory disorders can be a useful and sensitive biomarker to guide prioritization of testing in regions with high reported prevalence of OD/GD among COVID-19 patients. More standardization is also needed in the study designs, patient identification and data acquisition tools to be able to know and compare the exact prevalence of OD/GD in COVID-19

patients globally. Finally, more studies are needed to confirm that heterogeneity in the reported prevalence of OD/GD among COVID-19 patients can be attributed to differences in host and virus genotypes dominating different geographical regions.

Limitations

One limitation is that data from non-peer-reviewed and pre-print literature has been included in the present review. Although each included article was critically analyzed, peer-review adds another layer of trust. Also, there is great heterogeneity in the methods of identification of subjects suffering from OD or GD and the data collecting tools used, which in most studies depended on self-reporting unverified information and different questionnaires assessing different targets and rarely depended on well-standardized objective olfactory assessment tests.

Conclusion

There is great heterogeneity in the reported prevalence of OD/GD as COVID-19 symptoms. Caucasian COVID-19 patients seem to be much more susceptible to OD/GD than East Asians. Preliminary evidence suggests that differences in host or virus genotypes dominating different geographical regions may explain heterogeneity in the reported prevalence of OD/GD among COVID-19 patients, and more standardized studies are needed to explore this suggestion. Meanwhile, in regions with higher prevalence, the sudden onset of OD/GD, especially in the absence of nasal obstruction or any upper respiratory symptoms, can be useful as a sensitive early biomarker of COVID-19 that may help prioritization of COVID-19 testing and promote self-isolation which would reduce exposure to contagious but otherwise asymptomatic individuals who are much more difficult to identify.

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