Olfactory dysfunction: a highly prevalent symptom of COVID-19
with public health significance

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Abstract

Objective: COVID-19 is a global pandemic affecting millions of individuals, killing hundreds of thousands. Although typically described with characteristic symptoms of fever, cough, and shortness of breath, greater understanding of COVID-19 has revealed myriad clinical manifestations. Olfactory dysfunction (OD)—hyposmia and anosmia—has recently been recognized as an important symptom of COVID-19 and increasingly gained traction as a public health tool for identifying COVID-19 patients, in particular otherwise asymptomatic carriers who, unawares, may be major drivers of disease spread. The objective of this study is to review the scientific evidence about anosmia in COVID-19.

Data sources: PubMed, Google Scholar and Web of Science.

Review methods: Comprehensive literature search of primary studies pertinent to the objectives of this review using the chosen data sources.

Conclusions: Current evidence shows that OD is highly prevalent in COVID-19 with up to 80% of patients reporting subjective OD and objective olfactory testing potentially showing even higher prevalence. OD is frequently accompanied by taste dysfunction. Up to 25% of COVID-19 patients may experience sudden onset OD as the first symptom. A large proportion of COVID-19 OD cases may resolve over the period of a few weeks.

Implications for practice: Sudden anosmia should be considered to be a symptom of COVID-19. Assessing for sudden onset anosmia may increase sensitivity of COVID-19 screening strategies, in particular for identifying patients at the earliest
stages of disease. Since many cases of OD due to COVID-19 may resolve in the short term, conservative management including observation is reasonable, while advanced imaging is unnecessary.
The 2019 coronavirus disease (COVID-19) is caused by a novel coronavirus, referred to as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 was initially and is still most commonly described by characteristic symptoms of fever, cough, and shortness of breath. However, COVID-19 is now recognized to be highly heterogeneous in severity—ranging from asymptomatic (or symptoms too mild to be noticed) to severe acute respiratory distress syndrome and death—and in symptomatology, which extends to include otolaryngologic symptoms. While patients with the well-known and characteristic symptoms of COVID-19 may be readily identified (by themselves or others), patients experiencing nonclassical symptoms of COVID-19 may be missed and may serve as vectors for transmission, and therefore persistence, of the disease. In the last few weeks, anecdotal reports from around the world have suggested that olfactory dysfunction (OD)—in particular anosmia—may be an important symptom of COVID-19 and also a significant predictor of asymptomatic COVID-19 carriers.

Methods and Results
The PubMed, Google Scholar and Web of Science databases were searched with combinations of search terms including COVID-19, SARS-CoV-2, coronavirus, anosmia, hyposmia, olfactory dysfunction for any articles that were indexed up to April 18, 2020. While preprints were considered for discussion, only peer-reviewed articles are presented in the evidence table. Due to the rapid proliferation of peer-reviewed scientific evidence that may not yet be database-indexed, online forums
from the American Academy of Otolaryngology – Head and Neck Surgery and American Rhinologic Society were also used to identify studies. Only studies of COVID-19 patients were included, although case reports were not included in the final evidence table. Only articles in English were included. A total of 6 studies representing the existing peer-reviewed evidence on OD in COVID-19 were identified (Table 1).

Discussion

Incidence of olfactory dysfunction in relation to the COVID-19 pandemic

In March 2020, anecdotal reports from around the world described a dramatic increase in the recent incidence of OD, in particular anosmia, which seemed to parallel the spread of COVID-19. A study by Hopkins et al showed that over February and March 2020 in the UK, incidence of patient-reported OD followed an exponential increase similar to the incidence of COVID-19. A study by Bagheri et al, available as a pre-print, showed that the incidence of patient-reported OD across the 31 provinces of Iran since the onset of the COVID-19 epidemic there was highly correlated with the incidence of COVID-19 during that time. These studies provided strong circumstantial evidence for the relationship between OD and COVID-19.

Olfactory dysfunction as a symptom of COVID-19

Although the prevalence of nasal symptoms such as congestion or rhinorrhea in COVID-19 is reported on the order of 5%, OD has been reported as an
increasingly prevalent symptom of COVID-19. A short communication by Vaira et al first reported chemosensory dysfunction—anosmia or ageusia—in at least 19.4% of a cohort of 320 Italian COVID-19 patients.\(^5\) Another study of 59 hospitalized Italian COVID-19 patients found that 23.7% of patients complained of OD, the majority with concomitant taste alteration as well.\(^6\) Reported at the height of the COVID-19 epidemic in Italy and with the stated intention of raising awareness of chemosensory dysfunction as a symptom of COVID-19, the authors hypothesized that the prevalence of chemosensory dysfunction could be even higher given their limitations for assessment.

In fact, subsequent studies have suggested that prevalence of OD in COVID-19 is much higher. A multicenter European study of 417 COVID-19 patients by Lechien et al, representing the first systematically collected data published regarding OD in COVID-19,\(^7\) found that 85.6% of patients reported subjectively decreased sense of smell in association with COVID-19, which was closely correlated with gustatory dysfunction. Of those reporting decreased sense of smell, 79.6% reported a complete loss. A subsequent study by Yan et al described that of 59 patients presenting to their institution with flu-like symptoms and testing positive for COVID-19, 68% reported decreased sense of smell, which was also closely correlated with decreased sense of taste.\(^8\) In comparison, only 16% of a control group of 203 COVID-19 negative patients presenting with flu-like symptoms during the same time period reported a decreased sense of smell.\(^8\)

A high prevalence for OD in COVID-19 has also been described using objective testing of olfactory function. In a study by Moein et al, the mean University
of Pennsylvania Smell Identification Test score in 60 Iranian COVID-19 patients was 20.98 (indicative of severe microsmia) compared to 34.10 (indicative of normosmia) in 60 age-matched controls. Moein et al found that 59 of COVID-19 patients (98%) were experiencing at least some hyposmia: 8 (13%) with mild microsmia, 16 (27%) with moderate microsmia, 20 patients (33%) with severe microsmia, and 15 (20%) with anosmia. In comparison, only 18% of 60 age-matched controls showed evidence of hypmosia, all of which were quantified as mild microsmia. While the etiology of OD in COVID-19 remains unknown, two case reports have shown negative magnetic resonance imaging findings, with normal-appearing olfactory bulbs, although one case report found mucosal obstruction of the olfactory clefts on computed tomography.

Olfactory dysfunction as a predictor of COVID-19

In addition to being a highly prevalent symptom of COVID-19, anecdotal reports have suggested that anosmia may also be used as a predictor of COVID-19. In their study, Yan et al reported that in patients presenting with flu-like symptoms, OD was associated with COVID-19 with an adjusted odds ratio of 10.9. In contrast to the context of concomitant flu-like symptoms, a case report by Gane et al described a COVID-19 patient who presented with sudden onset anosmia but no other symptoms. Gane et al also described a series of 10 new patients presenting with OD during the COVID-19 pandemic, half of whom had other viral prodromic symptoms, and the other half reporting only anosmia.
Consistent with the observation of Gane et al, a recent study lead by Pr Dominique Salmon, MD, PhD (Hôtel Dieu, Paris), and Dr Alain Corré, MD (Hôpital Fondation Adolph de Rothschild, Paris)—the results of which were directly communicated to the authors of this commentary while the manuscript is in review—found that 94% of patients presenting to them with anosmia but no other nasal symptoms and none of the classical respiratory symptoms of COVID-19, tested positive for COVID-19. These findings suggest that during the COVID-19 pandemic, isolated sudden onset OD could be used to screen for and identify asymptomatic carriers.

The utility of anosmia to identify asymptomatic carriers must also be interpreted in the context of how often COVID-19 patients will only exhibit anosmia as a symptom. In Lechien et al’s 417-patient cohort, 11.8% reported OD as the first symptom of COVID-19. In comparison, OD occurred at the same time as other COVID-19 symptoms in 22.8% and after other COVID-19 symptoms in 65.4%. In another cohort of 237 COVID-19 patients with OD submitted to the American Academy of Otolaryngology—Head and Neck Surgery COVID-19 Anosmia Reporting Tool, anosmia was reported to be the first symptom of COVID-19 in 27% of patients. Thus, up to a quarter of COVID-19 patients could potentially be identified at the earliest stages of the disease only by screening for a history of sudden onset OD.

Resolution of olfactory dysfunction
Despite short follow up times inherent to the recent nature of the COVID-19 pandemic, OD will improve in a substantial fraction within 1-2 weeks in conjunction with improvement of infection.\textsuperscript{8,13} Kaye et al reported that 27\% of their 327-patient cohort with COVID-19 and OD experienced at least some improvement of OD with a mean time of 7.2 days.\textsuperscript{13} In comparison, Yan et al reported that 74\% of their 38-patient cohort with COVID-19 and OD experienced improved OD with resolving COVID-19.\textsuperscript{8}

**Limitations**

COVID-19 patients included in the current literature are heterogeneous with respect to recruitment, severity of disease and symptoms experienced. Understandably, patients with the most severe disease (e.g. patients in intensive care) are highly underrepresented in these initial studies. Moreover, there may be many other COVID-19 patient populations who are not yet captured and characterized due to limited testing. Finally, although OD appears to be highly predictive of COVID-19 during the COVID-19 pandemic, sensitivity and specificity are unknown and it is unclear how predictive value will change as prevalence of COVID-19 decreases.

**Implications for Practice**

OD—both subjectively and objectively assessed—is highly prevalent in COVID-19 and screening for COVID-19 should include assessment of OD. Presently, sudden onset OD should trigger COVID-19 precautions, including quarantining, and
consideration for testing (depending on local resources and availability) as well as contact tracing irrespective of accompanying flu-like symptomatology. Isolated sudden onset anosmia without nasal congestion or flu-like symptoms may identify up 25% COVID-19 patients at the earliest clinical stages of the disease and should be used to screen for asymptomatic carriers. Advanced imaging, at least in the short term during the pandemic, is unnecessary especially since a large proportion of patients may experience improvement of OD with resolution of COVID-19.
References


Table 1. Table of evidence

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Key outcome measures</th>
<th>Measurement tool</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaira et al⁵</td>
<td>320 patients with COVID-19</td>
<td>1. Anosmia 2. Ageusia</td>
<td>Not described 1. 19.4% prevalence of chemosensory dysfunction, without distinction of anosmia vs. ageusia.</td>
</tr>
<tr>
<td>Giacomelli et al⁶</td>
<td>59 patients with COVID-19</td>
<td>1. OD 2. Gustatory dysfunction</td>
<td>Patient reports 1. 23.7% of patients reported OD with 78.6 of those patients also reporting gustatory dysfunction</td>
</tr>
<tr>
<td>Lechien et al⁷</td>
<td>417 patients with mild to moderate COVID-19 recruited from 11 hospitals across Belgium, France, Spain and Italy</td>
<td>1. OD prevalence 2. Gustatory dysfunction 3. Associated nasal, systemic and pulmonary symptoms 4. Timing of OD relative to other COVID-19 symptoms 5. Time to resolution of OD</td>
<td>Patient reports 1. 85.6% prevalence of OD 2. Of patients reporting OD, 79.6% reported anosmia 3. 88.0% of gustatory dysfunction 4. OD occurred as the first symptom in 11.8% of cases 5. OD occurred at the same time as other symptoms in 22.8% 6. OD occurred after other COVID-19 symptoms in 65.4% 7. In the subset of clinically cured patients, 44% reported resolution of OD with almost three quarters experiencing resolution within first 8 days after resolution of COVID-19.</td>
</tr>
<tr>
<td>Yan et al⁸</td>
<td>59 patients with COVID-19 presenting with flu-like symptoms and 203 patients negative patients presenting with flu-like symptoms</td>
<td>1. OD 2. Taste loss 3. Resolution of OD</td>
<td>Patient reports 1. In COVID-19 patients, 68% reported OD and 71% reported taste loss 2. In COVID-19 negative patients, 16% reported OD and 17% reported taste loss, which was significantly less compared to COVID-19 patients. 3. In patients presenting with flu-like symptoms, OD was associated with COVID-19 with adjusted odds ratio of 10.9. 4. 74% of COVID-19 patients with OD experienced improvement of OD with improvement of COVID-19.</td>
</tr>
<tr>
<td>Kaye et al¹³</td>
<td>237 patients with COVID-19 and anosmia from around the world submitted to AAO-HNS Anosmia Reporting Tool</td>
<td>1. Timing of anosmia relative to other symptoms and diagnosis 2. Resolution of anosmia</td>
<td>Physician reports 1. Anosmia occurred as the first symptom of COVID-19 in 27%. 2. Anosmia was present in 73% prior to diagnosis 3. Anosmia contributed to COVID-19 testing in 40%. 4. At least some improvement of anosmia experienced by 27% with mean time of 7.2 days.</td>
</tr>
<tr>
<td>Moein et al⁹</td>
<td>60 Iranian patients with COVID-19 patients and 60 approximately age matched controls</td>
<td>1. OD</td>
<td>Patient reports and UPSIT 1. In the COVID-19 cohort, 35% of patients had smell/taste complaints while 0% of controls had these complaints. 2. COVID-19 patients had significantly lower UPSIT score (mean = 20.98 reflective of severe microsmia) compared to controls (mean = 34.10 reflective of normosmia) 3. 98% of COVID-19 patients had objective evidence of OD while only 18% of patients in the control cohort had evidence of OD.</td>
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</table>

OD = olfactory dysfunction
UPSIT = University of Pennsylvania Smell Identification Test