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2 **Olfactory dysfunction: a highly prevalent symptom of COVID-19**
3 **with public health significance**
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38 Keywords: Coronavirus; COVID-19; SARS-CoV2; SARS-CoV-2; anosmia; hyposmia;
39 olfactory dysfunction; olfactory function; olfaction; smell
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42

43 **Abstract**

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

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

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

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

62 **Implications for practice:** Sudden anosmia should be considered to be a symptom
63 of COVID-19. Assessing for sudden onset anosmia may increase sensitivity of
64 COVID-19 screening strategies, in particular for identifying patients at the earliest

65 stages of disease. Since many cases of OD due to COVID-19 may resolve in the short
66 term, conservative management including observation is reasonable, while
67 advanced imaging is unnecessary.

68

69

70 **Introduction**

71 The 2019 coronavirus disease (COVID-19) is caused by a novel coronavirus,
72 referred to as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).¹
73 COVID-19 was initially and is still most commonly described by characteristic
74 symptoms of fever, cough, and shortness of breath. However, COVID-19 is now
75 recognized to be highly heterogeneous in severity—ranging from asymptomatic (or
76 symptoms too mild to be noticed) to severe acute respiratory distress syndrome
77 and death—and in symptomatology, which extends to include otolaryngologic
78 symptoms. While patients with the well-known and characteristic symptoms of
79 COVID-19 may be readily identified (by themselves or others), patients experiencing
80 nonclassical symptoms of COVID-19 may be missed and may serve as vectors for
81 transmission, and therefore persistence, of the disease. In the last few weeks,
82 anecdotal reports from around the world have suggested that olfactory dysfunction
83 (OD)—in particular anosmia—may be an important symptom of COVID-19 and also
84 a significant predictor of asymptomatic COVID-19 carriers.

85

86 **Methods and Results**

87 The PubMed, Google Scholar and Web of Science databases were searched
88 with combinations of search terms including COVID-19, SARS-CoV-2, coronavirus,
89 anosmia, hyposmia, olfactory dysfunction for any articles that were indexed up to
90 April 18, 2020. While preprints were considered for discussion, only peer-reviewed
91 articles are presented in the evidence table. Due to the rapid proliferation of peer-
92 reviewed scientific evidence that may not yet be database-indexed, online forums

93 from the American Academy of Otolaryngology – Head and Neck Surgery and
94 American Rhinologic Society were also used to identify studies. Only studies of
95 COVID-19 patients were included, although case reports were not included in the
96 final evidence table. Only articles in English were included. A total of 6 studies
97 representing the existing peer-reviewed evidence on OD in COVID-19 were
98 identified (**Table 1**).

99

100 **Discussion**

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

102 In March 2020, anecdotal reports from around the world described a
103 dramatic increase in the recent incidence of OD, in particular anosmia, which
104 seemed to parallel the spread of COVID-19. A study by Hopkins et al showed that
105 over February and March 2020 in the UK, incidence of patient-reported OD followed
106 an exponential increase similar to the incidence of COVID-19.² A study by Bagheri et
107 al, available as a pre-print, showed that the incidence of patient-reported OD across
108 the 31 provinces of Iran since the onset of the COVID-19 epidemic there was highly
109 correlated with the incidence of COVID-19 during that time.³ These studies
110 provided strong circumstantial evidence for the relationship between OD and
111 COVID-19.

112

113 **Olfactory dysfunction as a symptom of COVID-19**

114 Although the prevalence of nasal symptoms such as congestion or rhinorrhea
115 in COVID-19 is reported on the order of 5%,⁴ OD has been reported as an

116 increasingly prevalent symptom of COVID-19. A short communication by Vaira et al
117 first reported chemosensory dysfunction—anosmia or ageusia—in at least 19.4% of
118 a cohort of 320 Italian COVID-19 patients.⁵ Another study of 59 hospitalized Italian
119 COVID-19 patients found that 23.7% of patients complained of OD, the majority with
120 concomitant taste alteration as well.⁶ Reported at the height of the COVID-19
121 epidemic in Italy and with the stated intention of raising awareness of
122 chemosensory dysfunction as a symptom of COVID-19, the authors hypothesized
123 that the prevalence of chemosensory dysfunction could be even higher given their
124 limitations for assessment.

125 In fact, subsequent studies have suggested that prevalence of OD in COVID-
126 19 is much higher. A multicenter European study of 417 COVID-19 patients by
127 Lechien et al, representing the first systematically collected data published
128 regarding OD in COVID-19,⁷ found that 85.6% of patients reported subjectively
129 decreased sense of smell in association with COVID-19, which was closely correlated
130 with gustatory dysfunction. Of those reporting decreased sense of smell, 79.6%
131 reported a complete loss. A subsequent study by Yan et al described that of 59
132 patients presenting to their institution with flu-like symptoms and testing positive
133 for COVID-19, 68% reported decreased sense of smell, which was also closely
134 correlated with decreased sense of taste.⁸ In comparison, only 16% of a control
135 group of 203 COVID-19 negative patients presenting with flu-like symptoms during
136 the same time period reported a decreased sense of smell.⁸

137 A high prevalence for OD in COVID-19 has also been described using
138 objective testing of olfactory function. In a study by Moein et al, the mean University

139 of Pennsylvania Smell Identification Test score in 60 Iranian COVID-19 patients was
140 20.98 (indicative of severe microsmia) compared to 34.10 (indicative of
141 normosmia) in 60 age-matched controls.⁹ Moein et al found that 59 of COVID-19
142 patients (98%) were experiencing at least some hyposmia: 8 (13%) with mild
143 microsmia, 16 (27%) with moderate microsmia, 20 patients (33%) with severe
144 microsmia, and 15 (20%) with anosmia. In comparison, only 18% of 60 age-
145 matched controls showed evidence of hypmosia, all of which were quantified as
146 mild microsmia. While the etiology of OD in COVID-19 remains unknown, two case
147 reports have shown negative magnetic resonance imaging findings, with normal-
148 appearing olfactory bulbs,^{10,11} although one case report found mucosal obstruction
149 of the olfactory clefts on computed tomography.¹¹

150

151 **Olfactory dysfunction as a predictor of COVID-19**

152 In addition to being a highly prevalent symptom of COVID-19, anecdotal
153 reports have suggested that anosmia may also be used as a predictor of COVID-19.
154 In their study, Yan et al reported that in patients presenting with flu-like symptoms,
155 OD was associated with COVID-19 with an adjusted odds ratio of 10.9.⁸ In contrast
156 to the context of concomitant flu-like symptoms, a case report by Gane et al
157 described a COVID-19 patient who presented with sudden onset anosmia but no
158 other symptoms.¹² Gane et al also described a series of 10 new patients presenting
159 with OD during the COVID-19 pandemic, half of whom had other viral prodromic
160 symptoms, and the other half reporting only anosmia.

161 Consistent with the observation of Gane et al, a recent study lead by Pr
162 Dominique Salmon, MD, PhD (Hôtel Dieu, Paris), and Dr Alain Corré , MD (Hôpital
163 Fondation Adolph de Rothschild, Paris)—the results of which were directly
164 communicated to the authors of this commentary while the manuscript is in
165 review—found that 94% of patients presenting to them with anosmia but no other
166 nasal symptoms and none of the classical respiratory symptoms of COVID-19, tested
167 positive for COVID-19.⁴ These findings suggest that during the COVID-19 pandemic,
168 isolated sudden onset OD could be used to screen for and identify asymptomatic
169 carriers.

170 The utility of anosmia to identify asymptomatic carriers must also be
171 interpreted in the context of how often COVID-19 patients will only exhibit anosmia
172 as a symptom. In Lechien et al’s 417-patient cohort, 11.8% reported OD as the first
173 symptom of COVID-19.⁷ In comparison, OD occurred at the same time as other
174 COVID-19 symptoms in 22.8% and after other COVID-19 symptoms in 65.4%. In
175 another cohort of 237 COVID-19 patients with OD submitted to the American
176 Academy of Otolaryngology—Head and Neck Surgery COVID-19 Anosmia Reporting
177 Tool, anosmia was reported to be the first symptom of COVID-19 in 27% of
178 patients.¹³ Thus, up to a quarter of COVID-19 patients could potentially be identified
179 at the earliest stages of the disease only by screening for a history of sudden onset
180 OD.

181

182 **Resolution of olfactory dysfunction**

183 Despite short follow up times inherent to the recent nature of the COVID-19
184 pandemic, OD will improve in a substantial fraction within 1-2 weeks in conjunction
185 with improvement of infection.^{8,13} Kaye et al reported that 27% of their 327-patient
186 cohort with COVID-19 and OD experienced at least some improvement of OD with a
187 mean time of 7.2 days.¹³ In comparison, Yan et al reported that 74% of their 38-
188 patient cohort with COVID-19 and OD experienced improved OD with resolving
189 COVID-19.⁸

190

191 **Limitations**

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

201

202 **Implications for Practice**

203 OD—both subjectively and objectively assessed— is highly prevalent in
204 COVID-19 and screening for COVID-19 should include assessment of OD. Presently,
205 sudden onset OD should trigger COVID-19 precautions, including quarantining, and

206 consideration for testing (depending on local resources and availability) as well as
207 contact tracing irrespective of accompanying flu-like symptomatology. Isolated
208 sudden onset anosmia without nasal congestion or flu-like symptoms may identify
209 up to 25% COVID-19 patients at the earliest clinical stages of the disease and should be
210 used to screen for asymptomatic carriers. Advanced imaging, at least in the short
211 term during the pandemic, is unnecessary especially since a large proportion of
212 patients may experience improvement of OD with resolution of COVID-19.
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Table 1. Table of evidence

	Patient population	Key outcome measures	Measurement tool	Main results
Vaira et al ⁵	320 patients with COVID-19	1. Anosmia 2. Ageusia	Not described	1. 19.4% prevalence of chemosensory dysfunction, without distinction of anosmia vs. ageusia.
Giacomelli et al ⁶	59 patients with COVID-19	1. OD 2. Gustatory dysfunction	Patient reports	1. 23.7% of patients reported OD with 78.6 of those patients also reporting gustatory dysfunction
Lechien et al ⁷	417 patients with mild to moderate COVID-19 recruited from 11 hospitals across Belgium, France, Spain and Italy	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	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.
Yan et al ⁸	59 patients with COVID-19 presenting with flu-like symptoms and 203 patients negative patients presenting with flu-like symptoms	1. OD 2. Taste loss 3. Resolution of OD	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.
Kaye et al ¹³	237 patients with COVID-19 and anosmia from around the world submitted to AAO-HNS Anosmia Reporting Tool	1. Timing of anosmia relative to other symptoms and diagnosis 2. Resolution of anosmia	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.
Moein et al ⁹	60 Iranian patients with COVID-19 patients and 60 approximately age matched controls	1. OD	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.

OD = olfactory dysfunction

UPSIT = University of Pennsylvania Smell Identification Test