Anosmia as a presenting symptom of SARS-CoV-2 infection in healthcare workers – a systematic review of the literature, case series, and recommendations for clinical assessment and management *

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Abstract

Background: Healthcare workers are at the forefront of the ongoing COVID-19 pandemic and are at high risk for both the contraction and subsequent spread of virus. Understanding the role of anosmia as an early symptom of infection may improve monitoring and management of SARS-CoV2 infection.

Methodology: We conducted a systematic review of the literature of SARS-CoV2 infection/COVID-19 and anosmia to help inform management of anosmia in healthcare works. We report a case series of healthcare workers, who presented with a loss of sense of smell secondary to COVID-19 infection to demonstrate management principles. RT-PCR was used to confirm COVID-19 positivity and psychophysical testing of olfaction was performed using the British version of the University of Pennsylvania Smell Identification Test, UPSIT.

Results: The systematic literature search returned 31 articles eligible for inclusion in the study and informed our recommendations for clinical assessment and management. All three healthcare professionals who presented with loss of sense of smell subsequently tested positive for SARS-CoV-2. Psychophysical testing of olfaction using the UPSIT confirmed mild and moderate microsmia in two, respectively, and normosmia at day 17 in one.

Conclusions: Olfactory (± gustatory) dysfunction is indicative of COVID-19 infection and thus has important implications in the context of healthcare workers, or key workers in general, who work in close contact with others if not recognised as suffering from COVID. This leads to a potentially higher likelihood of spreading the virus. In conjunction with our literature review these findings have helped with creating recommendations on the assessment and management of olfactory dysfunction during the ongoing COVID-19 pandemic, both for healthcare workers and patients.

Key words: coronavirus, SARS-CoV-2, COVID-19, olfaction disorders, anosmia, pandemic, coronavirus infection

Introduction

Post Viral Olfactory Loss (PVOL) represents approximately 11% of cases of olfactory dysfunction in the community[(1)] but typically accounts for 20-25% of cases presenting to specialist clinics[(2,3)]. Coronaviruses have previously been demonstrated to be among the respiratory viruses that can cause PVOL[(4)]. Increasing number of reports of COVID-19 positive patients describing a loss of smell and taste have been seen internationally since initial reports from China[(5)], Korea[(6)], Italy[(7)] and Iran[(8)]. These may be the only symptoms, early presenting symptoms, or be part of mild

flu-like symptoms[9,10]. This topic has also received significant press coverage, especially with regard to potential public health implications. The World Health Organisation has recently added anosmia to its list of official symptoms and as such, patients experiencing these symptoms need to follow self-isolation guidance. Importantly, individual healthcare institutions may or may not be following these guidelines and awareness of this update may be limited. It is known that the viral load is comparable between symptomatic and minimally symptomatic/asymptomatic individuals thus if people with anosmia were to have COVID-19, transmission is possible[11].

The debate is ongoing as to what extent loss of smell and taste in SARS-CoV-2 infection is caused by localised olfactory cleft oedema, architectural deformity of the olfactory neuroepithelium or direct neuroinvasion of the olfactory nerve pathways. In typical viral mediated olfactory loss, the pathophysiology involves loss of cilia of the olfactory sensory neurons[12]. Furthermore, the loss of taste more likely reflects loss of flavour perception due to loss of retronasal olfaction rather than the loss of the sense of taste per se.

There have been reports of increase in anosmia symptoms and a recent case report of anosmia in a healthcare worker in Madrid who was subsequently diagnosed with SARS-CoV-2. This raises questions regarding the significance of anosmia in COVID-19 - both generally in terms of anosmia management, but also of particular concern to healthcare workers, how to advise healthcare workers who present with such a symptom from a public health aspect in terms of isolation and testing.

Here we present the results of a systematic review of the currently available literature on anosmia in COVID-19 and provide a summary table of the relevant findings. Secondly, we present three representative cases of healthcare workers presenting to our clinics with anosmia as their primary symptom of COVID-19. Finally, combining the findings from the review and the case series together, we provide recommendations on how to adapt existing anosmia management protocols in the context of COVID-19, particularly focussing on healthcare workers.

Systematic review of the literature

A systematic literature search was performed on PubMed on 27 April 2020 using the following search terms: (((((((SARS-CoV-2) OR 2019-ncov) OR coronavirus) OR corona virus) OR COVID-19) OR COVID)) AND ((((((anosmia) OR hyposmia) OR loss of smell) OR smell) OR olfact*) OR cacosmia) OR dysosmia). We also screened BioRxiv and MedRxiv on for preprints related to anosmia in SARS-CoV-2. Inclusion criteria were papers describing reports of anosmia in patients in the context of COVID-19, regardless of patient demographics, number of cases, and method of anosmia assessment. Date criteria were from 31/12/2019 to 27/04/2020. We hand searched citing literature and references of included studies. Papers that did not provide patient level data were not included for data extraction. We did not search for or include articles in the lay press or online forums. We also did not screen studies reporting general clinical features of anosmia as a recent review from The Centre for Evidence Based Medicine has assessed these studies already and found the evidence base was inconclusive[13]. The authors did recommend incorporation of olfactory history and assessment in further studies. This conclusion was also reached by Lovato and colleagues who provide an overiew of upper respiratory tract symptoms in COVID-19[14]. Finally, any identified reviews were used to identify studies but were not themselves included in the data extraction. Data extraction included: number of patients, study method, onset of anosmia relative to COVID-19 symptoms, COVID-19 positivity and method of testing, time for recovery from anosmia, and summary findings. Formal evaluation and assessment of risk of bias of included papers was not performed.

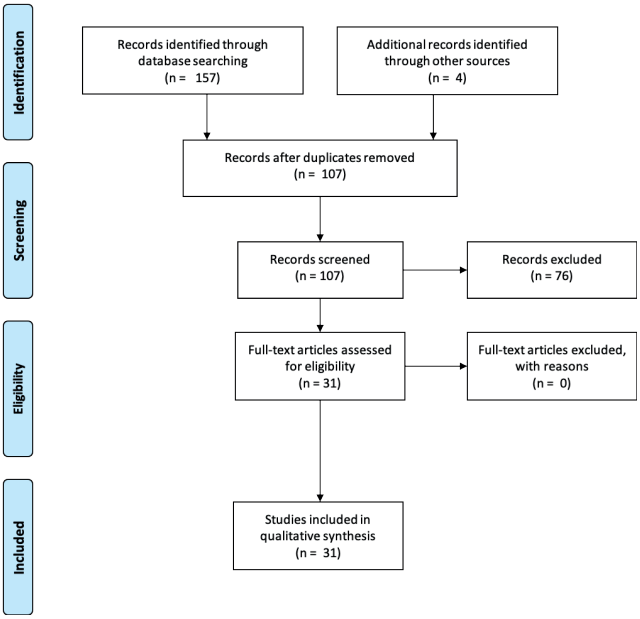

Figure 1. PRISMA flow diagram of literature search and screening for relevant studies.

We found 107 unique papers of which 31 were eligible for inclusion in the study (Figure 1). Summary findings of the included studies are in Supplemental Table 1 for reference. The 31 papers included work from multiple continents. The majority were cross sectional studies, case series or case reports. Diagnosis of smell dysfunction was variable and used a variety of published and custom designed self-reported surveys of anosmia/COVID-19 symptoms either in person, online, or via apps. Formal psychophysical testing of olfaction used the Nez-du-Vin, country specific UPSIT or the Sniffin' Sticks.

Table 1. Summary of case series.

Case #	Age/ Sex	Patient History	Other Symptoms	UPSIT Score	COV-ID-19 RT-PCR	Other Medical History
1	43/M	Presented with loss of smell, initial onset one week prior to presentation	Feeling hot and cold, runny nose, mild bilateral nasal obstruction, no cough, persistent olfactory dysfunction	25	Positive	Gastric sleeve operation, hernia repair, smoker (5/day)
2	37/M	Presented with loss of smell five days prior to presentation, subsequent metallic smell and taste	Recurrent temperature, myalgia, fatigue, dry cough, runny nose and sneezing	28	Positive	Septoplasty, thoracotomy and pleurectomy of right lung following spontaneous pneumothorax, toxoplasmosis of right eye
3	53/M	Presented with loss of smell, initial onset 2 days after flu-like symptoms	Mild flu-like symptoms, residual tiredness after 14 days self-isolation, early loss of smell (recovered)	34	Positive	

Anosmia is presenting as the primary symptom or as an early symptom in patients who have tested COVID+. In a European study, 11.8% of patients reported anosmia onset before other otorhinolaryngological symptoms[15]. In the American Academy survey, 26.6% reported it as an isolated initial symptom[16] and the Centre for Disease Control and Prevention has just added this to the symptoms related to COVID-19, but individual institutions may or may not be testing based on this symptom. Other surveys did not have a sufficient tested population. Thus, identifying olfactory dysfunction could potentially have a role in the diagnosis of COVID-19. One study formally assessed smell and taste loss in a stepwise regression model and found them to be strongly associated with COVID-19. In fact it was the strongest predictor from a list of other symptoms and had a positive predictive value of 67%[17]; the caveat of this study was that only 0.1% of all participants had been tested for COVID-19. Anosmia may also have potential to discriminate COVID-19 from other viral respiratory illnesses[18,19].

Where anosmia is reported in the context of COVID-19, due to the short time that has elapsed since the pandemic started, data on the recovery of olfactory function is not always available. In the studies that have reported it in COVID-19 tested patients, albeit from surveys, complete resolution was seen in 13% and partial resolution in 14%, with a mean time to improvement of 7.2 days[16]. This is lower than the recovery rates reported by Lechien and colleagues[15] who suggest a short term recovery rate of 44% in 59 patients who had clinically recovered from COVID-19, and also lower than the 73% that reported by Levinson and colleagues[20], although only 15 patients make up this cohort. Recovery seems to take place within a few weeks but this may be due to short follow up and recovery may happen in others over a longer timeframe. The coming months will begin to reveal whether COVID-19 will leave a larger burden of persistent PVOL patients in the community.

Correlations suggested between disease mild severity disease and anosmia are necessarily preliminary. Whilst some suggestions are made that anosmia is associated with milder disease[21,22], this could be confounded by the inability to assess/self-report anosmia in those patients with severe disease in intensive care settings. However, a higher viral load, potentially indicative of more severe disease, does seem to be associated with a shorter duration of anosmia[23].

Whether the underlying cause of anosmia is conductive or sensorineural was attempted to be addressed by two studies that assessed imaging of the olfactory system[24,25]. Anosmia was found to be obstructive in nature rather than neural with a normal olfactory bulb. However, the presence of nasal obstructive symptoms (albeit subjectively reported) in patients with anosmia varied widely in the included studies. The reports of ACE2 receptor expression in non-neuronal cells and supporting olfactory sustentacular cells may support this finding [26-29]. Alternatively, the virus could migrate from these cells if it were neurotropic[30,31].

Healthcare workers suffering from anosmia were reported in multiple studies and in the American Academy data, approximately a third of patients were healthcare workers(16). Whilst this could be due to selection bias as only healthcare workers could enter data into the reporting tool, it suggests that both anosmia and COVID-19 in healthcare workers is an issue that is important to consider. Below, we present three illustrative cases to highlight issues to consider in the assessment and management of healthcare workers with anosmia.

Case series

Three healthcare professionals, a 43-year-old male nurse, a 37-year-old male Specialty Registrar in Rheumatology and a 53-year-old male Consultant Anaesthetist, presented to our ENT

clinics with loss of their sense of smell and a history of other mild flu-like symptoms (Details in Table 1) in the last 3 weeks. In view of the emerging literature, we performed a COVID-19 real-time reverse transcription polymerase chain reaction (RT-PCR) swab test and confirmed COVID-19 infection. Formal assessment of their olfactory function was performed using the British version of University of Pennsylvania Smell Identification Test (UPSIT), a validated psychophysical test in line with the guidelines in the Position paper on olfactory dysfunction[32]. This confirmed moderate microsmia (UPSIT score of 25/40) in patient 1, mild microsmia (UPSIT score of 28/40) in patient 2 and the third patient told us that he felt that his sense of smell had already almost recovered at the time he was seen and he scored 34/40 on day 17. All three individuals were advised to contact occupational health for further advice, were given safety advice regarding his olfactory dysfunction, and referred to a website with validated patient information on their condition and guidance on olfactory training (www.fifthsense.org.uk).

Discussion and recommendations

The presence of anosmia in the context of COVID-19 raises three main questions. Firstly, if a person develops isolated anosmia, what is the likelihood they already have, or will go on to develop, COVID-19? Secondly, what is the best strategy for treatment for anosmia in the context of COVID-19 and what is the prognosis for recovery of olfactory function? Finally, what is the underlying mechanism and pathophysiology of the anosmia?

At present the answers to the above questions are limited until high-level robust evidence available. A global survey of COVID-19 related chemosensory impairment is currently underway: https://gcchemosensr.org.

The mechanism at present is also debated with some suggesting the SARS-CoV-2 virus is neurotropic but others arguing the expression of target receptors in non-neuronal olfactory/nasal region cells suggests a possible inflammation with an obstructive cause of anosmia. There is also the possibility that acquired mutations of SARS-CoV-2 have enabled the virus to alter its pathogenicity and which may play a role in altering disease presentation[33]. Nevertheless, the work presented here does highlight that anosmia in healthcare workers may be indicative of COVID-19. When combined with the preliminary evidence that anosmia is a strong diagnostic symptom, this has potentially important implications when anosmia is considered in the context of healthcare workers, or key workers in general. The ongoing potential contact with other people due to the nature of such professions means someone with COVID-19 is potentially at higher likelihood both of contracting the virus and of spreading the virus if they were to catch it – anosmia may be an early symptom of this. There are limitations in the evidence presently available. The majority of studies are cross sectional or retrospective with limited prospective follow up. Many cases rely on self-reporting and COVID-19 laboratory confirmed numbers are small. Where testing is performed, it relies on the RT-PCR test which the Centre for Evidence-Based Medicine reported to have as high as a 30% false-negative rate[34]. Finally, formal assessment of anosmia varied with multiple survey types used and assessment modalities hence comparability and evidence synthesis are limited to comparable studies.

Whilst the recent work by Hunter and colleagues[35] suggests that there is a comparable rate of COVID-19 positivity in front-line clinical staff compared with non-clinical staff in hospitals, the authors suggest this shows isolation and PPE measures are adequate at present to prevent nosocomial infections and the transmission may reflect that from the community. This is supported by a reduction coinciding with the UK wide lock-down timing. However, the authors only tested staff with new continuous cough and fever as per current PHE recommendations rather than staff screening for those with wider symptoms or if asymptomatic. Therefore, the work presented here is of relevance as it shows that testing may potentially need to be extended to a wider spectrum of symptoms, particularly if community transmission seems to be the prime vector. The other caveat is that a comparison with other institutions and control groups of non-hospital key-workers would also be helpful.

Our recommendations for the management of patients, particularly healthcare workers, with symptoms of hyposmia/anosmia during the COVID-19 crisis are guided by the Position Paper on Olfactory Dysfunction[3] and include:

- Discussion regarding isolation and testing for COVID-19 with institutional occupational health service.
- Full remote history asking about onset, duration, other COVID-19 symptoms, exposure risks, past otorhinolaryngological history, and general medical history.
- If no other red flag symptoms (such as facial pain, serosanguinous discharge, visual changes) and acute onset particularly in relation to flu-like symptoms during the COVID-19 pandemic, imaging (CT/MRI) is not indicated.
- Ideally psychophysical testing[30,32] but this may be limited by resource and default to self-reporting, although individuals can be asked to self-test at home against common food cupboard items. Psychophysical testing, which can be done remotely (e.g. country specific UPSIT)[36] will avoid direct contact with patients.
- Provide advice regarding safety precautions including need for gas alarm, smoke alarm, and care with use by dates for food. Patients can be directed to relevant online resources such as the Fifth Sense website.
- Current guidance is to avoid oral steroids due to the poten-

tial risk of worsening COVID-19, as evidence from previous SARS in 2004 where systematic corticosteroids led to an increase in viral shedding[37]. However, current trials, such as the RECOVERY trial for COVID-19 include systemic steroids in a treatment arm, so this advice may alter if these trials show evidence of benefit or at least no precipitation of deterioration in recipients. Intranasal steroids are unlikely to be harmful in patients already taking them but a fear of promoting viral shedding in new patients means advice currently is to avoid them.

- Provide advice regarding olfactory training (e.g. from organisations such as Abscent/Fifth Sense).
- Rhinology follow-up after crisis. Only consider an MRI olfactory protocol if there are any other concerning symptoms, but if there is a clear temporal history relating to the viral infection, especially where COVID+ve status is confirmed, an MRI scan is not indicated.

National organisations in the UK and USA have recommended the addition of anosmia as a diagnostic symptom in the WHO criteria and potentially isolating if new onset anosmia is experienced as a symptom. Future work regarding the diagnostic utility and prognosis in large all-comer cohort studies with sufficient laboratory-based testing will hopefully provide stronger evidence for ongoing diagnosis and care of these patients. Until this time, we hope the evidence summary and recommendations in this work will be of use to care providers, researchers and public health organisations in their work.

Conclusion

Loss of sense of smell and taste appears to be indicative of COVID-19 infection and has important implications in the context of healthcare workers, or key workers in general, who are in ongoing close contact with others due to their work. This leads to a potentially higher likelihood of contracting and spreading the virus. This literature review has helped to underline the clear link of loss of the senses of smell and taste during the ongoing COVID-19 pandemic, both for healthcare workers and patients. We hope our illustrative case series and recommendations can thus be applied to help manage these presentations of anosmia in the current climate until further evidence is available.

Authorship contribution

ML has led on the concept and written the initial draft with the help of DC, who conducted the systematic review. KJ, JL, SG, VJL, CP, and SJ helped writing the manuscript, reviewed final draft and advised on the clinical guidelines for the management of patients with symptoms of hyposmia/anosmia during the COVID-19 crisis.

Conflict of interest

The authors declare no conflicts of interest relevant to this work.

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SUPPLEMENTARY INFORMATION

Supplemental Table 1 Summary of findings from systematic literature review

Reference	Location	Method	Cohort	Summary of Findings	Further Details of Olfactory Dysfunction
Bagheri et al, 2020	Iran	Cross-sectional survey	n = 10069; mean age 32.5, 71% female; with new onset anosmia or hyposmia	Significant correlation between anosmia and COVID-19 positivity; sudden symptom onset in 76.2%	Nasal stiffness in 43.7%, rhinorrhea in 15.63%
Beltran-Corbellini et al., 2020	Spain	Case control study	n = 79 COVID+, mean age 61.6, 59.2% females; n = 40 influenza+, mean age 61.1, 52.5% female	New onset olfactory/taste disturbances more frequent among COVID+ (39.2%) than influenza+ (12.5%)	acute onset olfactory/taste disorder in 27%, as initial symptom in 35.5%; 80.6% with smell disorders; 45.2% anosmia, 29.0% hyposmia, 6.5% dysosmia; complete recovery (40%) after mean 7.4 days; partial recovery (16.7%) after mean 9.1 days; 12.9% reported concomitant nasal obstruction
Benezit et al, 2020	France	Cross-sectional survey	n = 259, 68 COVID+ by RT-PCR	45% hyposmic; strongest association seen with hypogeusia and hyposmia in patients without history of ENT disorders	
Drew et al, 2020	UK	Cross-sectional survey	n = 265,851 reporting COVID+ symptoms, RT-PCR in 0.2%; mean age 41, 75% female	Anosmia fifth most common symptom reported, more common than fever	
Eliezer et al, 2020	France	Case Report	n = 1, female in 40's	COVID+ by RT-PCR with dry cough, cephalgia, myalgia prior to anosmia	CT/MRI showed olfactory cleft obstructive inflammation, no changes to olfactory bulb, no nasal obstruction symptoms
Galougahi et al, 2020	Iran	Olfactory bulb scanning in COVID+ patient with anosmia	n = 1, 27-year-old male	MRI showed normal olfactory bulb volume, normal signal intensity	No sign of nasal congestion
Gane et al, 2020	UK	Case series	n = 11, mean age 37.6, 27% female, all with anosmia and symptoms of COVID	One 48-year-old male neurosurgeon with anosmia tested COVID+ by RT-PCR, anosmia as isolated symptom in n = 5, part of other possible COVID-19 symptoms in n = 6	
Giacomelli et al, 2020	Italy	Cross-sectional survey	n = 59; median age 60, 32% female; COVID+ hospitalised patients	11.9% hyposmic, 11.9% anosmic	20.3% reported taste/smell disturbance prior to hospital admission, 13.5% experienced symptoms during hospital stay
Gudbjartsson et al, 2020	Iceland	Targeted testing of high-risk individuals and population screening	n = 4551 (tested by RT-PCR); mean age 44.4 in first round screening, 42.0 in second round screening; 47.7% female	n = 528 were COVID+, 4.4% experienced loss of smell; none in population screening repoted loss of smell	
Gutierrez-Ortiz et al, 2020	Spain	Case Report	n = 2, 50 year-old-male and 39-year-old male	Patient 1: 2-day history of vertical diplopia, perioral paraesthesias and gait instability, diagnosed with Miller-Fisher Syndrome; reported anosmia with other COVID-19 symptoms; Patient 2 reported dysgeusia and had polyneuritis cranialis	Residual anosmia persisted despite treatment of MF Syndrome

Reference	Location	Method	Cohort	Summary of Findings	Further Details of Olfactory Dysfunction
Heidari et al, 2020	Iran	Case series	n = 23, COVID+ with anosmia, mean age 37.4, 65% female	83% reported anosmia as first symptom; low grade fever in 3 cases, mild myalgia and fatigue in 4 cases	Anosmia as only symptom in 16 cases, persisted for a few days
Hopkins et al, 2020	UK	Cross-sectional survey	n = 2428; median age 30-39, 73% female	74% of those tested for COVID-19 were positive (59/80); 13% reported anosmia prior to disease onset, 38.4% at same time, 48.6% after other symptoms	
Jang et al, 2020	South Korea	Case report	n = 1, 42-year-old male	anosmia at presentation, only sign in a contact of a COVID+ patient; onset 2 days after quarantine	isolated symptom; persisted longer than 2 weeks; no rhinorrhea or nasal obstruction
Kaye et al, 2020	International (USA, Mexico, Italy, UK and others)	Cross-sectional survey	n = 237, mean age 39.6, 54% female	Over 33% reported cases were from healthcare workers, anosmia noted in 73% prior to COVID-19 diagnosis	Anosmia was isolated initial symptom in 26.6%, complete resolution in 13%, partial resolution in 14%, mean time to improvement 7.2 days, nasal congestion prior to anosmia in 25%, rhinorrhea prior to anosmia in 18%
Klopfenstein et al, 2020	France	Retrospective series	n = 114 COVID+, n = 54 with anosmia; mean age 47, 67% female	47% confirmed COVID-19 reported anosmia	Anosmia never the first or second symptom; third presenting symptom in 38%; developed 4.4 days after infection onset; mean duration was 8.9 days, duration ≥ 7 days in 55%, ≥ 14 days in 20%; one patient had anosmia persisting beyond 28 days; rhinorrhea in 57%, nasal obstruction in 30%
Lechien et al, 2020	Europe	Cross-sectional survey	n = 417, COVID+, mean age 36.9, 63% female	85.6% reported olfactory dysfunction, 79.6% were anosmia, 20.4% hyposmic	Olfactory dysfunction prior to onset of general/ENT symptoms in 11.8%, after in 65.4%, same time in 22.8%; dysfunction persisted after resolution of other symptoms in 63%, n=76 did not experience nasal obstruction or rhinorrhea
Lechien et al, 2020b	Belgium	Cross-sectional study	n = 78, mean age 40.6, 59% female	62% anosmia 12 days with 87.5% COVID-19 positive; 38% > 12 days with 23% COVID-19 positive	52% anosmic, 24% hyposmic, 24% normosmic; of patients with anosmia, 79.1% reported nasal obstruction symptoms, 64.6% reported rhinorrhea, 75% reported postnasal drip
Levinson et al, 2020	Israel	Cross-sectional survey	n = 42, COVID+ hospitalised inpatients with mild disease; median age 34, 45% female	Anosmia reported in 35.7% of patients; n=14 reported both anosmia and dysgeusia, n=1 reported only anosmia	Anosmia and dysgeusia started median 3.3 days post disease onset; 73.3% with anosmia reported recovery, median 7.1 days for dysgeusia, 7.6 days for anosmia
Lorenzo-Vilalba et al, 2020	France/Spain	Case reports	n = 2, 85-year-old male and 80-year-old female	Anosmia presented early in disease; one patient died of ARDS after 5 days	85-year-old male experienced sudden onset of anosmia and fatigue prior to admission, died on day 6 after presentation; 80-year-old female had a 5-day history of taste loss prior to smelling problems and fatigue
Mao et al, 2020	China	Retrospective observational case series	n = 214, COVID+, mean age 52.7, 59.3% female	Smell impairment in 5.1%, 3/88 in severe patients, 8/126 in non-severe patients	Onset 1 day prior to admission in severe patients, 2 days prior to admission in non-severe patients
Marchese-Ragona et al, 2020	Italy	Case series	n = 6; patients presenting with hyposmia as main/only symptom; mean age 32.3, 67% female		1 patient had fever after smell dysfunction, 2 patients reported myalgia one day prior to onset of hyposmia and mild dry cough after hyposmia

Reference	Location	Method	Cohort	Summary of Findings	Further Details of Olfactory Dysfunction
Menni et al, 2020	UK	Cross-sectional survey	n = 579, COVID+, mean age 40.79, 69% female; n = 1123 controls, mean age 41.22, 74% female	Loss of smell and taste in 59.4% COVID+, 18.97% COVID-; positive predictive value = 61.7%	
Moein et al, 2020	Iran	Cross-sectional study	n = 120 hospitalised patients; mean age 46.6, 33% for COVID+; mean age 46.6, 33% female for controls	35% of COVID+ reported taste/smell complaint, 98.3% had olfactory dysfunction by UPSIT; no controls reported smell/taste problems, 18% had mild microsmia by UPSIT; mean UPSIT for COVID+ was 20.98, 34.10 for controls	
Ollarves-Carrero et al, 2020	Spain	Case report	n = 1, 40-year-old female	Anosmia presented 2 days after myalgia, headache, chills, abdominal pain and diarrhea; at same time as cough	Gradually improved and resolved after 14 days
Paoli et al, 2020	Italy	Case Report	n = 1, 31-year-old male	Anosmia after onset of other typical symptoms	
Spinato et al, 2020	Italy	Cross-sectional survey	n = 202 COVID+ patients; median age 56, 52.0% female	Change to smell or taste reported by 64.4%	Occurred before other symptoms (11.9%, at the same time (22.8%) or after other symptoms (26.7%); 34.6% with smell dysfunction also reported blocked nose
van Damme et al, 2020	Belgium	Case report	n = 1, 39-year-old female	Report of a nurse with onset of rash followed by pyrexia and headache, subsequently developed anosmia and dysgeusia	Anosmia onset 1 week after other symptoms, recovered after 1 week; also reported rhinorrhea
Wee et al, 2020	Singapore	Prospective study	n = 870 suspected COVID patients	17.9% of suspected patients tested positive; 22.7% of these had olfactory/taste disturbance; high specific of olfactory dysfunction as screening criterion for COVID-19 (98.7%) but lower sensitivity (22.7%)	3/35 presented with isolated anosmia; rhinorrhea in 28.5%; COVID+ patients had higher odds of olfactory/taste disturbance compared to those positive for other respiratory viruses (OR = 10.14, $p < 0.001$)
Xydakis et al, 2020	Unavailable	Letter	n = 1	COVID+ with anosmia and dysgeusia	Traditional nasal manifestations as seen with other upper-respiratory infections typically absent with COVID+, often no significant nasal congestion or rhinorrhea
Yan et al, 2020	USA	Cross-sectional survey	n = 59, COVID+, 49% female; n = 203 COVID-, 65% female	Olfactory dysfunction in 68% of COVID+, 16% of COVID-	22% reported anosmia at initial presentation of disease, 74% had return of function (18% <1 week, 37.5% by 1-2 weeks, 18% by 2-4 weeks); nasal obstruction in 47.5% of COVID+, 44.8% COVID-; rhinorrhea reported in 30.5% of COVID+, 40.9% of COVID-
Yan et al, 2020b	USA	Retrospective review	n = 128 COVID+ patients, median age 53.5, 65% female for admitted patients, 49% for outpatients	Anosmia strongly and independently associated with patients remaining in outpatient care; 10-fold less chance to be admitted than normosmia	Rhinorrhoea in 1 admitted patient, 15.7% of outpatients; nasal obstruction in 15.4% admitted patients and 30.4% of outpatients