REVIEW ARTICLE

A review of smell and taste dysfunction in COVID-19 patients

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ABSTRACT

Introduction: Multiple anecdotal reports suggest that smell and taste loss were early subclinical symptoms of COVID-19 patients. The objective of this review was to identify the incidence of smell and taste dysfunction in COVID-19, determine the onset of their symptoms and the risk factors of anosmia, hyposmia, ageusia or dysgeusia for COVID-19 infection.

Methods: We searched the PubMed and Google Scholar on 15th May 2020, with search terms including SARS-COV-2, coronavirus, COVID-19, hyposmia, anosmia, ageusia and dysgeusia. The articles included were cross sectional studies, observational studies and retrospective or prospective audits, letters to editor and short communications that included a study of a cohort of patients. Case reports, case-series and interventional studies were excluded.

Discussion: A total of 16 studies were selected. Incidence of smell and taste dysfunction was higher in Europe (34 to 86%), North America (19 to 71%) and the Middle East (36 to 98%) when compared to the Asian cohorts (11 to 15%) in COVID-19 positive patients. Incidence of smell and taste dysfunction in COVID-19 negative patients was low in comparison (12 to 27%). Total incidence of smell and taste dysfunction from COVID-19 positive and negative patients from seven studies was 20% and 10% respectively. Symptoms may appear just before, concomitantly, or immediately after the onset of the usual symptoms. Occurs predominantly in females. When occurring immediately after the onset of the usual symptoms, the median time of onset was 3.3 to 4.4 days. Symptoms persist for a period of seven to 14 days. Patients with smell and taste dysfunction were reported to have a six to ten-fold odds of having COVID-19.

Conclusion: Smell and taste dysfunction has a high incidence in Europe, North America, and the Middle East. The incidence was lower in the Asia region. It is a strong risk factor for COVID-19. It may be the only symptom and should be added to the list of symptoms when screening for COVID-19.

KEYWORDS:
COVID-19; SARS-COV-2; smell; taste; dysfunction

INTRODUCTION

The severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) or Coronavirus disease 2019 (COVID-19) has infected more than 5.2 million people with 330,000 over fatalities as of May 2020.[1] The outbreak was first detected in Wuhan, China in December 2019 and has rapidly spread globally over the last six months. It is transmitted via droplet inhalation through the upper respiratory tract and was declared a global pandemic by the World Health Organization (WHO) on 11th March 2020.

The typical general symptoms of COVID-19 are fever, cough, and shortness of breath. Other symptoms include sore throat, nasal congestion, body aches, myalgia, headaches, nausea and vomiting, diarrhoea and abdominal pain.[2] Anosmia and ageusia or smell and taste dysfunction are not listed symptoms as part of the screening criteria.

Since being declared a pandemic, there have been anecdotal reports suggesting that smell and taste loss were early subclinical symptoms of COVID-19. Otorhinolaryngology (ORL) or Ear, Nose and Throat (ENT) societies have alerted physicians to the risk of patients having COVID-19 with isolated smell or taste dysfunction before the general symptoms occur (i.e. fever, dry cough, fatigue and shortness of breath).[3]

In mid-March 2020, the German virologist Professor Hendrick Streeck, reported that more than two in three of 200 confirmed COVID-19 patients interviewed in a hospital reported loss of smell and taste.[4] France in a press release said anosmia without nasal obstruction is a pathognomonic sign of COVID-19 infection after their interview with 55 COVID-19 patients.[5] Iran showed a dramatic increase in complains of anosmia across multiple regions since the start of the coronavirus outbreak.[6]

Although some countries have passed their peak of infections, others such as Brazil, Russia, Peru and Mexico are seeing an increase in cases.[7] According to Professor Claire Hopkins, the President of the British Rhinological Society (BRS), in the UK, there were a significant number of essential workers who had anosmia or hyposmia but did not meet criteria for a swab test and were forced to go to work. These people potentially had COVID-19 and their diagnosis could have been missed thus contributing to the spread of disease.[8]

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As a result, this has led to the announcement of BRS on the 21st March 2020 to call for healthcare professionals to don adequate personal protective equipment (PPE) in view of strong evidence of anosmia being a valid symptom for COVID-19.[3] Meanwhile in the USA, the Center for Disease Control and Prevention (CDC) in April 2020 added loss of taste or smell to its list less common symptoms that may arise two to 14 days after exposure to the COVID-19 virus.[9] Furthermore, many nations have yet to include smell and/or test disorders as a screening symptom for COVID-19.

There were three objectives with the present review. Firstly, it was to identify the incidence or frequency of smell and taste dysfunction in COVID-19; secondly, to determine the onset of the smell and taste dysfunction whether it was before, during or after the general symptoms of COVID-19 (i.e., fever, cough, shortness of breath) and finally, to determine if smell and taste dysfunction is a significant risk factor for COVID-19.

MATERIALS AND METHODS

This literature review was narrative in nature. Latest manuscripts within the past six months (coinciding with the start of COVID-19) on COVID-19 from peer-reviewed journals were included. Searches was conducted using the PubMed and Google Scholar database on 15th May 2020.

Search terms used were "SARS-CoV-2 AND hyposmia OR anosmia AND coronavirus" (Search 1) and "SARS-CoV-2 AND ageusia OR dysgeusia AND coronavirus" (Search 2). Relevant references from individual articles were retrieved and included.

The inclusion criteria were cross sectional studies, observational studies and retrospective or prospective audits, letters to editor and short communications that included a study of a cohort of patients. Case reports, case-series, reviews, and interventional studies were excluded. Both published and unpublished (pre-print) materials were included.

Data from shortlisted papers were divided equally between four researchers, two each for Search 1 and Search 2 respectively who obtained full texts and reviewed the manuscript. Risk bias was minimised by adhering to the objectives of this study. Duplicate articles were removed. A second author re-reviewed the full text manuscripts. Significant and relevant results were tabulated based on authors, study designs, sample sizes, symptoms, age groups, gender, duration, and recommendations. Wherever possible results collected on smell and taste dysfunction were tabulated based on COVID-19 positive or negative patients with respective sample size.

Additional analysis was performed to identify the incidence or frequency of smell and taste dysfunction in COVID-19. Only case control studies with COVID-19 negative patients as a control were used for incidence calculation. The calculation of incidence is based on the total number of smell and taste disorders in COVID-19 positive patients/total number of Covid-19 positive and negative patients that were included.

In all, both searches revealed 630 results and a total of 16 manuscripts were included in this narrative review tabulated in Table I. The studies comprised of 3 prospective audits, 5 retrospective audits, 6 short communications and 2 pre-prints.[10-25] The studies were published between 25th February 2020 to 12th May 2020.

Anatomy and Physiology of Olfaction

The zone of smell of the classical olfactory system in the nose lies in the olfactory epithelium, located at the roof of the nasal cavity. It covers an area of about 5cm^2 on either side of the nose, including superior turbinates, septum and ethmoid bone. The structure of the nose is designed, in part, to direct inspired air toward the olfactory epithelium. The neuroepithelium is characterised by the presence of olfactory neurons whose axons project through the cribriform plate of the ethmoid bone, and synapse with neurons in the central olfactory nervous system. The group of axons form an olfactory tract that connects to olfactory bulb on the ventral surface of the frontal lobe. The axons then travel to the olfactory cortex in the inferior and medial temporal lobe. Some project to limbic system and hypothalamus, where smells associated with long-term memory and emotional response. Newer studies revealed a more extensive distribution of olfactory epithelium that involves the anterolateral part of middle turbinate and posterior nasal septum.[26]

Odorant particles are inhaled through the nose and carried by the turbulent airflow to the olfactory epithelium superiorly and dissolve into mucous membrane. These odorant molecules are transported by binding proteins to the olfactory receptors within the cell membrane of an olfactory dendrite. Binding of the odorants to the specific olfactory receptors induces graded membrane potential in the olfactory neurons, which transmits signals to the brain.

Besides the normal route, some of the odorants reach the olfactory epithelium by ascending through the nasopharynx and posterior choanae. This retronasal olfaction has contributed in part to the sensation of flavour during consumption of food and liquids.[26] This may explain the reason why taste sensation can be affected when the olfactory function is impaired.

Smell and Taste Dysfunction In COVID-19

Olfactory dysfunction presenting as anosmia or hyposmia has an overall prevalence rate of 3 to 20%. It usually affects males predominantly and is worse in the older age groups.[27-30] Olfactory dysfunction in the viral upper respiratory tract infections is not uncommon and is present in up to 30% of patients.[27] Causal viruses include rhinovirus, parainfluenza, adenovirus, Epstein-Barr virus and coronavirus.[31]

All reviewed studies involved positive or confirmed COVID-19 cases. Majority of studies had lab-based confirmation in the form of reverse transcriptase polymerase chain reaction (RT-PCR) of nasopharyngeal and/or throat swabs and Bronchial-Alveolar-Lavage (BAL).

There were a total of seven studies that looked into smell and taste dysfunction and compared its symptoms between COVID-19 positive and negative patients.[11,18-20,23-25] The total

smell and taste dysfunction complaints in COVID-19 positive patients was 5077, almost twice that of smell and taste dysfunction in non-COVID-19 patients at 2648 (ratio 1.9:1). There were 65.1% (5077/7798 patients) COVID-19 positive patients who had smell and taste dysfunction smell and taste dysfunction compared to only 21.2% (2648/12491 patients) who were COVID-19 negative with smell and taste dysfunction.

Therefore, the total incidence of smell and taste dysfunction from COVID-19 positive and negative from the seven studies above is 30 in 100 patients (30%). The incidence of smell and taste dysfunction among COVID-19 positive patients is 20 in 100 patients (20%). The incidence of smell and taste dysfunction among COVID-19 negative patients is 10 in 100 patients (10%).

In our review, only two studies reviewed anosmia and hyposmia alone.[19,23] The rest of the studies also reviewed ageusia and dysgeusia and documented a very close relation between smell and taste dysfunction. They found that among the COVID-19 positive patients the incidence of smell and taste dysfunctions ranged from 11% to 86%.[14,17] This was higher compared to COVID-19 negative patients where the incidence ranged from 12 to 27%.[11,18,20,24]

Smell and taste dysfunction in COVID-19 appeared to have different characteristics from the other viruses described above. They are often the first symptom to be reported in mildly symptomatic patients in COVID-19.[22] They seem to appear just before, concomitantly or immediately after the onset of the general symptoms of fever, cough, myalgia and shortness of breath. When appearing before the onset of the general symptoms, they can occur 11.8 to 58% of the time.[11,12,14,22,23] When occurring immediately after the onset of the general symptoms, the median time of onset was 3.3 to 4.4 days.[13,21] The symptoms of anosmia, hyposmia, ageusia and dysgeusia usually persist for a period of about seven to 14 days with a majority improving after two weeks.[11,13-16,25]

They are associated with mild nasal obstruction 13 to 50% of the time and usually have no other rhinological symptoms (i.e., nasal congestion, rhinorrhoea, itchiness, facial pain) evident by their relatively low SNOT-22 score in the Spinato et al. cohort (i.e., median score of four).[11,12,20-23,25] In some studies, olfactory dysfunction was the only symptom reported.[14,21] Predominantly women and younger patients presented with chemosensory dysfunction.[10-16,18-25] Patients with smell and taste dysfunction were reported to have a six to ten fold odds of having COVID-19.[18,25]

There were two studies reporting patients with COVID-19 with smell and taste dysfunction having able to differentiate sweetness, saltiness, and bitterness, controlled by specific taste afferents ranging between 60 to 88.9%. This suggests that COVID-19 may have an affinity or tropism to specific olfactory sensors.[11,32]

Demographic Distribution of smell and taste dysfunction in COVID-19

Then incidence of smell and taste dysfunction was higher in Europe (34 to 86%), North America (19 to 71%) and the Middle East (36 to 98%) when compared to the Asian cohorts (11 to 15%). Some authors believed that this was because there was a decreased focus on nasal obstruction, rhinorrhoea and chemosensory complaints in these cohorts due to the initial clinical impact, rapid spread and severity of the disease.[13,14]

However, a large epidemiological report of 1099 patients from China documented that cough (68%), fever (44%), fatigue (34%), and sputum production (34%) were the most prevalent symptoms.[2] Nasal congestion or rhinorrhoea accounted for 4-6% of their cohort that was similar to another study in China.[2,33] Tonsil swelling and throat congestion accounted for 2% of complains and sore throat 14%.[2]

Therefore it is possible that the clinical differences in patients are due to the affinity of the COVID-19 virus to different tissue sites in different ethnic groups as alluded by Lechien et al., or the possibility of a mutated viral genome in Europe and North America.[13,14]

Pathophysiology of Anosmia

Initially, it was thought that mechanical obstruction due to excess production of mucous during active infection was the cause of anosmia, however persistent anosmia in patients with normal acoustic rhinometry post infection suggests that there may be a different pathophysiology resulting in more lasting damage.[31]

COVID-19 enters into its human host by a cell surface receptor known as angiotensin-converting enzyme 2 (ACE2), which is expressed in the human airway epithelia, lung parenchyma, vascular endothelia, kidney cells, and small intestine cells.[34] ACE2 receptor binds to the S1 spike glycoprotein in the viral envelope. The virus then enters the host cell through endocytosis.

However, it requires a second protein known as transmembrane protease serine 2 (TMPRSS2). TMPRSS2 is a protease that resides in the endosomal compartment that primes and cleaves the S1 spike glycoprotein, allowing fusion of the viral envelope with the endosomal compartment of the host cell.[35] Respiratory viruses such as influenza A, parainfluenza and Japanese encephalitis have known to use the olfactory nerves to gain access to the central nervous system.[15,36] Similarly, SARS-coronavirus have shown intracranial trans-neural access via olfactory bulb in mice models following intranasal inoculation.[37] Therefore, it is believed that SARS-CoV-2 may share the same properties of its predecessors.

Studies from the 1960s have shown that coronovirus's are neuroinvasive and neurotropic. That means that it can penetrate the central nervous system (CNS) and infect neurons and glial cells and could induce an overreaction of the immune system.[38]

This has been seen in Wuhan, China where some patients with COVID-19 also showed neurologic signs, such as headache, nausea, and vomiting.[34] A recent study found expression of both ACE2 and TMPRSS2 in nasal respiratory tissue, as expected, but also in olfactory neuroepithelia, central nervous systems and lymphoid tissues.[39]

This was confirmed by another study that also found that nasal epithelial cells, including clusters of goblet cells and ciliated cells, have the highest expression among all investigated cells in the respiratory tree.[40] Moreover, as COVID-19 is an enveloped virus, its release does not require cell lysis. Thus, the virus might exploit existing secretory pathways in nasal goblet cells for low-level, continuous-release at the early stage with no overt pathology.[40]

There are also suggestions that besides ACE2, difference in levels of expression of spike S protein for viral entry as mentioned above and nucleoplasmid N protein for transcription may influence the behaviours of COVID-19 within different regions and ethnicity.[14]

Although, the exact mechanism of smell and taste dysfunction in COVID-19 is not known, there are a few theories out there. Firstly, it could be due to direct damage of the virus to the olfactory receptors.[41] Secondly, COVID-19 causes inflammation to the olfactory epithelium. The epithelium contains sustentacular cells that structurally support sensory neurons, provide nutrients, and maintain the salt and water balance. Therefore during an infection, damage of sustentacular cells could cause a disruption in the olfactory epithelium and degradation of sensory neurons leading to anosmia.[42] This was supported by a recent study that found that expression of both ACE2 and TMPRSS2 on the olfactory epithelium sustencular cells comparable to those observed in lung cells.[42] Thirdly, nasal subepithelial mucosal inflammation could prevent odours from reaching the olfactory mucosa.[43]

LIMITATIONS

This review is subject to several limitations. Firstly, most of the studies were retrospective in nature. For the studies that were prospective, some studies interviewed their patients through the telephone and questionnaires. Therefore, there was a possibility of recall bias regarding the accuracy of symptoms of patients.

Secondly, there was a lack in formal quantitative chemosensory testing and as such may have led to an overrepresentation of anosmia and ageusia.

Thirdly, smell and taste dysfunction in the COVID-19-positive patients were more likely to respond based on the increased media reporting of smell loss and/or desire to share their experience, as compared to the COVID-19-negative patients especially when obtaining data from telephone interviews and online questionnaires.[15,18] However, the argument against the above limitations was that anosmia, hyposmia, ageusia and dysgeusia were not ambiguous symptoms and would likely to be recalled by patients given the lack of these symptoms in COVID-19 negative patients.[15]

Fourthly, follow-up was reported in only five studies evident by the median recovery time of smell and taste dysfunction.[11,13-15,25] As such, the incidence of long term smell and taste dysfunction was not known.

AUTHORS' OPINIONS

Smell and taste dysfunction appear to be a common early clinical presentation especially in Europe, North America, and the Middle East. Olfactory dysfunction is highly prevalent and has a high sensitivity rate as an early marker for COVID-19.[11,13,18-25] In some cases anosmia or hyposmia may be the first and only symptom.[14,21]

The symptoms of anosmia, hyposmia, ageusia and dysgeusia could be a useful, harmless, inexpensive and efficient way to evaluate potential patients for COVID-19. This allows patients to be tested early for COVID-19 and self-isolate. It would also allow for healthcare workers to employ universal precautions when seeing these patients in clinic.[3] We anticipate that this would help aid early diagnosis and mitigate the spread of COVID-19. Therefore, we recommend the addition of anosmia, hyposmia, ageusia and dysgeusia to the list of criteria for screening of COVID-19.

The authors earlier set out to assess viral loads and smell and taste dysfunction but yielded no results. Although the majority used COVID-19 RT-PCR, they were mostly qualitative and not quantitative. Therefore, there needs to be studies on quantitative RT-PCR viral loads in association with anosmia/hyposmia scoring.

In light of suggestions of variation of ACE2, TMPRSS2, protein S and protein C, further studies should include tissue biopsies from the olfactory mucosa to gain a correlation (if any) between the presence of these receptors with hyposmia/anosmia.

Although questionnaires may be quick, a combination of a quantitative test (e.g., University of Pennsylvania Smell Identification Test - UPSIT, Sniffin Stick Test) and subjective questionnaires with elimination of confounding factors such as chronic rhinosinusitis and nasal polyposis may provide for a more robust study.

Lastly, we also recommend the avoidance of nasal endoscopy among patients with smell and taste dysfunction for the first two weeks of onset of symptoms in the absence of red flag symptoms, unless necessity dictates so with adequate PPE as they could potentially be infected with COVID-19.

CONCLUSION

Smell and taste dysfunction has a high incidence in Europe, North America and the Middle East. The incidence is lower in the Asia region. It is a strong risk factor for COVID-19. The symptoms may appear just before, concomitantly, or immediately after the onset of the general symptoms of COVID-19 and usually resolve within one to two weeks. They appear predominantly in the younger age group and female gender. Anosmia and hyposmia usually appear in tandem with ageusia and dysgeusia. These symptoms should be added to the list of symptoms when screening for COVID-19.

Table I: Reviewed manuscripts with results and recommendations

Author (Published) Article type	Region (State, Country)	Study Design/ Sample Size	Sample Size & S&TD Results	Symptoms onset (before, during, after)	Mean/ Median Age (years)	Gender	Duration	Level of care	Recommendation(s)
Tostmann et al. (23rd April 2020) *rapid communication*	Nijmigen, Netherlands	Cohort. Case controlled. Questionnaire, prospective	+ve COVID-19, n=79 Anosmia: 37 (46.8%) -ve COVID-19, n=190 Anosmia: 7 (3.7%)	n/a	n/a	F(>70%) *overall respondents*	n/a	n/a	Anosmia and muscle ache are strongest predictors, with high sensitivity (91.2%) and moderate specificity (55.6%). Targeted screening and isolation involving this population
Beltran-Corbellini et al. (22nd April 2020) *short communication*	Madrid, Spain	Multicentred, case controlled, telephone & inpatient questionnaire	+ve COVID-19 (n=79), **S&TD:31 (39.2%)** Anosmia:14 (45.2%) Hyposmia: 9 (29.0%) Dysosmia: 2 (6.5%) Ageusia: 14 (45.2%) Hypogeusia: 7 (22.6%) Dysgeusia: 8 (25.8%) +ve sweet/salt/bitter: 21 (67.7%) -ve COVID-19 (+ve Influenza, n:40), S&TD: 5 (12.5%) +ve sweet/salt/bitter: 5 (100%)	Acute: 21 (67.7%) Subacute: 10 (32.3%)	Mean: 52.6±17	M (60.8%)	Mean:7.1d SD: 3.1d	n/a	S&TD commoner in COVID-19 compared to influenza and to be used in COVID-19 suspicions and isolation
Mao et al. (25th February 2020) *retrospective audit*	Wuhan, China	Single centred retrospective.	+ve COVID-19, n=214 **Hypogeusia: 12 (5.6%)** **Hyposmia: 11 (5.1%)**	During	n/a	F(60%)	n/a	mixed	COVID-19 enters the CNS through hematogenous or retrograde neuronal route Patients with CNS symptoms are more severe with poorer prognosis
Lee et al. (11th May 2020) *brief communication*	Deagu, Korea	Home patients, retrospective telephone interviews,	+ve COVID-19, n= 3191 **Anosmia OR Ageusia: 488 (15.3%)** Anosmia & Ageusia: 254 (8%) Ageusia: 99(3%) Anosmia:135 (4%)	During	Mean: 36.5 (24.5 - 54)	F(67%)	anosmia & ageusia Median: 7d	mild - critical	Anosmia and ageusia are important for diagnosis of early COVID-19 Anosmia and ageusia for suspicion and diagnosis of asymptomatic to mild COVID-19

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Speth et al. (17th April 2020) *prospective audit*	Aarau, Switzerland	single centre, prospective, cross-sectional telephone questionnaire	+ve COVID-19: n=103 **S&TD:n=63 (61.2%)** [Mild=12.7% Moderate=12.7% Severe=81%] Hyposmia:14.6% Anosmia:46.6% Dysgeusia:25.2% Ageusia:65.2% taste dysfunction, n=67 (65%) [Mild=10.4% moderate=22.4% severe=67.2%]	After: 3d (median)	n/a	F (51.5%) M (48.5%) *overall respondents*	n/a	n/a	OD is highly prevalent early symptom and severe 30% - 50% of patients attributed symptoms of nasal congestion and rhinorrhoea younger age and female being associated with OD
Lechien et al. (6th April 2020) *prospective audit*	Multiple; Spain, Italy France	Multicentred (12), questionnaire, survey	+ve COVID-19:n =417 **Olfactory Disorder, n=357 (85.6%)** Anosmia: 284 (79.6%) Hyposmia: 73 (20.4%) Pantosmia (12.6%), Parosmia (32.4%) **Gustatory (Taste) Disorder, n:342 (88.8%)** Reduced: 78.9% Distorted/ unable taste: 21.1% Constant/ fluctuating: 72.8%/23.4%	Olfactory Before: 11.8% During: 22.8% After: 65.4% Unsure: 9.4% Gustatory: n/a	mean 37 (+/-11.4)	F (63%)	Hyposmia/ Anosmia 1-4d: 33% 5-8d: 39.6% 9-14d: 24.2% >15d: 3.3%	mild - moderate (excluding ICU)	loss of smell frequently occurs concomitant to loss of sense Sudden anosmia or ageusia are important symptoms COVID-19 Employ psychophysical or electrophysiological methods for assessing smell and taste
Yan et al. (24th April 2020) *retrospective audit*	California, USA	single institution, cross-sectional study, questionnaire	+ve COVID-19, n=59 **anosmia/hyposmia: 40 (68%)** **dysgeusia/ageusia:42 (71%)** -ve COVID-19, n=203 anosmia/hyposmia: 33 (16%) dysgeusia/ageusia: 34 (17%)	n/a	36.9±11.4	F (63%)	Anos/ hyposmia 29/40 (72.5%) improved <1 w:18%, 1-2 w:37.5%, 2-4 w:18%	low hospital admission	Anosmia/hyposmia, Ageusia/dysgeusia 10-fold more common in COVID-19 cases than non-COVID-19

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Moein et al. (17th April 2020) *prospective audit*	Iran	single institution, case-controlled study, inpatients, UPSIT test;	+ve COVID-19: n=60; OD: 59 (98%) anosmia: 35 (58%) moderate: 16 (27%) mild: 8 (13%) -ve COVID-19: n=60. normal:49 (82%) mild hyposmia: 11 (18%)	During/ Immediately after	46.55 (12.17)	M (66%)	n/a	n/a	anos/hyposmia, is a major marker for COVID-19 infection
Giacomelli et al. (26 March 2020) *correspondence*	Milan, Italy	Cross sectional survey, questionnaire.	+ve COVID-19: n=59. Dysgeusia: 5 (8.5%) Ageusia: 1 (1.7%) Hyposmia: 3 (5.1%) **S&TD: 20 (33.9%)**	before hospital: 12 (20.3%) during hospital: 8 (13.5%)	median 56	F (53%)	n/a	non ventilated	S&TDs are common in COVID-19 and may precede the onset of full-blown clinical disease
Levinson et al (11 April 2020) *pre print*	Israel	prospective, single centre, inpatient questionnaire survey phone/email	+ve COVID-19: n=42; anosmia: 15 (35.7%) dysgeusia: 14 (33%) **Anosmia & dysgeusia: 14 (33%)**	median: 3.3 d after other symptoms	median 34	M: 23 (54.7%) F: 19 (45.3%)	n/a	mild	Anosmia and dysgeusia more common in mild disease Anosmia and dysgeusia appeared early in third of patients (short-lived)
Aggarwal et al (29 April 2020) *retrospective audit*	USA	Retrospective study, single centre	+ve COVID-19, n=16 **S&TD: 3 (19%)** Anosmia: 3 (19%); Dysgeusia: 3(19%)	n/a	mean 67	M (75%)	n/a	n/a	n/a

Abbreviations: SD: Standard Deviation; OD: Olfactory dysfunction; F: Female; M: Male, d day; w: week, CNS: Central Nervous System; USA: United States of America; UK: United Kingdom, n/a; not applicable

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