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Review Article

# Olfactory dysfunction in COVID-19; Self-report or olfactory dysfunction test?

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## *Abstract*

***Background:*** COVID-19 developed a sudden onset of smelling disorders. Researchers used self-reported or special tests to study this issue. We aimed to investigate whether quantitative-test smell disorders have a considerable difference from self-reported or not.

***Methods:*** We searched 554 studies published between December 2019 to September 2020 by the PICO model. Our search strategies were based on MeSH terms in the electronic databases Web of Science (136 articles), Scopus (84 articles), and PubMed (334 articles). The duplicated articles were excluded, then the preferred reporting items for systematic reviews and meta-analysis guidance were utilized. Finally, we divided the studies into two (self-report (33 articles) and specific-test (9 articles)) groups.

***Results:*** 33 (80%) articles expressed olfactory dysfunction by self-report of patients and 9(20%) studies were conducted by a specific test. Only three studies, one in self-report; ((internal reliability, Cronbach $\alpha = 0.84$) and validity ($r = -0.60$, $p < 0.001$)) and two in specific-test groups; ((test-retest r=0.94) and another study (test-retest r >0.7)) conducted validity and reliability. Self-reported studies published a various range of prevalence (20% _97%) in patients with COVID-19. COVID-19 patients with a specific-test group were found to have a primary incidence of anosmia of over 65%, even reaching 98% depending on the types of tests.

***Conclusion:*** Self-reporting of COVID-19 detection can be affected by sociodemographic factors. Although self-reported questionnaires are economical and easy to use, standardized tests provide more reliable comparisons and professional assessments. Therefore, standardized tests are recommended for more accurate screening over self-reporting.

***Keywords:*** Anosmia, COVID-19, Smell, SARS-CoV-2.

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The first pandemic in 21 century was declared on March 11, 2020, by the World Health Organization (WHO), which was seen first in Wuhan, China (1). It was the third severe respiratory infection outbreak that coronaviruses were responsible for. After SARS-CoV which led to severe acute respiratory syndrome (SARS) in 2002-2003 and MERS-CoV which was related to the Middle East respiratory syndrome in June 2012, it was time for SARS-CoV-2 to widespread rapidly all over the world and caused the recent Coronavirus Disease 2019 (COVID-19) pandemic. SARS Cov-2, an enveloped plus-strand RNA virus, could contaminate both animals and humans. Droplet transmission, aerosols, and direct contact with nasal, oral, and even eye mucous secretions are the transitional pathways (2). More than 267 million cases led to about 5.287 million deaths all over the world were reported. Fever, dry cough, and tiredness consist of the most common triad but this virus is more complicated and could only appear through headache, nasal congestion, diarrhea, conjunctivitis, sore throat, skin rashes, discoloration of fingers and toes, and especially olfactory dysfunction (3).

Some patients may not recognize the disease and be asymptomatic and most symptomatic ones will not need hospital treatment. But unfortunately, some high-risk cases become seriously ill and develop hard breathing in case of pneumonitis or acute respiratory distress syndrome. This virus could stay 1 to 14 days (averagely 5.2 days) without any expressions and suddenly manifests and cause difficulties (3).

The sudden onset of different stages of smelling problems, related to SARS Cov-2, all over the world took physician's attention to this symptom. Soon, a significant raising in presenting anosmia and hyposmia as the only symptom of Covid-19 made the concern of the existence of many unknown and unnoticeable carriers and the rapid spread of the virus. So, detection of these patients is necessary as olfactory dysfunction can happen beforehand with other symptoms and could give this chance to patients to take action about the disease immediately (1).

The COVID-19 is a new challenge and the studies are in the beginning, it is felt necessary to have suitable tools for screening and correcting diagnosis of patients. Several studies were done and also some reviews tended to anosmia and hyposmia but to our knowledge, none of them were based on quantitative and validated tests. The self-report and different questionnaires on smell loss were the patient's detection strategy of most studies (3). In addition, the exact pathogenesis of the virus related to olfactory dysfunction is unclear. This finding could make good developments in therapeutic intervention.

## Methods

We selected 554 studies published between December 2019 to September 2020. Relevant literature was identified as follows: pertinent articles in the following electronic databases: Web of Science (136 articles), Scopus (84 articles), and PubMed (334 articles); we developed search strategies using keywords and MeSH terms (Covid-19 or Coronavirus or SARS-CoV-2 or Coronavirus Disease) and (Olfaction Disorders or Anosmia or Smell Disorder or Smell Disorders)).

The abstract of each article was carefully reviewed to detect appropriate publication; full-text articles were retrieved and read carefully, including all reference lists of all relevant articles to identify additional eligible publications; and references from previously retrieved articles and all eligible studies were also searched manually. The search strategy for studies using the PICO model (P, Problem, Patient or Population, I, Intervention, C, Comparison, Control or comparator, and O) is outlined in table 1. The previous study was used to define the scale (4). The inclusion of studies was based on whether they used one scale or compared different scales in Covid-19 patients or tested for olfactory dysfunction in the population.

Inclusion criteria were: clinical trials, prospective studies, retrospective cohort studies, cross-sectional studies; original research in adult human survivors. The study selection process is depicted diagrammatically in fig. 1. Retrospective cohort studies, prospective studies, cross-sectional studies, clinical trials, and original research in adult human survivors were the inclusion criteria. Figure 1 depicts the study selection process in a diagrammatic way. The following articles were not included: studies that were highly selected or treatment studies without incidence data; nonadult populations; single case reports; commentary articles; editorials; review articles; and full texts that are not in English or cannot be accessed. The extraction of descriptive data (first author, year of publication, place of study, studied patients, scale, type of instrument, and the result of the study) was done for each study. Dr Saheb Alzamani and Alijanpour independently extracted data and cross-checked the information to confirm the studies after reading each article carefully. We discussed any disagreement until we came to an agreement. If the disagreement persisted, Dr. Saadat was consulted. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance was used. Finally, included studied divided to self-reported group (with 33 researches) and specific test group (with 9 articles) (5). Finally, included studies were divided to self-reported groups (with 33 researches) and specific test group (with 9 articles).

## Results

After using the inclusion and exclusion criteria through 334 articles, we divided the remaining studies (42 ones) into two groups: self-report or specific test. Thirty-three (80%) articles expressed olfactory dysfunction by self-report of clients and 9(20%) studies were conducted via a specific test. Only three studies, one study in self-report; Carignan et al. (internal reliability, Cronbach $\alpha = 0.84$) and validity ($r = -0.60$, $p < 0.001$).) and two studies in a specific test group; Moein et al.'s study ((test_retest r=0.94) and Alijanpour et al.'s study (test_retest r >0.7) conducted validity and reliability which is shown in tables 2 and 3. Self-report studies reported a various range of prevalence of smell disorders (20%_97%) among patients with COVID-19 and in studies using specific test, the main incidence of anosmia in covid-19 patients were more than 65% even near 98% depending on the type of test.

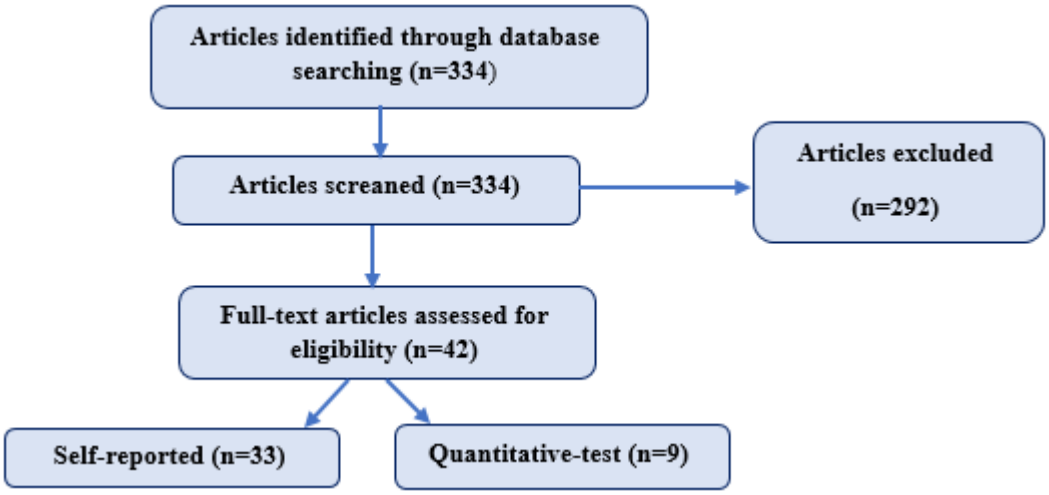


**Figure 1. The study selection process diagram**

**Table 1. Studies search strategy with picos model**

| *PICOS* | Definition |
|---|---|
| *P* | (‘covid-19’ OR ‘Coronavirus’ OR ‘SARS-CoV-2’ OR ‘Coronavirus Disease’) AND (‘Olfaction Disorders’ OR ‘Anosmia’ OR ‘Smell Disorder’ OR ‘Smell Disorders)). |
| *I* | (‘University of Pennsylvania Smell Identification Test’ OR ‘Iranian Version of University of Pennsylvania Smell Identification Test’ OR ‘means of the Connecticut Chemosensory Clinical Research Center orthonasal olfaction test’ OR ‘Sniffin Sticks’ OR ‘Short type of the Questionnaire of Olfactory Disorders- Negative Statements’ OR ‘Visual analog scale and questionnaire of olfactory disorders’ OR ‘American Academy of Otolaryngology–Head and Neck Surgery Anosmia Reporting Tool’ OR ‘ Global Consortium for Chemosensory Research questionnaire’) |
| *C* | (‘reliability’ OR ‘validity’ OR ‘sensivity’ OR ‘specify’ |
| *O* | (diagnose OR ‘impairment’ OR ‘screening’) |
| *S* | (‘randomized trial’ OR ‘cohort analysis’ OR ‘intervention study’ OR ‘longitudinal study’ OR ‘cluster analysis’ OR ‘crossover trial’ OR ‘cluster analysis’ OR ‘cluster analysis’ OR ‘major clinical study’)/de OR (cohort OR longitudinal OR controlled trial OR clinical trial OR crossover trial OR cluster analysis OR randomized trial). |

**Self-report:** In the current study, we categorize the online questioner, self-report, and filling questioner by interviewing as self-report. In Carignan et al.’s article, an age-matched case−control study, the odds ratio (OR) for the association of anosmia or dysgeusia or both with SARS-CoV-2 positivity was 20.0 (95% confidence interval [CI] 7.3– 54.6) and the difference between women (16.9, 95% CI 7.6–37.4) and men (26.9, 95% CI 8.7–82.8) was not significant (6). In an Iranian study by Jalessi M et.al, 23.91% of patients reported the olfactory loss, of whom 6.52% patients related it as the primary symptom. Anosmia was identified in 40.9% and hyposmia in 59.1%. Likert scale questionnaire with a five-point scale was chosen for olfaction and taste evaluation both at the disease onset and for follow-up (7). Hopkins C et.al designed an Online Survey to investigate smell disturbance. It was completed by 382 patients. 86.4% reported absolute anosmia and 11.5% complained of high degree smell loss. After 1 week, a follow-up survey showed that 80.1% had fewer symptoms, 17.6% were not changed and 1.9% had worsened (8).

**Short type of the questionnaire of olfactory disorders-negative statements:** In a multicenter European study by Lechien et.al, among 417 certain COVID-19 patients, 357 (85.6%) cases presented olfactory dysfunction according to the infection (79.6% anosmic and 20.4% hyposmic). The prevalence of olfactory disturbance was significantly more in females. The short version of the Questionnaire of Olfactory Disorders- Negative Statements (sQOD-NS) and the smell and taste item of the National Health and Nutrition

Examination Survey were utilized in this study to identify the olfactory impairment (9).

**Visual analog scale and questionnaire of olfactory disorders (QOD):** About 41% of subjects in Qiu C et al.'s study, represented smell and/or taste dysfunction (among 394 screened patients). According to the country, 32% in China, 69% in Germany and 49% in France were reported. Although the visual analog scale (10) was used to quantify the olfactory disorders, the presence and severity of hyposmia were expressed by a questionnaire on olfactory disorders(QOD). Olfactory dysfunction's characteristics are evaluated using QOD-P (parosmia statements) (11). In VAS among 113 participants, the mean score was 3.60 ± 3.62 (IQR, 0-7). The result of QOD in the QOD-P (parosmic statements) part was 40% ± 30% (IQR, 17%-60%) (11).

**Online questionnaire:** Through a self-administered online questionnaire by Gómez-Iglesias P et al., about 97.7% of 909 suspected COVID-19 patients reported olfactory impairment. In the questionnaire 82.8% chose anosmic part which were defined as no smell sensation, 15.6% were hyposmic as they had decreased sensation which at least were able to sense 2 types of odorants and 0.9% were dysosmic (they complain of unpleasant smell sense). At time of this study, only 7.6% had positive test for COVID-19 and other participants were included by susceptible symptom which had doctor's confirmations (12).

**American academy of otolaryngology–head and neck surgery (AAO-HNS) anosmia reporting tool:** Sayin.I et al., compared the olfactory dysfunction in (COVID-19)–positive subjects with COVID-19–negative ones using AAO-HNS. A significant difference in smell impairment was seen between two groups. (In COVID-19–positive group n = 46[71.9%] vs n = 17 [26.6%] for the COVID-19–negative ones, P = 0.001). In participants reported smell disorders, anosmia rates were not significantly different among two groups (n = 8 [12.5%] for the COVID-19–positive group vs n = 3 [4.7%] for the COVID-19–negative group, P = 0.115) but hyposmia and parosmia were significantly high in the COVID-19–positive group. 51.6% of COVID-19–positive group vs 15.6% of COVID-19–negative group, P = 0.001 reported hyposmia and [17.2%] for the COVID-19–positive group vs [3.1%] for the COVID-19–negative group, P = .008 complained of parosmia (13).

**Table 2. Category and sub category of Olfactory test in studies**

| Author's | Year | Aims | Outcome | Test | Item and category | Validity and reliability |
|---|---|---|---|---|---|---|
| Alijanpour | 2021 | Assess the olfactory dysfunction status in COVID-19 clients with standard Iran Smell Identification Test | One-hundred cases (42.2%) had hyposmia and 20 cases (8.4%) anosmia. Type of covid-19 sign and symptom were statistically significant with olfactory dysfunction. | Iranian verified version of Pennsylvania Smell Identification (IR-SIT) | 6 odorants, 5 or 6 accurate detection is normal, under 4 accurate answer is hyposmia and full false answer is anosmia<br>Cut point=5 | (test_retest r > 0.7) |
| Moein | 2020 | To assess the presence, magnitude, and frequency of confirmed COVID-19 patient's olfactory dysfunction. And determine whether the smell loss is related to the severity of disease, sex and age of the subjects. | Fifty-nine (98%) of the 60 patients exhibited some smell dysfunction thirty-five of the 60 patients (58%) were either anosmic or severely microsmic, 16 exhibited moderate microsmia, 8 mild microsmia and 1 normosmia | The University of Pennsylvania Smell Identification Test (UPSIT) | 40 odorants in form of microencapsulated "scratch and sniff" ones and classified olfactory impairment in 6 level as follows; Anosmia, severe microsmia, moderate microsmia, mild microsmia, normosmia and malingering<br>Cut point=31 | (test_retest r=0.94) |
| Vaira | 2020 | Objectively evaluate the gustatory and olfactory function, through the use of psycho-physiological objective tests, in COVID-19 patients | 73.6% of the patients reported having or having had chemosensitive disorders. Olfactory assessment showed variable degree hyposmia in 60 cases and anosmia in two patients. Gustatory assessment revealed hypogeusia in 33 cases and complete ageusia in one patient | The Connecticut Chemosensory Clinical Research Center (CCCRC) orthonasal olfaction test<br>Cut point=8 | Overall composite score (olfactory threshold + odor discrimination)<br><br>90-100 Normal<br>70-80 Mild hyposmia<br>50-60 Moderate hyposmia<br>20-40 Severe hyposmia<br>0-10 Anosmia | |

| Author's | Year | Aims | Outcome | Test | Item and category | Validity and reliability |
|---|---|---|---|---|---|---|
| Vaira | 2020 | Report and analyze the results of a large Italian multicenter study that objectively investigated chemoreceptive disorders in COVID-19 patients | Chemosensitive disorders self-reported by 256 patients (74.2%) but the 30.1% of the 89 patients who did not report dysfunctions proved objectively anosmic | The Connecticut Chemosensory Clinical Research Center orthonasal olfaction test (CCCRC) Cut point=10 | A butanol threshold assessment and a 10-items odor identification test using common odors | |
| Vaira | 2020 | // | // | Self-administered telephone test Cut point=9 | The olfactory threshold was determined using nine solutions with increasing concentration of denatured ethyl-alcoholThe olfactory discriminative capability was instead tested by means of seven groups of odorants, for each of which the patient expressed an evaluation from 0 (no discrimination) to 10 (normal discrimination | |
| Altin | 2020 | report the results from comprehensive olfactory and gustatory testing in a series of hospital in-patients with COVID-19 | Fifty (61.7%) COVID-19-positive patients had complaints related to olfaction within the case group, 22 individuals (27.2%) had taste malfunction | Sniffin' Sticks test Cut point=16 | 16 | |
| Lechien | 2020 | To investigate olfactory dysfunction (OD) in patients with mild coronavirus disease 2019 (COVID-19) through patient-reported outcome questionnaires and objective psychophysical testing | Total loss of smell was self-reported by 61.4% of patients. Objective olfactory testings identified 41 anosmic (47.7%), 12 hyposmic (14.0%), and 33 normosmic (38.3%) patients There was no correlation between the objective test results and subjective reports of nasal obstruction or postnasal drip. | Sniffin' Sticks test Cut point=16 | A total of 16 scents were presented patients were classified as normosmic (score between 12 and 16), hyposmic (Score between 9 and 11), or anosmic (score 8 or below). | |

**The global consortium for chemosensory research questionnaire GCCR):** Evaluation of the olfactory impairment in Parma.V et al.'s study was done by The Global Consortium for Chemosensory Research questionnaire (GCCR). 4039 improved COVID-19 cases were divided in two groups; first clinical assessments group and second the lab test ones. A large reduction in the sense of smell were reported in both groups. (79.7 ± 28.7 points on the 100-point scale; mean ± SD). Smell qualitative changes like Parosmia was not significantly different between two groups ( p = 0.463)( 14). Spadera.L et al. reported the Sudden Olfactory Loss (SOL) among 180 participants. Through an online questionnaire, smell disorder severity were classified into three parts; severe/total loss (severe hyposmia/anosmia) in 65.6% of patients (n = 118) , moderate (27.2%, n = 49)and slight form (7.2%,n = 13) (15). Souheil Zayet et al. divided their participants in two groups; Group 1- patients with positive RT-PCR for COVID-19(44%, n=95) and Group 2-the negative RT-PCR cases (56% n=122). Dysgeusia (65% vs 16%, $p < 0.001$) and anosmia (63% vs 15%, $p < 0.001$) were seen more frequent in G1 (PCR-positive) than in G2 (PCR-negative) (16).

**Specific olfactory dysfunction test:**

**The university of Pennsylvania smell identification test (UPSIT):** In Moein et al.'s study, 59 of 60 (98%) cases reported olfactory dysfunction (mean [95%CI] UPSIT score: 20.98 [19.47, 22.48]; controls: 34.10 [33.31, 34.88]; $p$ <0.0001). The University of Pennsylvania Smell Identification Test (UPSIT), is a reliable and well-validated (test-retest r = 0.94) test. Comparing this test with the same olfactory tests showed good correlation (17). Thirty-five

(58%) patients were either anosmic (15/60; 25%) or severely microsmic (20/60; 33%); 16 presented as moderate microsmia (16/60; 27%), 8 were mild microsmic (8/60; 13%), and 1 was normosmic (1/60; 2%).there was no significant difference between the test scores and severity of disease, gender, or comorbidities. Quantitative smell testing expressed that any form of smell disorders (not just anosmia), is an important marker for SARS-CoV-2 infection (17). Also in another study by Shima T et al.'s study, the UPSIT initial scores indicated that there was severe microsmia, with 96% showing measurable dysfunction; 18% were anosmic. The scores increased when tested again (initial and retest means (95%CIs) = 21.97 (20.84, 23.09) and 31.13 (30.16, 32.10; p<0.0001); there were no patients who had anosmia. Sixty percent of the retested participants had normal test scores after starting COVID-19 symptoms for five weeks. In almost one-third of cases, smell dysfunction remained after five weeks of symptom onset (17).

**IR-SIT**: It is the Iranian version of UPSIT that was used in Tabari et al.'s study to objectively identify smell disorders. Through IR-SIT test reports, 58% of inpatients were hyposmic (1–4 score) and no patients were pure anosmic. In this study, there was a significant correlation between olfactory impairment and severity of disease (OR 4, 95% CI: 1.166–13.728, p = 0.028). According to the criteria of disease severity (like SPO2 and the respiratory progressive disease course) 68 inpatients were divided in 2 groups, 48 patients had mild form of disease and 20 patients suffered from the severe form. The IR-SIT test demonstrated smell impairment in 80% of progressive type in comparison to those with mild illness (50%) (18). In Alijanpour et al.'s study in the North of Iran, after olfactory dysfunction test among 250 patients, 117 (49.4%) cases were normal, 100 cases (42.2%) were hyposmic and 20 (8.4%) cases were anosmic.

Different types of Covid-19 signs and symptoms (41 cases (31.8%) fever, 28 cases (21.7%) weakness and 15 cases (11.6%) dyspnea, P=0.0001) were statistically significant with olfactory dysfunction (19).

**Connecticut chemosensory clinical research center CCCRC**: 256 (74.2%) patients self-reported Chemo sensitive disorders but 30.1% of 89 participants who did not complain Chemo sensitive dysfunctions objectively proved as hyposmic. Also, 70% of participants who reported absolute resolution, proved hyposmic through objective test. In the early stages, 70.9% of patients were affected by severe form of olfactory dysfunctions (anosmia or severe hyposmia) and after 10 days, most of them were represented as mild and moderate hyposmia. They concluded that there is no statistically significant correlation between the COVID-19 severity and the existence or extent of chemosensitive dysfunctions. Although, suffering from chemosensitive disorders more than 7 days, showed significant correlation with the development of moderate and severe COVID-19 (20).

**Sniffin' Sticks" test**: In Jerome Ret al.'s study, 61.4% of patients self-reported total loss of smell while Objective olfactory testings identified 33 normosmic (38.3%) patients ‹12 hyposmic (14.0%) and 41 anosmic (47.7%) (21). Fifty (61.7%) COVID-19-positive patients had some complaining associated with olfaction in another study. Altin et al. concluded that there was statistically significant difference among the distribution of olfactory symptoms in the case group vs the control group (p < 0.001) (22). First, limitation of our study is related to the self-report articles, there is some bias in completing the questioner especially the online and telephone interview ones according to the misunderstanding or qualitative nature of questions.

The sample size of most articles was few. To the best of our knowledge, there is limited review studies working on comparison self-report with diagnostic test in the evaluation olfactory impairment among COVID-19 cases. We tried to find almost the most accurate tests which were used in the time of our study. Among self-report articles, those with reliable questionnaires and better methodology were chosen.

**Table 3. Different studies for detection of olfactory dysfunction by self-report or questionear**

| Author, years | Country | Aim | outcome | Instrument | Appraise of instrument |
|---|---|---|---|---|---|
| **Alex Carignan 2020 (6)** | Canada | To determine if anosmia and dysgeusia are distinct symptoms in individuals who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). | Olfactory and gustatory symptoms were found to be strongly associated with SARS-CoV-2 positivity. | Self-reported Mini Olfactory Questionnaire (Self-MOQ) | Internal reliability (Cronbach α = 0.84) validity (r = –0.60, p < 0.001). |

| Author, years | Country | Aim | outcome | Instrument | Appraise of instrument |
|---|---|---|---|---|---|
| **Maryam Jalessi 2020 (20)** | Iran | To determine the frequency of olfactory impairment and its outcome in hospitalized patients with positive swab test for COVID-19. | Sudden olfactory dysfunction and sinusitis are common among patients with COVID-19. The association between sinusitis and olfactory loss was not observed to be significant. | 7 Likert scale questions (five-point scale;0:nocomplaint,5:extremeseverepproblem) | _____ – |
| **Ibrahim Sayin 2020 (13)** | Turkey | To identify the taste and smell impairment in coronavirus disease 2019 (COVID-19)–positive subjects and compare the findings with COVID-19–negative subjects | There was a significant difference in the smell/taste impairment rates of the groups (n = 46% [71.9%] for the COVID-19–positive group vs n = 17 [26.6%] for the COVID-19–negative group, P = .001) COVID-19–positive subjects are strongly associated with smell/taste impairment | American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) Anosmia Reporting Tool | |
| **Jerome R. Lechien, 2020 (9)** | Belgium France Spain Italy | To investigate the occurrence of olfactory and gustatory dysfunctions in patients with laboratory-confirmed COVID-19 infection. | 85.6% and 88.0% of patients reported olfactory and gustatory dysfunctions, respectively. There was a significant association between both disorders ($p < 0.001$). The sQO-NS scores were significantly lower in patients with anosmia compared with normosmic or hyposmic individuals ($p = 0.001$). | National Health and Nutrition Examination Survey, and the short version of the Questionnaire of Olfactory DisordersNegative Statements | |
| **Patricia Gómez-Iglesias 2020 (18)** | Spain | A study of patients presenting olfactory/gustatory alterations in the context of SARS-CoV-2 infection in order to contribute to the understanding of this phenomenon. | Olfactory alterations are frequent in patients with SARS-CoV-2 infection and is only associated with nasal congestion in half of the cases. | Self-administered, anonymous online questionnaire | |
| **Claire Hopkins 2020 (19)** | | To characterise patients reporting new onset smell and taste disturbance during the COVID-19 pandemic and report on early recovery rates | | Online Survey | |
| **Souheil Zayet 2020 (17)** | France | To compare the symptoms of patients with positive and negative SARS-CoV-2 RT-PCR results and to determine the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each of these symptoms in regard to SARS-CoV-2 RT-PCR. | The specificity of anosmia and dysgeusia was respectively of 85%, and 84% specificity of the combination of anosmia and dysgeusia reached 91% for a positive PCR result. Dysgeusia and anosmia both had a positive predictive value of 77% for a positive RT-PCR result. The combination of these 2 symptoms had a positive predictive value of 83% for a positive SARS-CoV-2 RT-PCR result. | Self-questionnaire | |

| Author, years | Country | Aim | outcome | Instrument | Appraise of instrument |
|---|---|---|---|---|---|
| **Chenghao Qiu (15)** | China Germany France | to systematically characterize and compare olfactory and gustatory symptoms among COVID-19 adult patients and children | The incidence of olfactory and/ or gustatory complaints in COVID-19 patients in China, Germany, and France was 32%, 69%, and 49%, respectively (China vs Germany, P \ .001; China vs France, P = .002; Germany vs France, P = .029). Sixty-one of 394 (15%) of patients reported isolated olfactory dysfunction, and Ninety-three of 394 (24%) patients had both olfactory and gustatory dysfunction | A visual analog scale (10) of olfactory intensity and a questionnaire of olfactory disorders (QOD) | |

## Discussion

COVID-19 infection can also lead to the sudden loss of smell and taste (23). Therefore, identification of these symptoms could lead to investigate SARS-CoV-2 infection. The aim of this study was to investigate whether quantitative-test smell disorders has a considerable difference from self-reported or not. So it can report beneficial information about each ones and compare both to detect the most reliable way for smell dysfunctions.

In self-report study by Lechien et al., smell and taste impairment were expressed as a prevalent symptom in patients with mild to moderate COVID-19 infection. Although the sample size of the study was almost appropriate but the participants consisted of young and mild-to-moderate COVID-19 cases. Also the side effect of comorbidity and gender was not considered in the study (9). Carignan et al. demonstrated dysgeusia and anosmia as the most characteristic symptoms of SARS-CoV-2 infection. Although they used a validated questionnaire(Self-MOQ), the mental effect of publishing this theory of association between COVID-19 infection and olfactory dysfunction at the time of study, could not be denied especially as it was an unblinded study in which both case and control groups were aware of their RT-PCR test results (6). A case control study by Sayin et al. demonstrated that the olfactory and gustatory dysfunction was significantly higher in Covid19–positive group in contrast to COVID-19–negative subjects. Also, hyposmia/hypogeusia and parosmia/dysgeusia were more common than the other forms of smell impairments (13). Although the low sample size in each group and low average age of participants may have affected the result. Zayet et al. described that dysgeusia and anosmia were statistically more frequent in PCR-positive group compared with PCR-negative ones. Although they used a self-designed standard questionnaire, failure to report internal reliability and validity decreases the value (16). A strong relationship between olfactory alterations and SARS-CoV-2 infection has been reported in the literature of Gómez-Iglesias et al. No differences were expressed between definitive COVID-19 diagnosed patients and under quarantine participants (12). The online nature of the self-administered questionnaire used in this study, caused some limitations. First of all, the selection bias of young participants (mean age of 34.7) and internet accessed people, and also disability of hospitalized patients with severe symptoms to participate. There is no information of the questionnaire's reliability and validity, too. There were some differences among mentioned studies. For example, only Carignan et al. reported internal reliability and validity in their article (6). Also, in some studies (as Lechien and Carignan et al.' studies) the olfactory and gustatory dysfunctions were evaluated only among those who tested positive for COVID-19 while others like Sayin et al.'s (13) and Zayet et al.'s (16) studies were done, taste and smell impairment was compared between COVID-19 positive and negative subjects.

Quantitative olfactory testing by using UPSIT, in both Moein et al.'s studies, expressed that decreased smell ability is an important symptom related to SARS-CoV-2 infection. Although there were some cases with complete smell loss, the result of testing showed hyposmia as the major impairment. The other considerable finding was that only about one third of participants were subjectively aware of their smell impairment before testing (17). The mismatch between self-reported smell impairment and test results was seen in this study. Among the studies using olfactory test to evaluate smell disorders Alijanpour et al.'s (19) and Moein et al.'s (17) studies reported validity and reliability. Tabari et al. designed a study to find the association between smell dysfunction and severity of disease for the first time, by

using IR-SIT version. They also included both symptomatic and asymptomatic COVID-19 positive patients. Interestingly, they reported that smell loss has predictive value in disease severity and progression. Although limitation of low sample size might have affected the result (18). Lechien et al. had evaluated olfactory dysfunction both in objective and subjective aspect. The Sniffin' Stick test's result in about one third of cases with self-evaluated olfactory dysfunction, were normal. So, in this article, they resulted subjective reports overestimated smell loss in related to COVID-19 (21). Altin et al. in their case control study, concluded that hyposmia could be a reliable symptom in identifying pre-symptomatic patients, by using the Sniffin' Sticks test, the olfactory dysfunction in case group (positive covid_19 cases) were significantly different from the control group(negative covid- 19ones) (22). Vaira et al. concluded that in the early stages, there is no significant correlation between the severity of chemosensitive dysfunctions and its prospective prognostic value in determining the severity of the COVID-19 disease and clinical outcomes. In evaluation, the test's result in cause of smell impairment, at the initial time course of study, the severe form was the most frequent and by the passing of time, the disease decreases. In comparison to Sniffin Sticks and UPSIT, the researchers preferred the CCCRC test as it is less expensive and also determines the olfactory threshold. Actually it has also the potential to be used both in hospitalized patients and home quarantine ones as the home test kit through the dilution of butanol (24).

It has been observed that variations in methodology and case selection were evident in the studies (25). Patients with mild to moderate disease in some studies were entered and patients with severe disease were not included. The ability of defining various degrees of smell function by using such well-validated and sensitive test, causes more reliable correlation between the symptom and disease. Also, most of self-report study's limitations were recall bias, lack of case awareness, subject's prognosis of COVID-19's impact on smell sensation, non-validated questionnaire and poor methodology. Studies that mentioned validity and reliability were limited, and this requires considering methodology for study in this issue. The olfactory disorder questionnaire has been used more in the studies because of economic aspects and effortlessness for researches but using a special tool for recognizing smelling disfunction is advised as it is more professional and provides the ability to compare the results. Also, the detection of Covid-19 via self-report can be related to sociodemographic parameter of population. Therefore, the use of standardized tests instead of self-reports is recommended due to accurate screening.

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