

Screening for Olfactory Dysfunction in COVID-19 Patients Using Quick Smell Identification Test

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Abstract

Intro: To determine the prevalence of OD in the confirmed case with COVID-19 among our population using quick smell identification test (Q-SIT) as screening tool. **Methods:** Cross-sectional study carried out in Qatif area – Saudi Arabia among adult hospitalized patient with confirm COVID-19 during the period between May and July, 2020. All adults confirmed COVID-19 patients were interviewed for history of current disease and associated symptoms as well as performing Q-SIT. Participants who had history of olfactory dysfunction, and critical cases required ICU admission were excluded. **Results:** The prevalence of OD among COVID-19 cases was (16.3%) in our population using Q-SIT compared to (27.4%) for self-reported symptom. Females were having higher prevalence in compare to males (30.5% and 11.1%) respectively; which was statistically significant ($P < 0.001$). The patients reported higher prevalence of ageusia (31.9%) with significant association with OD ($P < 0.001$). Q-SIT showed high positive and negative predictive value in detecting OD among patients with COVID-19 (84% and 93% respectively). **Conclusion:** Q-SIT is a useful, validated and easy to apply tool for screening OD among patients with COVID-19. Some patients presented solely with this symptom which can occurs unnoticed in COVID-19 patients, and there for required objective test for detection.

Title: Screening for Olfactory Dysfunction in COVID-19 Patients Using Quick Smell Identification Test: Cross-sectional study

Abstract

Objective: To determine the prevalence of OD in the confirmed case with COVID-19 among our population using Quick Smell Identification Test (Q-SIT) as screening tool.

Design: Cross-sectional study carried out in Qatif area – Saudi Arabia among adult hospitalized patient with confirm COVID-19 during the period between May and July, 2020.

Setting: All patients were interviewed for demographic data, history of the current disease and associated symptoms as well as performing Q-SIT.

Participants: All confirmed COVID-19 patients, both male and female, and adults aged 18 years or above were included. Participants who had history of olfactory dysfunction, and critical cases required ICU admission were excluded. The sample size was estimated using the CDC tool (Epi Info[?]) to be 260 subjects.

Main Outcome Measures: The prevalence of OD among COVID-19 using Q-SIT as screening tool.

Results: The prevalence of OD among COVID-19 cases was (16.3%) in our population using Q-SIT compared to (27.4%) for self-reported symptom. Females were having higher prevalence in compare to males (30.5% and 11.1%) respectively; which was statistically significant ($P < 0.001$). The patients reported higher

prevalence of ageusia (31.9%) with significant association with OD ($P < 0.001$). Q-SIT showed high positive and negative predictive value in detecting OD among patients with COVID-19 (84% and 93% respectively).

Conclusions: Q-SIT is a useful, validated and easy to apply tool for screening OD among patients with COVID-19. Some patients presented solely with this symptom which can occurs unnoticed in COVID-19 patients, and there for required objective test for detection.

Key words: COVID-19, Olfaction Disorders, Odor, Prevalence, Smell test

Key points:

- Olfactory dysfunction can be the only presenting symptom of COVID-19. Hens, finding a validated screening tool for OD is valuable.
- Q-SIT is a Three-item microencapsulated odor identification psychophysical (objective) test.
- The prevalence of OD among COVID-19 cases was (16.3%) in our population using Q-SIT compared to (27.4%) for self-reported symptom.
- Q-SIT showed high positive and negative predictive value in detecting OD among patients with COVID-19 (84% and 93% respectively).
- Q-SIT is a useful, validated and easy to apply tool for screening OD among patients with COVID-19.

Introduction

With the emergence of Coronavirus disease 2019 (COVID-19) outbreak on December 2019¹, many researches have been published about its transmission, diagnosis, clinical presentation and management. Its presentation varies widely from mild to severe symptoms including severs pneumonia. Though the main reported COVID-19 symptoms include fever, headache, gastrointestinal symptoms, and respiratory symptoms.² Upper respiratory symptoms where not uncommon such as sore throat, rhinorrhea, complete or partial loss of smell (olfactory dysfunction-OD).³ Post viral Olfactory dysfunction (PVOD) Is caused by different viruses including Rhinoviruses, coronaviruses, parainfluenza viruses, and Epstein-Barr viruses.⁴ Many preliminary reports have suggested that smell and taste loss are potential early symptom or subclinical markers of COVID-19 infection. Several cross-sectional studies from many countries such as Iran, United Kingdom, Italy, Spain, Germany, European countries, France, and united states have been published about OD prevalence in COVID-19 patients.^{5,6} The incidence of OD in COVID-19 patients differs widely between these cross-sectional studies. ranging from 33.9 to 68%.⁵

A study from Spain using a self-reported questionnaire only without a validated olfactory test, found that the incidence rate of OD in COVID-19 patients was significantly more than OD in influenza patients (39.2% vs12.5%).⁷ Olfactory tests are categorized in to 3 types: subjective, psychophysical, and electrophysiological studies. Subjective testing can be performed through self-reporting method or as a part of quality of life outcome questionnaire eg. Sinonasal outcome test-22 (SNOT-22). Many tests have been utilized to assess the olfaction function objectively. These are the psychophysical tests which measure some or all the three olfactory parameters: the threshold, discrimination and identification. While subjective and psychophysical tests are used in most clinical and research, the electrophysiological studies like electroencephalography (EEG) and electro-olfactography (EOG) are having limited clinical use and mainly performed for medicolegal issues.⁸

One observational study from Saudi Arabia, found that self-reported loss of taste and smell was the most common presentation (47.5%.) in mild symptomatic COVID-19 patients.⁹ Objective (psychophysical test) has been available in few studies only, though it is considered to be the gold standard for diagnosis of OD.^{2,10,11} Moein et al reported that only 35% of their subjects were aware about their smell problem before doing objective test which indicate that self-reporting of the symptoms may be not enough and the incidence rate of OD is much higher than reported by the previous studies.¹⁰

This study aims to use Quick Smell Identification Test (Q-SIT) as screening tool to assess the prevalence of olfactory dysfunction in patients with confirmed COVID-19 infection in Qatif area, Eastern province, Saudi Arabia.

Materials and Methods

Study Design and Participants

This cross-sectional study was conducted in Qatif area, Saudi Arabia, during the period between May and July, 2020. Majority of our patients were severe cases hospitalized in Qatif central hospital wards, with positive results on reverse transcriptase polymerase chain reaction (RT-PCR) testing of COVID 19. Patients considered mild to moderate COVID-19, when there was no O2 requirements, no evidence of pneumonia but with other symptoms of covid19 e.g. fever. While Severe cases defined as the presence of [?] 1 of the following symptoms: Respiratory rate [?]30/min (adults), blood oxygen saturation [?]93%, PaO2/FiO2 ratio < 300, lung infiltrates >50% of the lung field within 24–48 hours.¹²

Our inclusion criteria included all confirmed COVID-19 patients (Saudi and nonSaudi), both male and female, and adults aged 18 years or above. Participants who had history of olfactory dysfunction, their age were below 18 years and critical COVID-19 pneumonia required intensive care unit admission were also excluded.

Sampling

According to the Saudi ministry of health, the estimated number of confirmed COVID-19 cases in the Qatif area during the study period was around 7000 cases.¹³ The sample size was calculated using the Centers for Disease Control and Prevention (CDC) tool (Epi Info[?] For Windows version 7.2). For confidence level of 90% the estimated sample size was 260 subjects.

Data Collection

We conducted a face-to-face interview with the participants. We Collected basic demographic, epidemiological and clinical data of hospitalized patients with COVID-19. Data on comorbidities, past medical and surgical history, olfactory dysfunction data were obtained. Quick- Smell Identification Test was performed in all patients.

Olfactory Testing

Olfactory function screening was done through Q-SIT. This is a Three-item microencapsulated odor identification test of standardized odors with five multiple choice options, one is “none/other” (Figure 1). Question one is testing chocolate odor, while the second is testing banana odor and third is for smoke odor.¹⁴

This test was chosen in particular because it is tear-off card test (disposable) so there is no concern about contamination and transmission of disease form COVID-19 patients. Moreover, it is fast and can be administered with in less than 1 minute.¹⁵ The test was validated against University of Pennsylvania Smell Identification Test (UPSIT). Though we disproved the validity of UPSIT in previous publication on our population, the three odorants used in Q-SIT are validated and accurately identified by our population.¹⁶ Cutoff point on one wrong answer gives better sensitivity and specificity with negative and positive predictive value of 98% ,43% respectively for detecting anosmia.¹⁴ Accordingly, we considered cutoff score of [?] 2 to be normal test and cutoff score of [?] 1 to be abnormal test for anosmia.

Statistical Analysis

Data were entered and analyzed using SPSS (version 25). The mean and standard deviation were calculated for numerical variables while count and percentages for categorical variables. Chi-square and Fisher’s exact test were used to test for significant difference and P-value [?] 0.05 considered statistically significant.

Reporting Guideline

We have followed The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement to write this study.

Ethical Approval

Informed written consent was obtained from each patient. The study was approved by the Institutional Research Ethic Committee in <Blinded for review>. Tests were performed with appropriate personal protective

equipment to ensure the examiner's safety.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Results

The patients' Characteristics

We interviewed a total of 275 patients with PCR- confirmed COVID-19 infection. Five patients were excluded (three patients aged less than 18 years, two patients reported previous history of OD). Of 270 patients, 250 patients (88%) were hospitalized with severe COVID-19 pneumonia. Only 20 patients (12%) reported mild symptoms and they were not hospitalized. The majority were in the age group 36-45 (30 %). The median age was 43 years, 198 (73.3%) were male. Most of our participants 177 (65.6 %) were Saudi (Table 1).

Clinical Features and Past History

Table 2 shows the presenting symptoms and comorbid illness of the participants. Fever was the most prevalent symptom in 218 patients (80.7%) followed by cough in 197 patients (73%). A total of 74 patients (27.4%) reported loss of smell; being the first symptom in 7%. Furthermore, 86 (31.9%) reported ageusia. The median duration for anosmia was 4 (1-15) days where as the median duration for ageusia was 5 (1-15) days. A total of 21 patients (7.8 %) reported past history of chronic rhinosinusitis or allergic rhinitis without OD.

Olfactory Tests

Q-SIT was used to screen all included patients regardless of the presence or absence of OD. Table 1 shows the Q-SIT scores of all participants. The prevalence of OD using Q-SIT was 16.3% (44 participants). Female were having higher prevalence in comparison to males (30.5% and 11.1%) respectively; which was statistically significant ($P < 0.001$). On the other hand, our results showed no significant association between age, nationality, or comorbid illness including chronic rhinosinusitis with self-reported anosmia or abnormal Q-SIT (Table 1). Furthermore, no significant association was found between anosmia and nasal blockage, postnasal drip, and rhinorrhea with olfactory dysfunction.

Among patients with abnormal Q-SIT, 37 patients (84%) subjectively reported OD at the time of the test. The recognition rate to question 1 (chocolate odor) was better than other two odors for patients with OD (Fig 2). Both ageusia and abnormal Q-SIT were present in 38.4% of patients with statistical significance ($P < 0.001$; Table 3).

In patients with anosmia at the time of Q-SIT administration, 75.5 % of the participants had abnormal Q-SIT when cutoff score [?] 2 was used; whereas 69.8% of the participants had abnormal Q-SIT when cutoff score [?] 1 was used (table 5b,5a). On the other hand, in patients without anosmia at the time of Q-SIT administration, 30.4 % of the participants had abnormal Q-SIT when cutoff score [?] 2 was used; whereas only 3.2% of the participants had abnormal Q-SIT when cutoff score [?] 1 was used. (Table 4).

Discussion

In our study, we found that the estimated prevalence of self- reported OD in our sample was 27.4 % while the prevalence of abnormal olfactory test was 16.3% which is lower than what was reported by most recent studies including studies using standard olfactory tests.⁵ Furthermore, we found that OD was more prevalent in females with confirmed COVID-19 infection which is similar to most published studies.

The low prevalence of OD in our study in comparison with other studies can be explained by the fact that the majority of our patients were hospitalized with severe COVID-19 pneumonia. So, the low prevalence could be explained by the delayed testing which led to the partial recovery of the olfactory dysfunction. While other studies examined patients with mild- moderate COVID-19 disease in their early stage. Moreover, psychophysical tests such as the Q-SIT evaluate one's sense of smell at a specific point in time, which could lead to an underestimation of the prevalence of OD. Jerome R. et al. showed that about 38.3% of patients with self-reported sudden-onset olfactory dysfunction found to be normosmic by the psychophysical Sniffin' Sticks test. we recorded similar finding of 30.2% having normal Q-SIT while they subjectively reported OD.¹⁷

When we measured the association between the Q-SIT and subjectively reported OD at the time of test, we found better positive predictive value and negative predictive value on a cutoff score [?] 1 (84% and 93% respectively) in compare to the cutoff score [?] 2. (Table 5) For that we have used the former cutoff in all previously mentioned calculations.

This study showed no significant association between olfactory dysfunction and nasal symptoms. This is supporting the hypothesis of direct invasion of the olfactory neurons by SARS-CoV-2 as the virus could be replicated in neural cell line U251 in vitro.¹⁸ That is against other hypothesis of olfactory cleft blockage due to inflammation or inflammatory cytokines affecting olfactory neural mucosa.⁶

It was expected to have significant association between OD and abnormal tasting (38.4%) as retronasal olfaction is the cause of most gustatory impairment.¹⁹ Moreover, the prevalence of gustatory impairment (31.8%) in our sample was higher than olfactory impairment. These data are supported by similar findings of an epidemiological survey conducted in four European countries.²⁰ while some studies differentiate between olfactory and gustatory dysfunction, others just report the prevalence of both anosmia and Ageusia as one symptom.^{7,21,22}

Strength and limitations

We have reported very valuable and validated objective tool for screening OD in patient with severe COVID-19. This is considered a strength to our study. Moreover, using an objective test avoids the response bias as patients can be influenced by the news that report smell and taste dysfunction in COVID-19 and overreported these symptoms.

On the other hand, this study has some limitations where most of our study population was having moderate to severe COVID 19 symptoms whom required hospitalization; for that mild cases were missed. Finally, duration of the symptoms and recovery rate were not assessed very well in this study.

Conclusion

Although the fever was considered the most frequent reported sign and symptoms in COVID 19 Patients, OD is one of the confirm symptoms to predict COVID-19 infection. Q-SIT is a useful, validated and easy to apply tool for screening OD specially in the current situation. Some patients have presented solely with this symptom usually in mild cases. Hence, primary physicians and otolaryngologist need to be aware of this putative presentation. Our study shows that anosmia can occurs unnoticed in COVID-19 patients, and there for those patients required objective and quantifiable test for detection.

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Figure 1: sample of the quick smell identification test card. Notice the tear-off slip with three questions on right side. Patient information and the answer key on the left side on the card.

Figure 2: Response rate to different odorants in Q-SIT among included patients.

Table 1. Patients Characteristics	Table 1. Patients Characteristics			
Characteristics	All Patients (n=270)	Normal Q-SIT (n=226)	Abnormal Q-SIT (n=44)	P value
Demographic data	Demographic data			
Age (Y) – mean (SD)	43 (±12)	44 (±12)	39 (±11)	0.109
18-25 – no. (%)	18 (6.7)	12 (5.3)	6 (13.6)	
26-35 – no. (%)	59 (21.9)	47 (20.8)	12 (27.3)	
36-45 – no. (%)	81 (30.0)	66 (29.2)	15 (34.1)	
46-55 – no. (%)	69 (25.6)	62 (27.4)	7 (15.9)	
56-65 – no. (%)	34 (12.6)	30 (13.3)	4 (9.1)	
>65 – no. (%)	9 (3.3)	9 (4.0)	0 (0)	
Sex				<0.001
Male – no. (%)	198 (73.3)	176 (77.9)	22 (50.0)	
Female – no. (%)	72 (26.7)	50 (22.1)	22 (50.0)	
Nationality				0.795
Saudi – no. (%)	177 (65.6)	143 (63.3)	34 (77.3)	
Arab, non-Saudi – no. (%)	9 (3.3)	7 (3.1)	2 (4.5)	
Indian – no. (%)	25 (9.3)	23 (10.2)	2 (4.5)	
Pakistani – no. (%)	19 (7.0)	17 (7.5)	2 (4.5)	
Bangladeshi – no. (%)	19 (7.0)	16 (7.1)	3 (6.8)	
Filipino – no. (%)	14 (5.2)	13 (5.8)	1 (2.3)	
Others– no. (%)	7 (2.6)	7 (3.1)	0 (0)	
Abbreviations: Q-SIT, quick-smell identification Test.	Abbreviations: Q-SIT, quick-smell identification Test.	Abbreviations: Q-SIT, quick-smell identification Test.	Abbreviations: Q-SIT, quick-smell identification Test.	Abbreviations: Q-SIT, quick-smell identification Test.

Table 2. Clinical Features and Past History

Clinical Features

Partial Anosmia – no. (%).

Complete Anosmia – no. (%).

Anosmia as The First symptom – no. (%).

Ageusia – no. (%).

Rhinorrhea – no. (%).

Nasal blockage – no. (%).

Fever – no. (%).

Cough – no. (%).

Sore throat – no. (%).

SOB – no. (%).

Diarrhea – no. (%).

Headache – no. (%).

Sputum production – no. (%).

Asthenia – no. (%).

Loss of appetite – no. (%).

Arthralgia – no. (%).

Myalgia – no. (%).

Abdominal pain – no. (%).

Nausea – no. (%).

Vomiting – no. (%).

Ear pain – no. (%).

Past History

Chronic sinusitis – no. (%).

Nasal polyp – no. (%).

Allergic rhinitis – no. (%).

DM – no. (%).

HTN – no. (%).

COPD – no. (%).

Asthma – no. (%).

CKD – no. (%).

CLD – no. (%).

CVD – no. (%).

GERD – no. (%).

Hypothyroidism – no. (%).

Depression – no. (%).

Autoimmune disease – no. (%).

Sinus surgery – no. (%)

Smoking – no. (%)

Abbreviations: Q-SIT: quick- smell identification Test; SOB: Shortness of Breath; DM: diabetes mellitus; HTN: Hypertension

Table 3: Q-SIT and Ageusia

Q-SIT	Ageusia		Ageusia P value
	Yes	No	
Normal – no. (%).	53 (61.6%)	173 (94%)	<0.001
Abnormal – no. (%).	33 (38.4%)	11 (5.99%)	<0.001

Total	86	184	270
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Table 4: correlation between subjectively reported smell impairment and Q-SIT using different cutoff point scores

Q-SIT	Anosmia During Smell Test Yes	Anosmia During Smell Test No	Anosmia During Smell P value
Cutoff score [?] 2	Cutoff score [?] 2	Cutoff score [?] 2	Cutoff score [?] 2
Normal score -no. (%)	13 (24.5)	151 (69.6)	<0.001
Abnormal score -no. (%)	40 (75.5)	66 (30.4)	<0.001
Cutoff score [?] 1	Cutoff score [?] 1	Cutoff score [?] 1	Cutoff score [?] 1
Normal score -no. (%)	16 (30.2)	210 (96.8)	<0.001
Abnormal score -no. (%)	37 (69.8)	7 (3.2)	<0.001
Total	53	217	270

Table 5: Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) Q-SIT using different cutoff point scores in relation to subjectively reported smell impairment.

Q-SIT	Sensitivity	Specificity	PPV	NPV
Abnormal score with cutoff score [?] 2	75.5%	69.9%	37.7%	92%
Abnormal score with cutoff score [?] 1	69.9%	96.8%	84%	93%

Q-SIT™

The Quick Smell Identification Test™

Patient:

Date:

Age:

Smoker:

IF YES Packs/day: IF YES Years:

Current Smell or Taste Problem?

Score:

Examiner:

See instructions if patient's score is less than 3.

ATTACH TO PATIENT RECORD

☐ Lemon

☒ **Chocolate**

☐ Strawberry

☐ Pepper

☐ None / Other

☐ **Banana**

☐ Peanut

☐ Rose

☐ Paint Thinner

☐ None / Other

☐ Peanut

☒ **Smoke**

☐ Chocolate

☐ Soap

☐ None / Other

A. This odor smells most like:

Lemon
Chocolate
Strawberry
Pepper
None / Other

B. This odor smells most like:

Banana
Peanut
Rose
Paint Thinner
None / Other

C. This odor smells most like:

Peanut
Smoke
Chocolate
Soap
None / Other

9

