



## Prevalence of olfactory dysfunction in COVID-19 patients

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### ABSTRACT

**Background:** Nowadays COVID-19 has become a pandemic in which global society experience multiple difficulties in management. It seems that olfactory dysfunction is one of the early occurring symptoms of this viral infection and many patients just show this symptom after they got infected. Considering so, olfactory dysfunction especially a decline in olfaction could potentially be used for screening purposes and preventing the disease to spread.

**Materials and Methods:** 50 PCR-verified SARS-CoV-2 infected participants were assessed about their olfactory function adequacy using a Modified Version of the University of Pennsylvania Smell Identification Test (UPSIT) for the Iranian population called Iran Smell Identification Test (Iran-SIT). Participants scores were compared against normal population scores in this test and possible correlations of age and scores were explored as well.

**Results:** Participants with SARS-CoV-2 infection generally obtained lesser scores in the mentioned test which means they experience a decline in olfactory function more, significantly. Aging also has a negative correlation with olfaction adequacy.

**Conclusion:** Based on this article's finding, olfactory function decrease is more frequent among SARS-CoV-2 infected people and potentially could be a suggestive indicator for screening programs. This indicator should be interpreted concerning patients' age.

**Keywords:** COVID-19; Olfactory dysfunction; Anosmia; Early detection.

## Introduction

The Coronavirus Disease 2019 (COVID-19) is a name that was appointed to a pandemic forming disease that started from china and was spread all over the world [1]. Till now, COVID-19 claimed more

than 1,390,000 lives [2] and it continues to be a threat to global society, especially elders and people with predisposing factors such as chronic disease, cardiovascular disease, or immunomodulatory states [1].

Rapid transmission [3], lack of optimally effective medical treatment [4], and high load of affected patients who demand medical care [5] made COVID-19 an uncontrolled global pandemic. Well-known symptoms of COVID-19 are fever, cough, dyspnea, myalgia and arthralgia, sputum production, and headache [6]. Many affected patients are asymptomatic or show non-specific symptoms which makes it hard to track and control this disease spread [6].

Olfactory dysfunction with emphasis on anosmia is one of the most prevalent and early occurring symptoms of the infection which many patients experience as their first and sometimes the only symptom of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [7]. Some researchers suggest that anosmia is a better indicator of SARS-CoV-2 infection than routine indicators used by clinicians [6,7] and potentially could be used more efficiently for screening purposes.

Olfactory dysfunction following a viral infection is a popular phenomenon that occurs following an inflammatory reaction in the nasal mucosa [8]. Some members of the coronavirus family alongside rhinoviruses and Epstein-Barr virus are among the most common viral causes of olfactory dysfunction [8]. After starting COVID-19, some researchers reported that many patients with SARS-CoV-2 infection had complaints about olfactory symptoms specially anosmia as a very early sign of their infection [6,7]. Loss of olfaction was also reported repetitively as the only symptom of some COVID-19 patients in the literature [7].

COVID-19 currently is diagnosed to be a disease of debate in case of treatment [4] and many controversies are among clinicians about proper approaches to affected patients management. Similar to other medical conditions, prevention is preferred to treatment in the case of COVID-19 but SARS-CoV-2 is an easily transmitting viral infection because of both the rapid onset of infectivity phase of the virus and also a large fraction of asymptomatic or minimally and non-specifically symptomatic patients [6]. Early detection and isolation of SARS-CoV-2 infected people will help healthcare systems to control the pandemic more efficiently [3] and it seems that detection of olfactory dysfunction and especially loss of olfaction (Anosmia) could be used as a potential screening field of action for the mentioned purpose. The current study aims to determine the fraction of SARS-CoV-2 infected people in the Iranian population.

## Methods and Materials

A total number of 50 SARS-CoV-2 infected patients referred to Shariati Hospital have entered the study. All of the participants were diagnosed to have SARS-CoV-2 by polymerase chain reaction (PCR) study. All of the participants were aged between 25 and 70 and None of the participants have neither altered level of consciousness nor prior medical condition with olfactory system involvement such as Alzheimer's disease or Parkinson's Disease. None of the participants received any medical care such as medications or procedures like intubation which potentially could interfere with the study. The study objectives and procedure were explained to participants and they declared their agreement to enter this study by signing a written consent. All institutional and ethical approvals were obtained before the beginning of the study.

Participants were assessed about their olfactory changes using a Modified Version of the University of Pennsylvania Smell Identification Test (UPSIT) for the Iranian population called Iran Smell Identification Test (Iran-SIT) [9]. All assessments were done by the same pre-trained examiner as an attempt for bias reduction. All sanitary considerations were carefully followed for patient's safety and also potential bias reduction. Participant's olfactory function was assessed using IRAN-SIT and documented for further interpretation. According to IRAN-SIT, Olfactory function adequacy can vary between 0 and 25. Based on IRAN-SIT, People who obtained grades less than 9 were categorized as Anosmia Group. Participants with grades in the range of 10-13 and 14-18 were categorized as Severe Microsomnia and Mild Microsomnia Groups, respectively. At last, participants with higher than 19 grades were appointed to Normosmia Group. Afterward, acquired data of the participants were compared with data which Taherkhani et al. (2015) reported as the normal status of Iranian olfactory function measured by IRAN-SIT. Statistical analyses were done using IBM SPSS v.21 software package [10]. Kruskal-Wallis equality-of-populations rank test was utilized to compare our results on COVID-19 patients with results of the normal population reported by Taherkhani et al. Pearson correlation test were used in search of possible correlation of age and IRAN-SIT scores.

## Results

All participants have done the test successfully. Statistical analysis showed that there is a negative correlation between aging and decline in olfactory

function as demonstrated in figure 1. Table 1 shows the statistical results of such a relationship. Besides, It seems that there is a statistically significant difference between normal population scores and COVID-19 patients scores of olfactory function adequacy measured

by the IRAN-SIT test ( $P=0.05$ ) (table 2). It seems that people infected with SARS-CoV-2 generally have less olfactory functionality in comparison to the normal population.

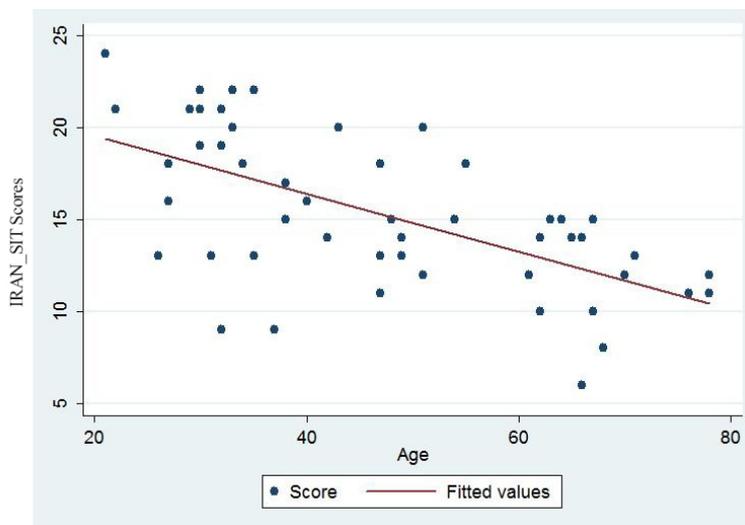


Figure 1. Negative trend between IRAN\_SIT Scores and Age in participants.

	Age	Score
Age	1.0000	
Score	-0.6138	1.0000
	0.0000	

Table 1. Negative Correlation between Age and IRAN-SIT Scores in Sars\_Cov\_2 infected participants.

Agegr	Obs	Rank Sum
25-29	4	122.50
30-34	11	325.50
35-39	5	123.50
40-44	4	129.50
45-49	5	139.50
50-54	3	76.00
60-64	5	100.00
65-69	10	111.50

Table 2. Results of Kruskal-Wallis equality of populations rank test. PCR-verified Sars\_cov\_2 infected participants were compared with the normal Iranian population.

## Discussion

Many people that were infected with SARS-CoV-2 have experienced anosmia or different degrees of decline in olfactory systems functionality [6] which as said before is not specifically a complication of SARS-CoV-2 infection and this condition can occur following different viral infections [8]. Inflammation of olfactory epithelium causes damage to the free nerve endings and chemosensory receptors in olfactory mucosa which leads to an anosmic or hyposmic experience in patients with an upper respiratory viral infection. SARS-CoV-2 also causes such a symptom which is not specific as explained, but in the pandemic, the situation could have usages in screening and epidemic control. In the case of COVID-19, rapid transmission of the disease made it hard to control. This rapid spreading has an important role in pandemic development; especially considering that many infected cases are clinically asymptomatic or minimally symptomatic and/or show non-specific and constitutional signs and symptoms which made it hard to early detect the disease. In this situation, the exact definition of highly sensitive biomarkers could be beneficial. Such biomarkers should also be easy to use and easy to teach so amateur volunteers can use them in companion with healthcare providers to maximize screening capacities. On the other side and with special attention to low-income society and social classes, cheap biomarkers will be favored so that economical limitation cannot interrupt the screening procedure. Many healthcare systems planned their screening programs based on symptoms like fever, dyspnea, and/or other symptoms [11] but there are other suggestions in the literature. Based on published researches a recent complaint of anosmia or any other form of olfactory dysfunction is one of the candidates for early detection of disease in subclinical stages [7]. Olfactory dysfunction occurs commonly and early in these patients and many patients only have complaints about olfactory dysfunction in absence of other COVID-19 related symptoms [7].

Considering the fact that most of the infected cases got infected by reservoirs without overt signs, Early detection of affected people and isolating them from the rest of the population can greatly facilitate combating the disease spread and its following epidemics [12]. Anosmia and other olfactory hesitations are easy to detect and can be informed about by self report of the suspected referees. Olfactory function assessment can be done easily by non-expert examiners which keeps diagnostic and screening human errors minimal. On the other side, the economical burden of this assess-

ment is negligible. High sensitivity, easy assessment ability, and also low cost of olfactory assessment make it a good candidate for screening purposes in the pandemic situation of SARS-Cov-2. Our study findings suggest that there is a significant difference in olfactory function adequacy of SARS-CoV-2 infected people and their corresponding healthy controls (see table 2); as table 2 shows, PCR verified cases of COVID-19 experience significantly more difficulties in olfaction in comparison to the healthy control group. it seems that similar to other mentioned viral infections, SARS-CoV-2 infection also causes a decline in olfactory function via inflammatory responses in the nasal mucosa. These findings can be used as a clue for further investigations about the possibility of this suggestion that relying on a decline in olfactory functionality could be utilized screening and early isolation of SARS-CoV-2 infected cases from the rest of the community and breaking the transmission chain by that.

Despite our use of the IRAN-SIT test as a standardized quantitative test for measuring the adequacy of olfactory function, clinical assessment of olfactory dysfunction necessarily does not require sophisticated tests or devices and practitioners could be informed about it by precise history taking and a brief olfactory neurological examination [13] which is quite a time and energy-saving considering the huge load of medical care demand which caused improper workload to healthcare workforce these days. This ease of assessment makes olfactory function adequacy testing a fast and potentially more effective clinical tool compared to routine methods of assessment for medical practitioners. The low specificity of olfactory adequacy decline will not cause concerns because in the pandemic situation of SARS-COV-2 which occurred recently, maximizing sensitivity considering COVID-19's great negative influence on human welfare, economic system, and its life-threatening importance is a reasonable strategy and low specificity could be tolerated until successful control of the pandemic.

We also have found that by normal aging processes, SARS-CoV-2 infected people also show a negative trend of olfaction adequacy (Figure 1). This negative trend is relatively strong ( $r=0.6$ ) which was shown in the result section in detail (see table 1). In figure 1 a negative trend is seen so that by aging the olfactory adequacy declines. This means that over the years, the olfactory function normally declines and some degrees of olfactory dysfunction are acceptable. This finding is in line with our prior knowledge [14] and has clinical significance. Practitioners should keep in mind this

physiological decline while assessing olfaction adequacy in suspected cases of SARS-CoV-2 infection. Such a trend will complicate olfactory function adequacy interpretation in elders and possibly reduces its specificity in older patients. Considering this, precise history taking and attending the chronic or acute pattern of the loss of olfaction or past similar experiences or medical conditions that can interfere with this decline could be beneficial. At last, the authors of this article suggest further investigations on this topic with a bigger study population and more precise categorization of SARS-CoV-2 infected patients which may provide a solid basis for the medical practice of COVID-19 management as a highly attended medical situation during these days.

### Conclusion

The SARS-CoV-2 infection has a significant correlation with a decline in olfactory function of infected ones. This correlation could potentially be used for screening purposes in asymptomatic or minimally symptomatic suspected cases of SARS-CoV-2 infection.

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### Conflict of Interests

There is no conflict of interest to declare.

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