The Journal of Laryngology & Otology

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Sudden loss of smell and taste: clinical predictors of coronavirus disease 2019 infection

A Jain[1], J Kaur[1], N Kahlon[2], M Singh[3], A K Rai[1], M Hans[4], V M Hans[4], S Dhankar[5], S Kumar[5] and A K Pandey[2]

Departments of [1]ENT, Faridabad, India, [2]Physiology, Faridabad, India, [3]Community Medicine, Faridabad, India and, [4]Dentistry, Employees' State Insurance Corporation ('ESIC') Medical College and Hospital, Faridabad, India and [5]Employees' State Insurance Corporation Medical College and Hospital, Faridabad, India

Main Article

Dr A Jain takes responsibility for the integrity of the content of the paper

Cite this article: Jain A *et al*. Sudden loss of smell and taste: clinical predictors of coronavirus disease 2019 infection. *J Laryngol Otol* 2022;**136**:747–749. https://doi.org/10.1017/S0022215122000986

Accepted: 12 April 2022
First published online: 27 April 2022

Key words:
COVID-19; Gustatory Perception; Olfactory Impairment; Sensitivity; Specificity

Author for correspondence:
Dr Avani Jain, Department of ENT, ESIC Medical College and Hospital, Faridabad, India
E-mail: avanijain87@hotmail.com

Abstract

Objectives. This study aimed: to evaluate the association between coronavirus disease 2019 infection and olfactory and taste dysfunction in patients presenting to the out-patient department with influenza-like illness, who underwent reverse transcription polymerase chain reaction testing for coronavirus; and to determine the sensitivity, specificity, and positive and negative predictive values of olfactory and taste dysfunction and other symptoms in these patients.

Methods. Patients presenting with influenza-like illness to the study centre in September 2020 were included in the study. The symptoms of patients who tested positive for coronavirus on reverse transcription polymerase chain reaction testing were compared to those with negative test results.

Results. During the study period, 909 patients, aged 12–70 years, presented with influenza-like illness; of these, 316 (34.8 per cent) tested positive for coronavirus. Only the symptoms of olfactory and taste dysfunction were statistically more significant in patients testing positive for coronavirus than those testing negative.

Conclusion. During the pandemic, patients presenting to the out-patient department with sudden loss of sense of smell or taste may be considered as positive for coronavirus disease 2019, until proven otherwise.

Introduction

The coronavirus disease 2019 (Covid-19) has been the topic of discussion since its outbreak worldwide. Its causative agent is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strain. It is diagnosed by real-time reverse transcription polymerase chain reaction testing of nasopharyngeal and oropharyngeal swabs.[1] The respiratory illness caused by this virus varies in presentation in terms of severity, ranging from mild self-limiting influenza-like illness to life-threatening pneumonia.

Sudden loss of smell and taste are now known symptoms of Covid-19, and are included in the diagnostic guidelines. Smell and taste dysfunction may appear in the initial stages of viral infection and in asymptomatic patients.[2] During the pandemic, in developing countries, testing facilities may be limited, particularly in rural areas and in states with high numbers of cases. In such scenarios, patients' description of symptoms is heavily relied upon, and sudden loss of smell and taste may indicate Covid-19 infection.

This study aimed to evaluate the association between Covid-19 infection and olfactory and taste dysfunction in patients presenting to the out-patient department with influenza-like illness, who underwent reverse transcription polymerase chain reaction testing for Covid-19 infection. We also calculated the sensitivity, specificity, and positive and negative predictive values of olfactory and taste dysfunction and other symptoms in these patients.

Materials and methods

This cross-sectional study was carried out in the month of September 2020 at Employees' State Insurance Corporation Medical College and Hospital, Faridabad, India. All patients presenting with influenza-like illness to the study centre during the study period were included. Patients were excluded from the study if they were aged below 12 years or above 70 years, had pre-existing anosmia or dysgeusia, or had a history of: nasal or oral surgery, radiotherapy in the oral and nasal cavities, psychiatric and neurological disorders, or chronic rhinosinusitis.

The demographic characteristics of all the patients presenting with influenza-like illness were documented at presentation. A detailed history of all the symptoms was

taken, including: malaise, cough, fever, sore throat, diarrhoea, breathlessness, nasal blockage, and loss of smell and/or taste.

All the patients underwent reverse transcription polymerase chain reaction testing for Covid-19 using nasopharyngeal swabs. The test results were reported as positive or negative. The symptoms of patients who tested positive for Covid-19 were compared to those who tested negative.

The sensitivity, specificity, positive predictive value and negative predictive value of each symptom was calculated. Descriptive data were presented as numbers and proportions. Statistical analysis was conducted using Epi Info™ version 7 software. The chi-square test was used to analyse differences between the group proportions. A *p*-value of less than 0.05 was considered statistically significant.

Results

During the study period, 909 patients, aged 12–70 years, presented with influenza-like illness to the study centre. This included 602 males (66.2 per cent) and 307 females (33.8 per cent). Of the 909 patients, 316 (34.8 per cent) tested positive for Covid-19. This included 222 males (70.3 per cent) and 94 females (29.7 per cent).

The various symptoms of patients with influenza-like illness are shown in Table 1. In patients with positive results on reverse transcription polymerase chain reaction testing, the symptoms reported were: fever (52.2 per cent), malaise (27.8 per cent), cough (25.9 per cent), sore throat (19.6 per cent), nasal discharge (9.5 per cent), breathlessness (4.7 per cent) and diarrhoea (0.9 per cent). Among the patients, anosmia or hyposmia was reported by 24.7 per cent, dysgeusia was reported by 20.3 per cent, and olfactory or taste dysfunction was reported by 30.7 per cent of patients.

In our study, only the olfactory and taste dysfunction symptoms were statistically more significant in patients who tested positive for Covid-19 on reverse transcription polymerase chain reaction testing compared to those who tested negative, as follows: hyposmia or anosmia (24.7 per cent *vs* 4.6 per cent, $p < 0.0001$), dysgeusia (20.3 per cent *vs* 5.4 per cent, $p < 0.0001$), and olfactory or taste dysfunction (30.7 per cent *vs* 5.7 per cent, $p < 0.001$). There were no other significant differences between the patients with positive and negative Covid-19 results in terms of clinical features.

The sensitivity, specificity, and positive and negative predictive values of all the symptoms are shown in Table 2. Olfactory or taste dysfunction was reported by 131 patients; of these, 97 tested positive for Covid-19, indicating a high specificity of 94.3 per cent. Sudden-onset olfactory disturbance was reported by 105 patients, of whom 78 tested positive for Covid-19. Sudden-onset gustatory disturbance was reported by 96 patients, of whom 64 tested positive for Covid-19. This depicted high specificity values of 95.4 per cent and 94.6 per cent for olfactory dysfunction and gustatory dysfunction, respectively, in Covid-19 infection.

Discussion

Sudden loss of smell and taste in Covid-19 infection is being extensively studied during the pandemic. The mechanism of olfactory dysfunction in Covid-19 infection is probably the result of nasal mucosal oedema, olfactory epithelial damage (including neural and non-neural epithelium) and the involvement of central olfactory pathways. The virus may target angiotensin-converting enzyme 2 (ACE2) expressing cells of the olfactory epithelium and/or taste buds via a cytopathic effect.[3]

- In our study, specificity for olfactory and taste dysfunction was very high
- Specificity values were 95.4 per cent for hyposmia or anosmia, 94.6 per cent for dysgeusia, and 94.3 per cent for olfactory or taste dysfunction
- Patients presenting with sudden loss of smell or taste during the pandemic may be considered coronavirus-positive until proven otherwise
- This may help in isolating patients early in the disease course, and may be beneficial in countries with limited resources and testing facilities, and with large numbers of cases
- However, sudden loss of smell or taste cannot replace a diagnosis made by reverse transcription polymerase chain reaction testing

The diagnosis of Covid-19 requires detection of SARS-CoV-2 RNA in respiratory samples by reverse transcription polymerase chain reaction testing. However, this is cumbersome and time-consuming. Furthermore, during the pandemic, in places with high population density and a lack of healthcare facilities, such testing may not be feasible. The collection of nasopharyngeal and oropharyngeal swabs, and their transport in viral transport medium at the appropriate temperature to the molecular biology laboratory for reverse transcription

Table 1. Symptoms of patients with influenza-like illness

Symptoms	Patients with symptoms* (*n* (%))	Covid-19 positive† (*n* (%))	Covid-19 negative‡ (*n* (%))	*P*-value
Fever	50.8 (462)	52.2 (165)	50.1 (297)	0.577
Malaise	24.6 (224)	27.8 (88)	22.9 (136)	0.106
Sore throat	17.9 (163)	19.6 (62)	17 (101)	0.364
Cough	27.9 (254)	25.9 (82)	29 (172)	0.352
Diarrhoea	1.2 (11)	0.9 (3)	1.3 (08)	0.756
Breathlessness	3.7 (34)	4.7 (15)	3.2 (19)	0.272
Nasal discharge	9 (82)	9.5 (30)	8.8 (52)	0.717
Anosmia or hyposmia	11.6 (105)	24.7 (78)	4.6 (27)	<0.0001
Dysgeusia	10.6 (96)	20.3 (64)	5.4 (32)	<0.0001
Olfactory or taste dysfunction	14.4 (131)	30.7 (97)	5.7 (34)	<0.001

*$n = 909$; †$n = 316$; ‡$n = 593$. Covid-19 = coronavirus disease 2019

https://doi.org/10.1017/S0022215122000986 Published online by Cambridge University Press

Table 2. Sensitivity, specificity, and positive and negative predictive values of symptoms

Symptoms	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Fever	52.2	49.9	35.7	66.2
Malaise	27.8	77.1	39.3	66.7
Sore throat	19.6	83	38	66
Cough	25.9	71	32.3	64.3
Diarrhoea	0.9	98.7	27.3	65.1
Breathlessness	4.7	96.8	44.1	65.6
Nasal discharge	9.5	91.2	36.6	65.4
Anosmia or hyposmia	24.7	95.4	74.3	70.4
Dysgeusia	20.3	94.6	66.7	69
Olfactory or taste dysfunction	30.7	94.3	74	71.9

PPV = positive predictive value; NPV = negative predictive value

polymerase chain reaction, may be troublesome. In addition, there may be long delays in running the tests and reporting the results in areas with high incidence. In such situations, we must rely on the clinical presentation of the patient, including the sudden-onset loss of smell and/or taste.

Sudden-onset loss of smell and/or taste usually presents early in Covid-19 infection, and may also be present in otherwise asymptomatic patients. This could be of importance in rural areas with no testing facilities, in areas with a high incidence of Covid-19 infection, and while awaiting reverse transcription polymerase chain reaction reports. The early identification of individuals with Covid-19, and their isolation, may help prevent the spread of infection.

In our study, the general symptoms of patients with positive Covid-19 results (on reverse transcription polymerase chain reaction positive) were: fever (52.2 per cent), malaise (27.8 per cent), cough (25.9 per cent), sore throat (19.6 per cent), nasal discharge (9.5 per cent), breathlessness (4.7 per cent) and diarrhoea (0.9 per cent). These symptoms are similar to those reported in other studies.[4,5] In our study, breathlessness was reported only by 4.7 per cent of patients; this is probably because they were out-patients, and thus without any respiratory distress. Hyposmia or anosmia was reported by 24.7 per cent of patients, dysgeusia was reported by 20.3 per cent of patients, and olfactory or taste dysfunction was reported by 30.7 per cent of patients. This prevalence of olfactory and gustatory dysfunction in Covid-19 patients is similar to findings of other studies conducted in India.[5,6] However, a higher prevalence of olfactory and gustatory dysfunction has been reported in the European population.[7,8]

In the current study, the specificity of olfactory and taste dysfunction was very high, with values of: 95.4 per cent for hyposmia or anosmia, 94.6 per cent for dysgeusia, and 94.3 per cent for olfactory or taste dysfunction. The positive predictive values for a positive Covid-19 result (on reverse transcription polymerase chain reaction testing), were: 74.3 per cent for hyposmia or anosmia, 66.7 per cent for dysgeusia, and 74 per cent for olfactory or taste dysfunction.

Zayet *et al.*[9] reported the positive predictive values for a positive Covid-19 result (on reverse transcription polymerase chain reaction testing based on a nasopharyngeal sample) as 76.9 per cent for anosmia, 76.5 per cent for dysgeusia, and 72.2 per cent for anosmia and/or dysgeusia. The specificity values were 85.2 per cent for anosmia, 84.4 per cent for dysgeusia, and 77.9 per cent for anosmia and/or dysgeusia. La Torre *et al.*[10] reported specificity values of 93.3 per cent for anosmia, 92 per cent for ageusia, and 97.3 per cent for anosmia plus ageusia. The positive predictive values were 73.3 per cent for anosmia, 66.7 per cent for ageusia, and 85.7 per cent for anosmia plus ageusia.

Reverse transcription polymerase chain reaction testing for SARS-CoV-2 is very specific for Covid-19. However, its main limitation is its varied sensitivity of 56–83 per cent. The false-negative test result may be due to an incorrect sampling technique or delayed testing, as viral load may decrease during the second week of the disease. In such cases, the patients' clinical symptoms may be relied upon, particularly symptoms of olfactory and taste dysfunction, as these have high specificity and a high positive predictive value. It is likely that patients who report olfactory or taste dysfunction, but with negative results on reverse transcription polymerase chain reaction testing, may actually have Covid-19 (false-negative result), and, therefore, the positive predictive value for these symptoms may be higher. In such cases, the patients should be isolated as early as possible to prevent further spread of infection. It may be useful to use other diagnostic tools, such as serology or a computed tomography scan, or to get a deeper respiratory sample, in order to confirm the diagnosis.

Competing interests. None declared

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https://doi.org/10.1017/S0022215122000986 Published online by Cambridge University Press