SUDDEN LOSS OF SMELL AND TASTE: CLINICAL PREDICTORS OF COVID-19 INFECTION

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ABSTRACT

OBJECTIVES: To evaluate the association of COVID-19 infection and olfactory and taste dysfunction (OTD) in patients presenting to the OPD with ILI undergoing RT-PCR testing for COVID-19. To determine the sensitivity, specificity, positive and negative predictive value of OTD and other symptoms in these patients.

METHODS: The patients presenting with ILI to the study centre in September, 2020 were included in the study. The symptoms of RT-PCR positive patients were compared to those of RT-PCR negative patients.

RESULTS: During the study period, 909 patients, aged 12-70 years, reported with ILI, out of which 316 (34.8%) patients tested COVID-19 positive. Only the symptoms of olfactory and taste dysfunction were statistically more significant in RT-PCR positive patients than in RT-PCR negative patients.

CONCLUSION: During the COVID-19 pandemic, patients presenting to the OPD with sudden loss of sense of smell or taste may be considered as COVID-19 positive, until proven otherwise.

Key words: COVID-19; gustatory; olfactory; sensitivity; specificity
INTRODUCTION

The Coronavirus disease 2019 (COVID-19) has been the topic of discussion ever since its outbreak worldwide. Its causative agent is severe acute respiratory syndrome coronavirus 2 strain (SARS-CoV2). It is diagnosed by real time reverse transcriptase polymerase chain reaction (RT-PCR) test on nasopharyngeal and oropharyngeal swab\(^1\). The respiratory illness caused by this virus varies in presentation in terms of severity ranging from mild self-limiting influenza like illness (ILI) 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 number 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.

The aim of this study was to evaluate the association of COVID-19 infection and olfactory and taste dysfunction (OTD) in patients presenting to the OPD with ILI undergoing RT-PCR testing for COVID-19 infection. We also calculated the sensitivity, specificity, positive and negative predictive value of OTD and other symptoms in these patients.
METHODOLGY

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 the patients presenting with ILI to the study centre during the study period were included. Patients below 12 years and above 70 years of age, those with pre-existing anosmia/dysgeusia, history of nasal or oral surgery, radiotherapy in oral and nasal cavities, psychiatric and neurological disorders and chronic rhinosinusitis were excluded from the study.

The demographic characteristics of all the patients presenting with ILI were documented at presentation. Detailed history of all the symptoms was taken including: malaise, cough, fever, sore throat, diarrhoea, breathlessness, nasal blockage, loss of smell and taste. All the patients underwent testing for COVID-19 by RT-PCR test of nasopharyngeal swab. The result of RT-PCR test was reported as positive or negative. The symptoms of RT-PCR positive patients were compared to those of RT-PCR negative patients.

The sensitivity, specificity, positive predictive value and negative predictive value for each symptom was calculated. Descriptive data was presented as numbers and proportions. Statistical analysis was done using epi info version 7 software. Chi square was used to test the difference between the group proportions. A p value of less than 0.05 was taken as statistically significant.
RESULTS

During the study period, 909 patients, aged 12-70 years, reported with ILI to the study centre. This included 602 males (66.2%) and 307 females (33.8%). Out of the 909 patients, 316 (34.8%) patients tested COVID-19 positive. This included 222 males (70.3%) and 94 females (29.7%).

The various symptoms of patients with ILI are mentioned in Table 1. In patients who were RT-PCR positive, the symptoms reported were fever (52.2%), malaise (27.8%), cough (25.9%), sore throat (19.6%), nasal discharge (9.5%), breathlessness (4.7%) and diarrhoea (0.9%). Loss of smell was reported by 24.7% patients; loss of taste was reported by 20.3% patients; loss of smell or taste was reported by 30.7% patients.

In our study, only the symptoms of olfactory and taste dysfunction were statistically more significant in RT-PCR positive patients than in RT-PCR negative patients: hyposmia/anosmia (24.7% vs 4.6%, p<0.0001), dysgeusia (20.3% vs 5.4%, p<0.0001), olfactory of taste dysfunction (30.7% vs 5.7%, p<0.001). There was no significant difference in other clinical features between RT-PCR positive and negative patients.

The sensitivity, specificity, positive and negative predictive value of all the symptoms are mentioned in Table 2. Olfactory or taste dysfunction was reported by 131 patients, out of whom 97 tested COVID-19 positive; indicating a high specificity of 94.3%. Sudden onset olfactory disturbance was reported by 105 patients, out of whom 78 tested COVID-19 positive. Sudden onset gustatory disturbance was reported by 96 patients out of whom 64 tested COVID-19 positive. This depicted high specificity of 95.4% and 94.6% 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.

The diagnosis of COVID-19 requires detection of SARS-CoV2 RNA in respiratory samples by RT-PCR. However, this is cumbersome and time consuming. During the pandemic, in places with high population density and lack of health care facilities, this may not be feasible. The collection of nasopharyngeal/oropharyngeal swabs and their transport in viral transport medium at the appropriate temperature to the molecular biology lab for RT-PCR may be troublesome. Also, there may be long delay in running RT-PCR tests and reporting in areas with high incidence. Therefore, in such situations, we can rely on clinical presentation of the patient, including acute 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 may be of importance in rural areas with no testing facilities, in areas with high incidence of COVID-19 infection, and while RT-PCR reports are awaited. Early identification of such patients and their isolation may help in further preventing the spread of infection.

The general symptoms of COVID-19 patients (RT-PCR positive) in our study were fever (52.2%), malaise (27.8%), cough (25.9%), sore throat (19.6%), nasal discharge (9.5%), breathlessness (4.7%) and diarrhoea (0.9%). These symptoms were similar to those reported in other studies. In our study, breathlessness was reported only by 4.7% patients, probably because they were outpatients, thus without any respiratory distress. Hyposmia/anosmia was reported by 24.7% patients; dysgeusia was reported by 20.3% patients; loss of smell or taste was reported by 30.7% patients. This prevalence of olfactory and gustatory dysfunction in COVID-19 patients was similar to other studies done in India. However, a higher prevalence of olfactory and gustatory dysfunction has been reported in the European population.

In our study, the specificity of olfactory and taste dysfunction was very high: hyposmia/anosmia was 95.4%, dysgeusia was 94.6%, and olfactory or taste dysfunction was
94.3%. The positive predictive value of hyposmia/anosmia was 74.3%, dysgeusia 66.7%, and olfactory or taste dysfunction 74%, for a positive COVID-19 RT-PCR. Zayet et al\textsuperscript{9} reported the positive predictive value of anosmia, dysgeusia, and anosmia and/or dysgeusia as 76.9%, 76.5% and 72.2%, respectively, for a positive COCID-19 RT-PCR on nasopharyngeal sample. The specificity of anosmia, dysgeusia, and anosmia and/or dysgeusia was 85.2%, 84.4%, and 77.9%, respectively. La Torre et al\textsuperscript{10} reported the specificity of anosmia, ageusia, and anosmia plus ageusia as 93.3%, 92% and 97.3%, respectively. The positive predictive value of anosmia, ageusia and anosmia plus ageusia was 73.3%, 66.7% and 85.7%, respectively.

RT-PCR for SARS-CoV-2 is very specific for COVID-19. However, its main limitation is its varied sensitivity of 56-83%. The false negative RT-PCR may be due to incorrect sampling technique or delayed testing, as viral load may decrease during the second week of the disease. In such cases, clinical symptoms of the patient may be relied upon, particularly symptoms of olfactory and taste dysfunction, as they have a high specificity and high positive predictive value. It is likely that the patients who reported olfactory or taste dysfunction and tested negative by RT-PCR, may actually have COVID-19 (false negative RT-PCR), and therefore, the positive predictive value of these symptoms may be higher. In such cases, the patients should be isolated as early as possible to prevent the further spread of infection. It may be useful to use other diagnostic tools- serology or CT scan, or to get a deeper respiratory sample to confirm the diagnosis.

SUMMARY

- In our study, the specificity of olfactory and taste dysfunction was very high: hyposmia/anosmia was 95.4%, dysgeusia was 94.6%, and olfactory or taste dysfunction was 94.3%.
- This study shows that during the COVID-19 pandemic, patients presenting to the OPD with sudden loss of sense of smell or taste may be considered as COVID-19 positive, until proven otherwise.
- This may help in isolating patients early in the course of the disease.
- It may be beneficial in countries with limited resources and testing facilities, and with large number of cases. However, sudden loss of smell or taste cannot replace a diagnosis by RT-PCR.
REFERENCES


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# Table 1. Symptoms of patients with ILI

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Patients with symptoms (n=909)</th>
<th>COVID-19 positive (n=316)</th>
<th>COVID-19 negative (n=593)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>50.8% (462)</td>
<td>52.2% (165)</td>
<td>50.1% (297)</td>
<td>0.577</td>
</tr>
<tr>
<td>Malaise</td>
<td>24.6% (224)</td>
<td>27.8% (88)</td>
<td>22.9% (136)</td>
<td>0.106</td>
</tr>
<tr>
<td>Sore throat</td>
<td>17.9% (163)</td>
<td>19.6% (62)</td>
<td>17% (101)</td>
<td>0.364</td>
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<tr>
<td>Cough</td>
<td>27.9% (254)</td>
<td>25.9% (82)</td>
<td>29% (172)</td>
<td>0.352</td>
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<td>Diarrhoea</td>
<td>1.2% (11)</td>
<td>0.9% (03)</td>
<td>1.3% (08)</td>
<td>0.756</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>3.7% (34)</td>
<td>4.7% (15)</td>
<td>3.2% (19)</td>
<td>0.272</td>
</tr>
<tr>
<td>Nasal discharge</td>
<td>9% (82)</td>
<td>9.5% (30)</td>
<td>8.8% (52)</td>
<td>0.717</td>
</tr>
<tr>
<td>Anosmia/Hyposmia</td>
<td>11.6% (105)</td>
<td>24.7% (78)</td>
<td>4.6% (27)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>10.6% (96)</td>
<td>20.3% (64)</td>
<td>5.4% (32)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Olfactory or taste dysfunction</td>
<td>14.4% (131)</td>
<td>30.7% (97)</td>
<td>5.7% (34)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table 2. Sensitivity, specificity, positive predictive value, and negative predictive value of symptoms.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (PPV) (%)</th>
<th>Negative predictive value (NPV) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>52.2</td>
<td>49.9</td>
<td>35.7</td>
<td>66.2</td>
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<tr>
<td>Malaise</td>
<td>27.8</td>
<td>77.1</td>
<td>39.3</td>
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<tr>
<td>Sore throat</td>
<td>19.6</td>
<td>83</td>
<td>38</td>
<td>66</td>
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<tr>
<td>Cough</td>
<td>25.9</td>
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<tr>
<td>Diarrhoea</td>
<td>0.9</td>
<td>98.7</td>
<td>27.3</td>
<td>65.1</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>4.7</td>
<td>96.8</td>
<td>44.1</td>
<td>65.6</td>
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<tr>
<td>Nasal discharge</td>
<td>9.5</td>
<td>91.2</td>
<td>36.6</td>
<td>65.4</td>
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<tr>
<td>Anosmia/Hyposmia</td>
<td>24.7</td>
<td>95.4</td>
<td>74.3</td>
<td>70.4</td>
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<tr>
<td>Dysgeusia</td>
<td>20.3</td>
<td>94.6</td>
<td>66.7</td>
<td>69</td>
</tr>
<tr>
<td>Olfactory or taste dysfunction</td>
<td>30.7</td>
<td>94.3</td>
<td>74</td>
<td>71.9</td>
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