

The incidence of anosmia in patients with laboratory-confirmed COVID 19 infection in India: An observational study

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Abstract

Background and Aims: Acute loss of smell or anosmia is a common and sometimes the only symptom observed in patients with coronavirus disease-2019 (COVID-19). The objective of the study was to determine the prevalence, time of onset, and duration of anosmia in patients with COVID-19 infection and the association of anosmia with other symptoms and eosinophil count.

Material and Methods: Two hundred patients with laboratory-confirmed COVID-19 infection, who were asymptomatic or mildly symptomatic were assessed for olfaction with a nonirritant odor. The presence of anosmia was recorded, and a questionnaire integrating the anosmia reporting tool was filled. Patients with anosmia/hyposmia were followed telephonically at 7 and 14 days for resolution of anosmia and other symptoms. The presence of anosmia was correlated with eosinophil count.

Results: Of the 200 COVID-19 patients, 87% were symptomatic. More than half of the patients had fever (56%). Anosmia was observed in 30% of the patients and hyposmia in 4% of patients. In 41% of the patients, olfactory loss was reported before diagnosis. The mean duration of anosmia was 7.8 (\pm 5) days; 97% of patients recovered with a resolution of symptoms within 2 weeks. Ageusia was the most commonly and significantly associated symptom with anosmia (66%, n = 45) followed by sore throat (41%), and rhinorrhea (28%). The symptoms in both the sexes were comparable. Absolute eosinophil count of $<40/\mu\text{L}$ was observed in 59 patients (29.5%) and an absolute eosinophil count of 0 in 17 patients (8.5%). Among the 68 anosmic patients, 36 (47%) patients had eosinopenia, which was statistically significant.

Conclusion: Anosmia is an early and sometimes the only symptom in approximately one-third of the patients with COVID-19 infection. Eosinophil count should be checked in anosmic patient with suspicion of COVID-19 infection. Objective tools for olfactory and gustatory assessment should be brought into practice for early and prompt diagnosis to control the spread of the disease.

Keywords: Ageusia, anosmia reporting tool, anosmia, COVID-19, eosinophil count

Key findings

- Incidence of anosmia in patients with COVID-19 in the Indian population is 34%
- The anosmia report tool developed by the AAO-HNS has good face validity and could be used for detecting

anosmia in patients with COVID-19

- Anosmia and ageusia affect the quality of life and recover with time. Reassurance and olfactory training may help patients
- Eosinophil count should be checked in an anosmic patient with a suspicion of COVID-19 infection.

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Introduction

The coronavirus disease 2019 (COVID-19) is a global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has so far resulted in over 15 lakh deaths worldwide.^[1] In India, the disease has affected more than 9.6 million people and has caused 1.4 lakh deaths.^[2]

The clinical symptoms of COVID-19 infection are nonspecific, like other viral respiratory infections such as fever, cough with or without sputum production, dyspnea, myalgia, arthralgia, headache, diarrhea, rhinorrhea, and sore throat. Patients with mild symptoms may rapidly progress to severe symptoms within a short period. The concern of rapid viral transmission by ambulatory patients with minimal to no symptoms underlines the importance of identifying early or subclinical symptoms of COVID-19 infection.^[3]

Sudden onset olfactory dysfunction may be the only presenting feature in some patients with COVID-19 infection, especially in the initial stage of the disease.^[4] Complete and partial loss of smell known as anosmia and hyposmia respectively, are commonly experienced by patients with COVID-19. However, unlike other viral infections, olfactory dysfunction associated with COVID-19 infection is often not associated with rhinorrhea or nasal obstruction. Although the exact pathogenesis remains elusive, olfactory epithelial damage and central nervous system involvement have been described as the probable cause.^[5] High angiotensin-converting enzyme-2 (ACE-2) and transmembrane protease serine 2 (TMPRSS-2) expression in nasal epithelial cells allows for a wide viral entry and thus damage to olfactory sensory neurons. Invasion of the olfactory bulb has also been hypothesized as a mechanism of virus-induced anosmia.^[6]

Anosmia/hyposmia is often associated with loss (ageusia) or alteration (dysgeusia) of taste sensation. Loss of smell and taste adversely affects the appetite as well as the mood and may negatively impact the patient's quality of life.

Tests for the assessment of loss of smell/taste can be performed easily, and questionnaires can be made for the same. Understanding the time of onset and association of smell/taste loss in COVID-19 may help facilitate screening and early isolation of cases.

Eosinopenia is a common finding in COVID-19 and has a high sensitivity for the prediction of COVID-19 infection in symptomatic patients. So, it may be a potential biological indicator of SARS-COV-2 infections.^[7]

There is insufficient literature available regarding the presence of olfactory symptoms in COVID 19 patients in the Indian

population. We carried out this study to ascertain the prevalence of anosmia and its onset and duration in patients with COVID-19 presenting to a dedicated COVID facility and correlate its existence with other symptoms and laboratory investigations.

Material and Methods

We carried out this observational study in 200 asymptomatic or mildly symptomatic, laboratory-confirmed patients through reverse transcriptase-polymerase chain reaction test. These patients were admitted to a dedicated COVID facility in India for isolation and/or observation. Patients were enrolled in the study after obtaining patients' consent and ethical approval from the Institutional Ethics Committee. Convenience sampling was carried out. The olfaction was assessed. The patients were blindfolded and asked to identify the odor of scented soap by sniffing it. We chose to assess olfaction with only one scent because of the technical difficulties in assessing olfaction in the COVID area, and our patients were also not well versed with fragrances used in a typical olfaction assessment test. The presence of anosmia or hyposmia was recorded. After seeking permission, the Anosmia Reporting Tool developed by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), Infectious disease, and Patient Safety Quality Improvement Committees was adopted because of its adequate face validity, and a questionnaire was formulated.^[8,9] The details of the patient's age, gender, associated comorbidities, and presence of symptoms related to COVID-19 infection, and history regarding the onset of anosmia were recorded. Those patients who had anosmia/hyposmia were followed at 7 and 14 days for resolution of anosmia and other symptoms telephonically. Complete blood count was performed in all the patients as a routine investigation, and the eosinophil count was reviewed. The presence of anosmia was correlated with eosinophil count. Absolute eosinophil count less than 40/ μ L was considered as absolute eosinopenia.^[10]

The results were analyzed by using statistical software SPSS (version 17, IBM Corporation, New York, United States). Descriptive statistics were used for the categorical variables and were reported as numbers, percentages, or mean. Continuous variables were expressed as mean with standard deviation (SD). Chi-square or Fisher exact tests were performed for qualitative variables.

Results

The mean age of the patients was 37.4 (\pm 11) years, and 151 (75.5%) were males. The most frequent comorbidities were hypertension (14%, n = 28), diabetes mellitus (9%,

n = 18), and coronary artery disease (2%, n = 4). Twenty-five patients were smokers. Risk factors for contracting COVID-19 infection such as a positive history of contact with a COVID-19 infected individual, residence in containment zones, health care professional involved in nursing, driving an ambulance, sanitation work, and security work were present in 75.5% (n = 151) of the patients. Eighty seven percent (n = 174) patients were symptomatic while 13% (26) patients were asymptomatic. More than half of the patients infected with COVID-19 had fever (56%). [Table 1] Other symptoms observed were fatigue and myalgia (38%), sore throat (29.5%), dry cough (27.5%), rhinorrhea (15%), headache (10%), cough with expectoration (8.5%), and dyspnea (7%). Diarrhea, chest pain/heaviness, and anorexia were other uncommon symptoms reported by the patients (<5%). Anosmia was observed in 30% (60) of the patients and hyposmia in 4% (8) of the patients. It was mostly seen after the establishment of diagnosis (59%, n = 40), 2–3 days after diagnosis in the majority. However, anosmia was also reported before diagnosis in 41% (n = 28) patients. The mean duration of anosmia was 7.8 (\pm 5) days. Anosmia/hyposmia resolved within 7 days in 65% of patients (n = 44) and within 2 weeks in 32% of patients. However, hyposmia lasted beyond 2 weeks in 2 patients, and it resolved within 1 month of diagnosis. Of the 68 patients with anosmia/hyposmia, ageusia was the most commonly and significantly associated symptom with it (66%, n = 45). Other statistically significant symptoms associated were sore throat (41%) and rhinorrhea (28%). More than half of the patients with anosmia had fever (59%). Myalgias and fatigue and dry cough were associated with anosmia/hyposmia in 41% and 29.4% of the patients, respectively. Expectoration and cough (9%), headache (6%), dyspnea (7%), anorexia, and chest heaviness were less commonly associated with anosmia (<5%). [Table 2] The symptoms in both the sexes were comparable. Ninety-seven percent of patients recovered with a resolution of symptoms within 2 weeks. [Figure 1] Blood investigations were reviewed in all the patients. An absolute eosinophil count of $<40/\mu\text{L}$ was observed in 59 patients (29.5%) and an absolute eosinophil count of 0 in 17 patients (8.5%). Among the 68 patients with anosmia, 36 patients had eosinopenia as well, which was statistically significant.

Discussion

We have observed 200 patients with COVID-19 infection and found anosmia/hyposmia in 34% (68) patients. Males (75.5%) outnumbered the female patients. The patients in our study were younger than previously reported (mean age of 37.4 ± 11 years). We observed that ageusia was

Table 1: Demographic profile, comorbidities, and symptoms in patients with COVID-19

Characteristics	Number
Age (years): Mean (SD)	37.4 (\pm 11)
Sex	
Male	151 (75.5%)
Female	49 (24.5%)
Comorbidities	
Smoker	25 (12.5%)
Hypertension	28 (14%)
Diabetes mellitus	18 (9%)
Coronary artery disease	4 (2%)
Risk factors	
Positive contact history	151 (75.5%)
Symptomatic patients	174 (87%)
Symptoms	
Anosmia	60 (30%)
Hyposmia	8 (4%)
Ageusia	48 (24%)
Fever	112 (56%)
Myalgia/fatigue	76 (38%)
Dry cough	55 (27.5%)
Sore throat	59 (29.5%)
Rhinorrhea	30 (15%)
Dyspnea	14 (7%)
Cough with expectoration	17 (8.5%)
Headache	20 (10%)
Diarrhea	7 (3.6%)
Chest pain/heaviness	6 (3%)
Anorexia	1 (0.5%)

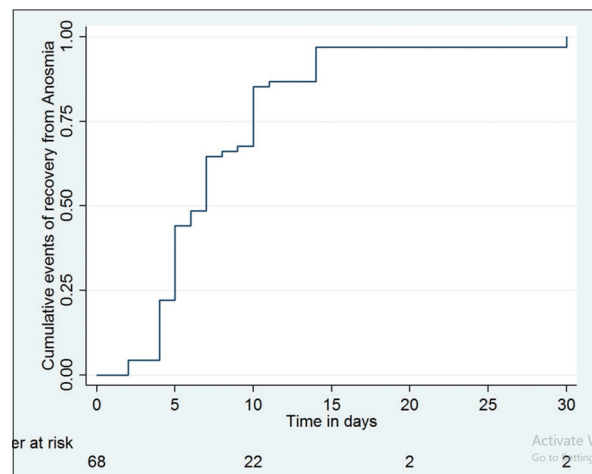


Figure 1: Kaplan Meyer graph of recovery from anosmia in patients with COVID-19

an associated symptom in 66% of patients with olfactory dysfunction (anosmia/hyposmia).

The incidence rate of olfactory dysfunction varies from 33.90%–68% with female dominance in various studies. In European COVID-19 patients, the prevalence of olfactory and gustatory dysfunction was substantially higher. Hornuss

Table 2: Details of COVID-19 patients having anosmia/hyposmia

Patient with Anosmia/Hyposmia	Total: 68
Age (years): Mean (SD)	36 (± 9.74)
Sex	
Males	54 (79.4%)
Females	14 (20.6%)
Mean duration (days)	7.8 (± 5)
The minimum duration of anosmia	2 days
The maximum duration of anosmia	30 days
Symptoms associated with anosmia/hyposmia	
Ageusia	45 (66%)
Fever	40 (59%)
Sore throat	28 (41%)
Myalgia/fatigue	28 (41%)
Dry cough	20 (29.4%)
Rhinorrhea	19 (28%)
Headache	4 (6%)
Dyspnea	5 (7%)
Cough with expectoration	6 (9%)
Chest heaviness	2 (3%)
Anorexia	1 (1.4%)
Onset of anosmia/hyposmia	
Before diagnosis	28 (41%)
1 day before	6 (9%)
2 days before	19 (28%)
3 days before	3 (4%)
After diagnosis	40 (59%)
1 day after	1 (1.4%)
2 days after	20 (29.4%)
3 days after	19 (28%)
Resolution of anosmia/hyposmia	
Within 7 days	44 (65%)
Within 14 days	22 (32%)
Beyond 14 days	2 (3%)

et al. reported anosmia in 40% of the patients and hyposmia in 44% of the patients with a mean age of 58 ± 17.5 years in the German population having COVID-19 disease.^[11]

In a study carried out in France, 47% (n = 54) reported anosmia among 114 patients with confirmed COVID-19 infection, and out of these 54 patients, 46 patients (85%) had dysgeusia. The mean age of the patients was $47 (\pm 16)$ years.^[12] Vaira *et al.* noted olfactory dysfunction in 19.4% of the 320 patients with COVID-19 infection in Italy.^[13]

Lechien *et al.* conducted a multicentric study on 417 mild-to-moderate patients with COVID-19 in Europe and have observed a higher rate of olfactory (85.6%) and gustatory dysfunctions (88%). They have also found a statistically significant association between the two disorders.^[4]

Asian countries also have reported symptoms of anosmia although in fewer numbers, and this has been an area of

research as well. Of the 214 patients hospitalized with COVID-19 in Wuhan, Mao *et al.* identified anosmia in 11 (5.1%) and ageusia in 12 (5.6%) patients.^[14] Data from South Korea suggests that 30% of COVID-19 positive patients had anosmia as the primary presenting symptom.^[6] Ethnic and racial disparity, the difference in expression of ACE2 and TMPRSS2 in different tissues due to genetic polymorphism, and mutation of viral proteins (such as surface protein, spike S protein, and nucleocapsid N protein) may affect the symptoms and outcomes in COVID disease.^[15,16]

Lee *et al.* reported sudden onset anosmia in 15.7% of the patients who were asymptomatic or having mild COVID-19 disease in South Korea. The olfactory and gustatory symptoms were most reported in the female population (69%) and a younger age group (36.5 ± 17.5 years).^[17]

In Iran, 48.23% of COVID-19 patients reported anosmia/hyposmia. The onset of anosmia was sudden in 76.24% of patients. A total of 83.38% of these patients were having concomitant dysgeusia (decreased taste sensation) and anosmia.^[18]

In our study, 28% of patients with anosmia/hyposmia had symptoms of rhinorrhea. However, a French study showed a higher percentage of patients with rhinorrhea (57%) along with anosmia. Lechien *et al.* stated that among the 18.2% of the patients without nasal obstruction or rhinorrhea, 79.7% were having hyposmia or anosmia.^[4]

In our study, more than half of the patients with anosmia had fever (59%). Other associated symptoms were sore throat (41%), myalgias and fatigue (41%), and dry cough (29.4%). Headache, dyspnea, cough with expectoration, anorexia, and chest heaviness were not commonly associated with anosmia (<10%). Diarrhea although reported in patients with COVID-19 infection, was not associated with anosmia in any patient.

Klopfenstein *et al.* also observed other symptoms in patients with anosmia/hyposmia although in higher numbers as follows Fatigue (93%), cough (87%), headache (82%), fever (74%), myalgia (74%), and arthralgia (72%). Diarrhea was also present in almost half of the anosmic/hyposmic patients.^[12]

In our patient population, anosmia was mostly seen after 1 to 3 days of diagnosis of COVID-19 infection (59%, n = 40). However, symptoms of anosmia were also reported before diagnosis in 41% (n = 28) of the patients. Lechien *et al.*^[4] also noted the appearance of olfactory symptoms before (11.8%) as well as after (65.4%) the onset of infection and development of other symptoms. However, Klopfenstein

et al., stated that anosmia developed around 4.4 ± 1.9 (1–8) days after the diagnosis of infection.^[12]

The mean duration of anosmia in our patients was $7.8 (\pm 5)$ days. Anosmia/hyposmia resolved within 1 week in 65% of patients ($n = 44$) and within 2 weeks in 32% of the patients. However, hyposmia lasted beyond 2 weeks in 2 patients. The patients called back and informed us of the resolution of anosmia at 1 month. Lechien *et al.*, observed the recovery of anosmia in 72.6% of their patient population within the first 8 days of the disease. The early olfactory recovery rate was 44.0%.^[4] Lee *et al.*, also found the duration of anosmia to be $7 (\pm 4)$ days.^[17]

Klopfenstein *et al.*, found out that the mean duration of anosmia was $8.9 (\pm 6.3 [1–21])$ days, and 98% of patients recovered within 28 days. The duration was ≥ 7 days for 55% and ≥ 14 days for 20%, one patient had not recovered at the end of the follow-up (after 28 days).^[12]

Most studies have reported recovery of olfaction and taste without treatment. In our study, also the patients received no specific treatment for anosmia/hyposmia. General measures like steam inhalation (patients with rhinorrhea), oral paracetamol (in case of fever), multivitamin supplements, and vitamin C were prescribed to the patients as per our treatment protocol. In addition, patients should be reassured regarding the recovery of a sense of smell and taste. Lechien *et al.*, described that no treatment was received by 70% of the patients with olfactory dysfunction; nasal (8.1%) and oral corticosteroids (2.5%) for anosmia and L-carnitine (1.4%) for gustatory dysfunction in few patients.^[4] Although administering steroids (both local application and systemic steroids) is a common practice for treating anosmia, intranasal steroids have not shown to have a positive effect on olfactory dysfunction, whereas significant improvement in olfaction has been observed with systemic steroids.^[19]

Patients with severe COVID-19 disease have been reported to have eosinopenia, raising the concern of its association with the disease severity.^[20,21] We found an absolute eosinophil count of $<40/\mu\text{L}$ in 59 patients (29.5%) and an absolute eosinophil count of 0 in 17 patients (8.5%) although our patients were asymptomatic or mildly symptomatic.^[22]

Eosinopenia along with raised C-reactive protein may prove as a useful aid in triaging the suspected patients with COVID-19 from other patients in fever clinics with the same clinical presentation. Li *et al.* have described a high sensitivity of eosinopenia (74.7%) for predicting positive SARS-CoV-2 cases.^[23]

A study carried out by Andreozzi *et al.* in patients with SARS-CoV-2 and influenza A infection (total = 91)

revealed a total eosinophil count of $<50/\mu\text{L}$ in 69 patients and undetectable eosinophil count in 44 patients. Eosinopenia could be due to COVID-19 or flu. Severe eosinopenia should raise the possibility of COVID-19 if there is no flu.^[24]

However, eosinophil responses in COVID-19 infection may differ in patients receiving treatment for asthma and hypereosinophilic syndrome due to the possibility of drug-induced eosinopenia.^[25] More research is warranted to understand whether in patients with COVID-19 eosinopenia will progress into critical illness.

Limitations of our study

There are few limitations of our study such as it was a single center study and only mildly symptomatic/asymptomatic patients were enrolled. Sick and intubated patients were not enrolled as it was not feasible and ethically not allowed. Therefore, we do not know the incidence of anosmia in sick and intubated patients with COVID-19. All our patients recovered fully and none of them had persistent anosmia.

Conclusions

Olfactory and gustatory losses are common and sometimes the only findings in patient with COVID-19 and may be missed in the absence of other symptoms. These patients are less likely to go for COVID-19 testing and may spread the disease. Eosinophil count should be checked in an anosmic patient with a suspicion of COVID-19 infection. More objective tools need to be developed and used for early assessment and prompt diagnosis to control the spread of the disease. Whether a patient remains infective after the resolution of anosmia is a question for further study. Multicentric studies are warranted to establish the prevalence and characteristic features of olfactory dysfunction.

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Conflicts of interest

There are no conflicts of interest.

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