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Alteration of Smell and Taste Sensations in Covid-19 Positive Patients: A Prospective Cohort Study in Western India

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Abstract Loss/alteration of Smell and taste sensation is common in CoViD-19 infection. We conducted present study to find out the frequency, onset and severity of these lost sensations and their recovery in mild, moderate and severe COVID 19 positive patients in our setup. A questionnaire based study on 574 COVID-19 positive patients admitted in a dedicated COVID hospital between September-November, 2020 were followed up until their sensations recovered completely or maximum for two months. Fever was the most common symptom reported. Loss of smell and taste sensation is seen in 200 (34.84%) and 269 (46.86%) patients respectively; 163 (28.4%) developed both. Males were affected significantly more than females (p = 0.030 and 0.027). Approximately 1/4th patients [49 (24.5%) and 55 (20.45%)] reported loss of smell and taste sensation as their first symptom. Most common taste sensation lost was salty 191 (71.0%). Loss of smell sensation is seen maximally in mild cases and the

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difference among mild, moderate and severe cases is statistically significant (p = 0.00001); while the difference in loss of taste among all three grades of severity is statistically insignificant (p = 0.0770). Most of the patients [smell (142; 71%) and taste (198; 73.6%)] recovered after 2 weeks of onset of lost sensations while 96.5% (193/200) and 98.1% (264/269) patients reported complete recovery of smell and taste sensations after two months of onset. Present study shows that high percentage of COVID-19 positive patients develop loss of either one or both of smell and taste sensations but recovery is fast and complete in most of them.

Keywords Altered Smell and Taste · Chemosensory deficit · COVID-19 · SARS-COV-2 · Recovery

Introduction

COVID-19 was characterised by the World Health Organisation (2020) as a global pandemic and health emergency on March 11, 2020, which led to a world wide concern [1]. The disease is caused by a new coronavirus (SARS-CoV-2) from a potential bat origin [2] and from which viral genome was rapidly characterized [3]. In January 2020, angiotensin-converting enzyme 2 (ACE2) was identified as the functional receptor for SARS-CoV-2, present in multiple human organs including the central nervous system [4]. Viral entry occurs, after the proteolytic cleavage of the spike (S) protein by the transmembrane protease TMPRSS2 [5, 6]. Interestingly, ACE2 and TMPRSS2 show an extremely high expression in characteristic cells of the nasal epithelium, goblet, and ciliated cells. These cells are the candidates as loci of original viral infection and possible reservoirs for dissemination; in addition, SARS-CoV-2 is an enveloped virus that does not require cell lysis for viral release. Thus, the virus might exploit existing secretory pathways in nasal goblet cells for low-level, continuous release at the early stage with no overt pathology [7].

Smell impairment was first observed among other neurologic manifestations of COVID-19 in hospitalised patients [8] and subsequently has been reported to be a common symptom in patients with mild disease [9, 10]. There are many known causes of acquired smell loss include URTI by respiratory viruses (adenovirus, rhinovirus, coronavirus, influenza), traumatic brain injury, upper airway inflammation (rhinitis, rhinosinusitis), and neurodegenerative (Parkinson and Alzheimer) diseases while minor causes are intracranial/ sinonasal tumors, drugs, exposure to toxic substances, irradiation, or iatrogenic factors [11]. The onset of smell and/or taste loss is often abrupt in COVID infection and, unlike other upper respiratory tract infections, it often occurs in the absence of nasal obstruction [12, 13] The prevalence of loss of smell widely ranged from 10% to over 80% in European countries [14]. A systematic review and meta-analysis reported a pooled prevalence of 52.7% and 43.9% for olfactory and gustatory dysfunction, respectively in patients with COVID-19 infection [15].

L A Vaira C Hopkins et al. reported that within the first 4 days of COVID-19 symptom onset, 84.8% of patients had chemo sensitive dysfunction. Specifically, severe olfactory and gustatory disorders affected 60.9% and 40.6 percent of patients, respectively [16]. Another study by Vikas gupta et al. reported that out of 387 COVID-19 patients, 167 (43.15%) patients had olfactory disfunction, 153 (39.53%) patients had gustatory disfunction and 105 (27.1%) patients had both [17].

In a study done by Valeria Dell Era et al. 49.5% and 50.4% patients declared full recovery of smell and taste respectively at 14th day of infection, with a median recovery time of ten days [18]. Vikas Gupta et al. reported that they found complete recovery of smell and taste in 96.4% and 96.73% patients respectively by 8 weeks of onset [17].

As limited data is available on prevalence, severity, and recovery pattern of involvement of smell and taste sensation in mild, moderate, and severe SARS-CoV-2 patients from India, present study is planned to estimate the same in patients from western part of India.

Methodology

This prospective, analytical questionnaire base study was conducted from September 2020 to January 2021. It recruited adult patients (18 years or more) who tested positive and treated for SARS-CoV-2 RNA by RT-PCR on nasopharyngeal and throat swabs, admitted in a dedicated COVID hospital in western India between September to November, 2020. Enrolled patients were followed up for two months at pre-defined intervals.

Pregnant women, children (< 18 years), patients with history of previous smell andlor taste disorders, allergic rhinitis, rhino sinusitis and dementia (who cannot report functional symptoms) were excluded from study. Patients who did not complete two months of follow-up were also excluded from the analysis.

The study was conducted with the approval of ethical committee of the hospital and informed consent was obtained verbally for telephonic interview. Patients were allowed to leave the interview in between also if they wish so.

A questionnaire was developed which was validated by two subject experts and revised as per their feedback. It was administered telephonically by principal investigator in native language and responses were recorded in Google form simultaneously.

Information was collected regarding age, gender, medical history (Co-morbidities and risk factors) general symptoms (fever, cough, difficulty in breathing, headache, body ache, abdominal pain, loose motion, vomiting, weakness and loss of appetite), ENT symptoms with special references to reduced, complete loss or altered sensation of taste and smell, their duration and recovery pattern separately. Information regarding altered smell and taste sensations before COVID infection, past medical or surgical conditions or co-medications that can cause altered smell or taste sensation, history of nasal allergy and smoking habit was also collected.

Patients were enrolled in the study at the time of discharge from the hospital. Subsequent calls were made after 2 weeks, one month and two month after discharge.

Statistical analysis: spread sheet was generated from Google forms and continuous variables were expressed as mean and standard deviation (SD). Categorical variables were expressed as numbers and percentages. strength of association for categorical variables has been calculated by chi square test.

Results

We recruited 605 patients; out of those, 31 patients were excluded from the final analysis as they could not be followed up completely (lost to follow-up; 5.12%). The mean (SD) age of 574 patients analyzed was 46.60 (14.63)years; Male: female ratio was found to be 2.1:1. Out of all the admitted patients, 176 (30.7%) received oxygen therapy through mask, 49 (8.54%) were admitted in Intensive Care

Unit, and 11 (1.9%) received oxygen therapy through noninvasive ventilation. None were treated by invasive ventilation. Fever was the most common presenting symptom. All the general symptoms and ENT symptoms are summarized in Table 1. Patients presented with various comorbidities are depicted in Fig. 1. Figure 2 is showing various symptoms patients were suffering with even after 14 days of illness. Of all the respondents, 20 (3.5%) were regular smoker.

Two hundred seventy nine (48.6%) of 574 respondents, reported a chemosensory deficit, out of which, 207 (36.1%) had sudden onset while 72 (12.5%) had gradual loss of sensations.

Two hundred (34.84%) patients reported a change in smell perception while 269 patients (46.86%) reported change in taste perception. 163 (28.4%) patients reported alteration in both smell and taste sensations. Their onset, type of involvement and recovery pattern is shown in Table 2. Those who had altered taste sensation, 191 (71.0%) lost the salty taste sensation, 108 (40.15%) lost sweet sensation, 87 (32.34%) lost bitter and 60 (22.30%) lost sour sensation. Many patients had loss of more than one taste sensation. After two months follow-up, 07 (3.5%) patients reported that their smell sensation is not recovered

 Table 1 Various general and ENT symptoms at the time of presentation

S No	Symptoms	N (%) n = 574				
	General symptoms					
1	Fever	470 (81.9)				
2	Cough	284 (49.5)				
3	Difficulty in breathing	170 (29.6)				
4	Headache	109 (19)				
5	Bodyache	234 (40.8)				
6	Abdominal pain	21 (3.7)				
7	Loose motion	45 (7.8)				
8	Vomiting	35 (6.1)				
9	Weakness	181(31.5)				
10	Loss of appetite	75 (13.1)				
	ENT symptoms					
1	Change/Loss of smell	200 (34.8)				
2	Change/Loss of taste	269 (46.9)				
3	Change/Loss of smell and taste both	163 (28.4)				
4	Nasal blockage	78 (13.6)				
5	Running nose	57 (9.9)				
6	Ringing in ears	3 (0.5)				
7	Sore throat	143 (24.9)				
8	Hearing loss	3 (0.5)				
9	No ENT symptoms	212 (36.9)				

while 05(1.9%) patients had incomplete recovery from taste sensation (Table 2).

Loss of sensations was seen more in males as compared to females. Male: female ration for altered smell and taste sensation was 1.63:1 (124 vs. 76/200) and 1.72:1 (170 vs. 99/269) which was statistically significant (p value of 0.030 and 0.027) respectively.

Among 200 patients who experience altered smell sensation, 40 (20%) patients reported nasal blockage and 20 (10%) patients reported running of nose.

For sub-group analysis, we divided patients into mild, moderate, and severe groups as per clinical guidelines of ICMR and Ministry of Health and Family Welfare, Government of India, to compare frequency and recovery pattern of smell and taste dysfunctions among these groups.

Mild disease group includes patients (n = 338) with upper respiratory tract symptoms with or without fever without shortness of breath/hypoxia and admitted in COVID ward for observation and symptomatic treatment. Moderate disease group (n = 176) includes patients with breathlessness and SpO2 90% to 93% on room air and required oxygen by face mask. Severe disease group included 60 patients who presented with breathlessness, SpO2 < 90% on room air and respiratory rate > 30/minute. They were admitted in HDU/ICU and required high flow oxygen or non invasive ventilation. A comparative table (Table 3) shows that the loss of smell sensation is seen maximally in mild cases and the difference among mild, moderate and severe cases are statistically significant (p value 0.00001); while the difference in loss of taste sensation among all three grades of severity is statistically insignificant (p value 0.0770).

Discussion

This prospective analytical study was undertaken to assess the involvement of smell and taste sensation, its duration, and recovery pattern in RTPCR positive COVID-19 patients, and also to compare these amongst mild, moderate and severe cases.

In present study, 34.84% (200/574) patients reported alteration/loss of smell, while 46.86% (269/574) patients reported alteration/loss of taste sensation. Larco et al. reported that the frequency of anosmia in COVID-19 affected persons ranged between 22 and 68% and frequency of taste dysfunction from 20 to 33% [19]. Another series of 417 patients with COVID-19 reported the involvement of smell and taste sensation in 85.6% and 88.0% respectively which is much higher than reported in present study [20]. Paolo Boscolo-Rizzo et al. reported prevalence of smell and taste dysfunction in 66.3% patients in their case series of 202 patients [21] Mullol et al. showed

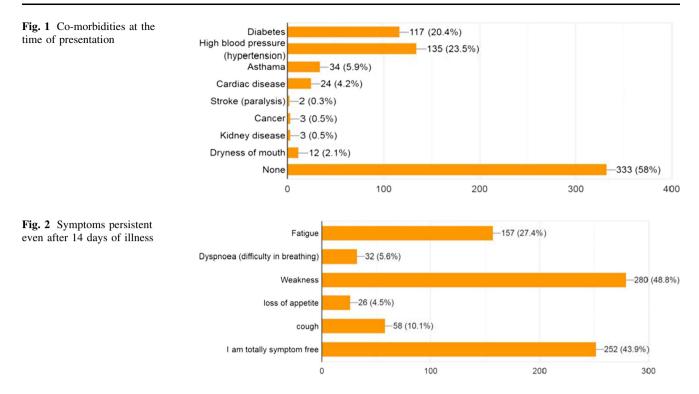


Table 2 Analysis of involvement of smell and taste sensation and their recovery pattern

S	Variables		Sensations affected	
No		Smell (n = 200) N (%)	Taste (n = 269) N (%)	
1	Onset of altered sensations	As first symptom	49 (24.5)	55 (20.45)
		Within 7 days of onset of illness	136 (68.0)	182 (67.66)
		Between 7 to 14 days of illness	15 (7.5)	32 (11.89)
2	Type of involvement	Partial loss of sensation	73 (36.5)	120(44.61)
		Complete loss of sensation	115 (57.5)	96 (35.69)
		Altered sensations	12 (6.0)	53 (19.70)
3	Onset of improvement in sensations	Within 7 days of onset of altered 1 sensation	79 (39.5)	107 (39.78)
		7 to 14 days of onset of altered sensation	99 (49.5)	132 (49.07)
		After 14 days of onset of altered sensation	22 (11.0)	30 (11.15)
4	Complete recovery	After one week of onset of altered sensation	68 (34.0)	85 (31.59)
		After two weeks of onset of altered sensation	74 (37.0)	113 (42.00)
		After one month of onset of altered sensation	33 (16.5)	54 (20.07)
		After two months of onset of altered sensation	18 (9.0)	12 (4.46)
		Incomplete/No recovery even after two months of follow-up	07 (3.5)	05 (1.9)

a high variability of smell or taste dysfunction ranging from 5 to 98% depending on the methodology used in the study and country [22]. A meta analysis based on data from 24 studies on 8438 patients reported prevalence of olfactory and gustatory dysfunction in 41.0% and 38.2%, respectively [23]. Another study done on 718 patients reported that 101 (14%) patients experienced either altered smell or taste, with 52 (7%) experiencing both altered smell and taste. Seventy-seven (10.7%) patients had altered smell and 76 patients had altered taste sensation (10.5%) [24].

	Smell sensation			Taste sensation		
	Smell sensation preserved (%)	Smell sensation lost (%)	Lost smell sensation recovered (%)	Taste sensation preserved (%)	Taste sensation lost (%)	Lost taste sensation recovered (%)
Mild disease $(n = 338)$	193 (57.2)	145 (42.8)	139 (95.8)	169 (50)	169 (50)	167 (98.8)
Moderate disease $(n = 176)$	139 (79)	37 (21)	36 (97.3)	106 (60.22)	70 (39.7)	69 (98.57)
Severe disease $(n = 60)$	42 (70)	18 (30)	18 (100)	30 (50)	30 (50)	28 (93.33)
	P = 0.00001			P = 0.0770		

Table 3 Loss of smell and taste sensations in mild, moderate and severe cases

We observed a clear male predominance in our study as 62% (124/200) male and 38% (76/200) female patients reported altered smell sensation while 63.1% (170/269) male and 36.8% (99/269) female patients reported alteration in taste sensation which is in contrast with other studies presenting female predominance [25].

Out of 60 patients with severe disease, altered smell was found in 30% (18) patients and altered taste was seen in 50% (30) patients with 100% recovery in altered smell and 93.33% in altered taste within 2 months. Andrea mazzatenta et al. conducted a study on 100 patients with severe CoViD-19 infection who were on assisted breathing with oxygen therapy, reported that smell impairment occured in 95% of patients, while 47% showed taste dysfunction [26].

There is paucity of data among severely affected patients as the description of anosmia and dysgeusia may seem unnecessary when clinicians deal with critically ill patients (Yang et al. 2020) [27]. Furthermore, details of symptoms are difficult to obtain when patients are critical.

Present study reports 68% (136/200) patients developed onset of loss of smell and 67.66% (182/269) patients develop altered taste sensation within seven days of onset of illness. A study done by Claire hopkins et al. found that 60% (229/382) and 94.8% patients reported onset of anosmia and reduced sense of taste respectively in less than 1 week [28].

Gluseppe mercante et al. found a significant association between nasal obstruction (38.2%) and runny nose (40.2%) with severe reduction of taste and smell [29] in our study only 20% (40/200) patients reported nasal blockage and 10% (20/200) patients reported running of nose. In 2007, Suzuki et al. demonstrated that coronavirus may be detected in the nasal discharge of patients with olfactory dysfunction. They observed that some patients with normal acoustic rhinometry did not recover their olfaction, suggesting that nasal inflammation and related obstruction were not the only etiological factors underlying the olfactory dysfunction in viral infection. This could explain the presence of olfactory dysfunction without nasal congestion [30].

We observed that most of patients with altered smell 96.5% (193/200) and taste 98.1% (264/269) sensation recovered to normal after two months of onset. A study done by Jerome R. Lechien et al. showed 79.5% of patients recovered normal smell sense within 2 months following the onset of loss of smell [31]. Pradipt ranjan sahoo et al. reported that 92% patients regained olfaction and 96% regained taste sensation, on follow-up at the 2 weeks of the PCR positivity [24]. The varied time taken for the recovery in different patients may be due to the various pathophysiological mechanisms causing damage to neuronal tract. Studies have suggested that COVID-19 could be neuro invasive in the central structures of the olfactory system [32]. Mao et al. [33] suggested 3 possible means of entry of SARS-CoV-2 into the brain; via olfactory nerves in the nasal cavity, through interaction with angiotensinconverting enzyme-2 (ACE-2) receptor in the brain, and through cytokine storm-induced blood-brain barrier disruption. This variability of the virus's potential entry into and damage to peripheral and central structures of the olfactory system may result in varied presentations.

Fever (81.9%) was most common symptom found in our study followed by cough (49.5%), body aches (40.8%) and dyspnea (29.6%). kadhiresan jayashree et al. reported fever (30%) as most common symptom followed by headache (18%) and cough (18%) in their COVID-19 positive patients [34].

The strength of present study is the adequate sample size of patients. We have also compared the frequency, duration and recovery of smell and taste alterations among mild, moderate and severe cases of COVID19 positive patients which to the best of our knowledge, no study has compared and published the data. It has got its limitations too: it was self reported loss of sensations rather than their objective assessment. Secondly, we lost 31 (5.12%) patients who could not complete all the follow-ups but even this is well within the acceptable range.

Conclusions: The present study confirms the high prevalence of olfactory and gustatory disorders in COVID-19 infection. Smell and taste loss may be used as indicators of potential infection and early identification may help to reduce the risk of spread, especially in asymptomatic /pre symptomatic cases. It also concludes that majority of patients recovers completely within two months of onset of altered sensations.

Declarations

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval All procedure performed in the study were in accordance with the ethical standards of the institution.

Informed Consent Informed consent was obtained from all individual participant in the study.

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