



Prospective Analysis of the Chronology of Smell and Taste Dysfunction in COVID-19 Positive ENT Doctors

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Abstract Olfactory and gustatory dysfunction has been reported as an early presentation in COVID-19. We intent to analyze the chronological outline of these chemosensory disturbances in term of onset, progression and resolution in ENT doctors with COVID-19. In six symptomatic otolaryngologists who tested positive for SARS-CoV-2, detailed symptomatology of olfactory and gustatory dysfunction was collected prospectively on regular basis till a period of at least three months. Due to their awareness, sensitivity and reliability, even mild and transient relevant symptomatology could be recorded accurately. Olfactory and gustatory dysfunction was universally present in all the six otolaryngologists. The onset of the symptoms was in first week and resolved completely within 4 weeks in four of them. In two doctors the recovery of olfactory dysfunction to near normal level was delayed and prolonged over 2 and 3 months. The pattern of involvement of basic tastes like sweet, salt, sour and bitter as well as food temperature and texture etc. pointed towards involvement of the gustatory mucosa with non-uniform involvement of the papilla and taste receptors. One of the doctors also experienced reappearance of parosmia and phantosmia in the 3rd month following complete disease resolution. Due to their expertise in the field of Otolaryngology, the recruited doctors represented the precise pattern of progression and resolution of olfactory and gustatory

dysfunction in COVID-19. Larger studies are needed to validate our reported universal presence of these symptoms with complete recovery rate following disease resolution.

Keywords Anosmia in COVID-19 · Hyposmia · Phantosmia · Dysgeusia · Hypogeusia · Otolaryngologists

Introduction

The coronavirus disease 2019 (COVID-19) is a viral pandemic spreading at a rapid pace across the globe. Common presentation of COVID-19 includes fever, cough, myalgia, sore throat, rhinorrhea, headache, shortness of breath and diarrhea [1, 2]. Anosmia and dysgeusia has been reported by many otolaryngologists across the world as early symptoms of COVID-19. The incidence of olfactory and gustatory dysfunction in COVID-19 has been reported as 19–88% [3–6]. However, the chronological outline of these chemosensory disturbances in COVID-19 is limited due to retrospective nature of studies and unavailability of long-term follow-up. In this prospective study on six COVID-19 positive symptomatic ENT doctors, we have analyzed the pattern of evolution and resolution of olfactory and gustatory changes till a minimum of three months.

Materials and Methods

This case series is based on the analysis of prospectively recorded data related to smell and taste disturbances experienced by 6 symptomatic COVID-19 positive otorhinolaryngologists. With due permission from institutional ethical committee, we documented the symptomatology of these doctors who consented to provide detailed

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and accurate relevant data for analysis and publication. The 6 doctors experienced symptoms while being actively involved in ENT out-patient department and operation theatre while following the recommended protocol on the usage of personal protective equipment as per the institute. Following their positive result on reverse transcriptase polymerase chain reaction (RT-PCR) testing for SARS-CoV-2, five of them were hospitalized in isolation wards and one doctor opted for home isolation. During their disease course, they were contacted telephonically on daily basis for their general symptoms as well as symptoms related to smell and taste. Being otorhinolaryngologists, they could notice and report precisely about their smell and taste dysfunction with regard to onset, progression and recovery on day-to day basis for at least three months.

Results

The demographic and basic disease related details are listed in Table 1. All infected doctors experienced mild disease severity as per the WHO Interim Guidelines for Clinical Management of COVID-19. All the doctors received symptomatic treatment based on the evidence available at that point of time as well as local health authority guidelines. The first presenting feature in all the doctors were fever and myalgia. The incidence of other symptoms were as follows: cough—3 patients, diarrhea—3, headache—2, sore throat—3, nasal congestion—3, and rhinorrhoea in 1 patient. All of them experienced asthenia for a variable period of time (7–45 days) starting from first day of symptom onset to 7 days after symptom onset.

Half of the doctors had smell as well as taste disturbances with onset within 3 days of being symptomatic and rest three doctors reported onset of anosmia within the first week. The onset, progress and resolution of smell dysfunction of all the doctors is briefed in Table 2. Four of the doctors reported anosmia and two experienced hyposmia. All the 6 doctors had taste disturbances in the form of

hypogeusia in five and dysgeusia in three of them. The onset of these symptoms were within first 6 days in all of them. Complete loss of taste was reported by one doctor who experienced significant hyposmia. The rest of the doctors, though had anosmia, experienced hypogeusia or dysgeusia. One doctor experienced dysgeusia (persistent bitterness in the mouth) only on the second day. The recovery pattern of each basic taste function along with sensations mediated by the trigeminal nerve is mentioned in Table 3.

In the first doctor, 11 weeks after the symptom onset and following complete symptomatic relief, complaints of phantosmia (strong odour of onion) and significant parosmia to all food items and day-to-days items like skin creams, body odour etc. appeared. These symptoms quickly progressed and was reported as unbearable making all the food items unpalatable by the doctor which lasted for 10 days. The symptoms gradually improved over next 6 days making the doctor symptom free on day 16. All the basic tastes were intact and the doctor did not experience any other symptoms. During this phase, repeat RT-PCR for COVID-19 was negative and the antibodies against the virus was more than 10 Index which was done during 7th week (4 weeks before the symptom recurrence).

Discussion

The literature on COVID-19 reports of smell and taste disturbances in a widely variable proportion of patients, ranging from 15.7 to 88% [5, 7]. This small case series limited to six Otolaryngology doctors with COVID-19 infection finds smell and taste disturbances to be universally noted by all. Otolaryngology doctors are likely to be precisely aware of symptoms related to smell and taste, and hence the sensitivity and accuracy of these symptoms are therefore best captured in this case group. This case group also provided all the insight into the patients'

Table 1 Demographic and basic disease related details of all cases

Demographic and overall disease related details	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age/sex	29/female	31/male	32/female	28/male	27/male	27/female
Co-morbidity	None	None	None	None	None	None
Symptom severity	Mild	Mild	Mild	Mild	Mild	Mild
Type of exposure (high risk/low risk/intermediate)	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Initial presentation	Fever, sore throat, myalgia	Fever, diarrhea, malaise	Fever, myalgia, malaise	Fever, malaise, headache	Fever, malaise, sore throat, cough	Fever, myalgia, nasal congestion

Table 2 The chronology and character of olfactory disturbances in all cases

Smell related symptoms/signs (in days starting from the day of onset of first symptom(s) as day 1)	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Day of onset and type	3, hyposmia	3, phantosmia (persistent smell of vomitus)	3, anosmia	7, anosmia	5, anosmia	6, hyposmia
Days of maximal dysfunction and type	4 and 5, anosmia	4–11, significant hyposmia (some smells like floor cleaners and deodorant perceived minimally)	3–16, anosmia	7–12, anosmia	5–25, anosmia	6–8, hyposmia
Improvement course in days	6 till 26	12 till 25	17 till 90	13 till 20	26–60	9,10
Duration (onset to maximal recovery)	24 days	23 days	88 days	14 days	55 days	5 days
Complete recovery	Yes	Yes	Almost	Yes	Almost	Yes
Associated nasal symptoms/signs and duration	Rhinorrhea: 2–4 Nasal congestion: 5–13	Nasal congestion: 5–7	None	None	None	Nasal stuffiness, 1–6

prospective on olfactory and gustatory dysfunction relevant to Otolaryngologists.

Smell and taste disturbance are much less likely in other illnesses presenting with upper respiratory catarrh or pharyngitis and fever. The commonly associated viruses with such dysfunction are rhinovirus, parainfluenza virus, corona virus and Epstein-Barr virus [8]. However, approximately 1% of patients suffer from permanent anosmia which has been correlated with reduced number of olfactory receptors, decreased volume of olfactory bulb and hypometabolism in the areas of central olfactory projections [9–14]. A recovery rate over many years has been quoted as one third to two third of all patients with viral upper respiratory infections [15, 16].

Among COVID-19 positive patients, these chemosensory dysfunction appear within initial three days in 85% of cases [17]. The incidence of phantosmia and parosmia has been reported as 12.65% and 32.4% respectively [5]. The gustatory dysfunction in the form of hypogeusia and ageusia has been found in 78.9% and 21.1% of patients, respectively [5]. Taste disturbances co-existing with smell disturbances have been reported in 55% of cases and in 1.5% of cases without any smell related symptoms [17]. The short term recovery rate for smell disturbances has been quoted as 44% and the median recovery time for both the chemosensory dysfunction has been noted as 7 days, whereas most of the patients recover within 3 weeks [5, 15].

As most of the reported studies are retrospective, the symptoms of trivial smell and taste related disturbances may suffer from unawareness, underestimation and recall bias, which was present in 7.6% of patients as reported by Leichien et al. [5]. This limitation has been addressed in our small prospective series where even minimal and

transient symptoms were reported. Hence, a higher incidence of smell and taste disturbances in COVID-19 positive cases may be expected as compared to already reported in literature. As all the doctors were followed up till complete recovery and as maximum as three months after first symptoms, we noticed 100% recovery rate in both smell and taste disturbances in this series as compared to the reported 15% and 59.7% incidences of no recovery rate in taste and smell disturbances respectively [17].

The onset of taste dysfunctions in our series, was within first three days in three of the doctors and maximum dysfunction lasted just for a day. Recovery trend started early and all of them reported complete recovery by the end of 4–5th week. One doctor who presented with gastrointestinal symptoms, experienced slightly delayed onset ageusia which lasted for a week, but recovered completely by 4th week. Recovery of taste function was reported as complete following appreciation of aroma of food items and not following complete return of just the basic taste sensations. Recovery of food flavors roughly corresponded with recovery of smell function by 75–80% as reported by the otolaryngologists in this case group. We noticed that the more is the total duration of maximal chemosensory dysfunction, the longer is the recovery time. Also, though the onset of both smell and taste dysfunction had a similar temporal pattern, there was no specific association between the recovery trend and duration.

The different basic taste dysfunction combinations could not be explained by affected specific types of papilla over the tongue mucosa responsible for sensing specific tastes. The third doctor had affected salty and bitter taste but not sweet whereas both salt and sweet taste are perceived by fungiform papillae. Similarly, involvement of different sensory nerves carrying the taste sensations from different

Table 3 The character and chronology of gustatory dysfunction in all cases

Symptoms/signs (Day 1 is the day of onset of first symptom related to COVID-19)	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Day of onset of gustatory dysfunction, type	3, hypogeusia	3-dysgeusia, hypogeusia	3-dysgeusia, hypogeusia	2-dysgeusia (persistent bitter taste)	5-(hypogeusia to bitter taste)	6, hypogeusia to bitter, sweet, sour
Day of maximal dysfunction, type	3, significant hypogeusia	6–12, ageusia	3-hypogeusia and dysgeusia	2	5, 6 hypogeusia	6, 7 hypogeusia
Improvement pattern noticed (on day)	4 till 26	13–30	4 till 17 for hypogeusia 4 till 35—dysgeusia	2	7	8–10
Complete recovery	Yes	Yes	Yes	Yes	Yes	Yes
Total duration of dysfunction (in days)	24	28	35	1	2	5
Other oral symptoms and signs	Sore throat: 1–4	Median glossitis, Burning sensation on food intake: 15–19	Sore throat: 20–25	None	Sore throat: 1–4	None
Loss and recovery pattern for salt taste	Complete loss—day 3, recovery started on day 8, recovered on day 9	Hypo—day 4,5, complete loss: 6–12, recovery started on day 15, complete recovery day 20	Hypo—day 3, complete recovery—17	–	–	–
Loss and recovery pattern of sweet	Complete loss—day 3, recovery started on day 8, recovered on day 9	Hypo—day 5, complete loss: 6–12, recovery started on day 15, complete recovery day 20	No loss	–	–	Hypo, 6, 7, recovery started on 8 and complete recovery by 10th day
Loss and recovery pattern of sour	Reduced—day 3, recovery started on day 8, complete recovery day 9	Complete loss—4–18 Recovery started on day 19, complete recovery on day 20	No loss	–	–	Hypo, 6, 7, recovery started on 8 and complete recovery by 10th day
Loss and recovery pattern for bitter	Reduced—day 3, recovery started on day 8, complete recovery day 9	Complete loss:4–18 Recovery started on day 19, complete recovery on day 20	Hypo—day 3, recovery—17	–	Hypo, day 5,6	Hypo, 6, 7, recovery started on 8 and complete recovery by 10th day
Sense of food temperature/texture/pain	hotness of chilies and raw onions not perceived	Persistent burning sensation	Loss of cooling sensation after using menthol-based gargle	Intact	Intact	Intact

parts of the tongue also could not explain the pattern of taste disturbances in our series. Type 1 gustatory receptors are associated salt and sweet taste, type 2 receptors with sour and type 3 with bitter taste sensation. Involvement of specific types of taste receptors also could not explain the dysfunction pattern. There was overlapping pattern of basic

taste disturbances due to dysfunction of multiple types of receptors and the loss of salt and bitter taste with preserved sweet taste in the third doctor could not be explained by the receptor concept alone as suggested by many studies [18–20]. However, type 3 receptor dysfunction was universally present in the doctors who experienced hypo/

ageusia. We also noticed that the sense of temperature and hotness of chilies was lost in two of our doctors suggesting the disease involvement of the tongue mucosa which also perceive the temperature, pain and texture sense through the papillae and further carried by branches of trigeminal and glossopharyngeal nerve. After analyzing all the possible mechanisms of taste dysfunction based on the involvement of individual types of taste, dysfunction of the gustatory mucosa by virus with non-uniform dysfunction of different types of tastes and sensation from the tongue seems the most probable explanation. Also, virus infiltration of the oral mucosa may be associated with salivary transmission of the novel corona virus which may result in disease transmission through shared food items and cutlery when not disinfected properly.

In one of the doctors, the occurrence of phantosmia and parosmia 11 weeks after onset of COVID-19 and complete disease recovery may represent a delayed neurological sequelae though we could not undertake a neuroimaging study during this symptomatic recurrence. No such incidences have been reported till date regarding delayed onset smell or taste dysfunction after disease resolution. Reactivation of the viral activity in the involved nerves and central nervous system when the antibody level declines in the blood, may explain this type of symptoms as seen in cases of herpes virus induced Bell's palsy and Ramsay Hunt syndrome. However, this postulation need further research to be proved or disproved.

The limitations associated with this study are the small number of cases and lack of objective tests to quantify the olfactory and gustatory disturbances. The disease severity was mild in all the six doctors in this case series; hence we cannot generalize our results to all the cases of COVID-19.

Conclusions

Presence of olfactory and gustatory dysfunction in all the COVID-19 positive symptomatic otolaryngologists in our prospective case series, indicates towards the possible universal occurrence of chemosensory disturbances in COVID-19. We also noticed universal recovery of the chemosensory dysfunction in this case group. Based on the pattern of taste disturbances, involvement of gustatory mucosa may explain the non-uniform combination and severity of different taste as well as trigeminal nerve mediated sensations. Following complete disease resolution, we report the first instance of phantosmia and parosmia 11 weeks after disease onset with no other accompanying symptoms of COVID-19.

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Declarations

Conflict of interest The author(s) declare that they have no conflict of interest.

Ethical Approval Approved by institute Ethical Committee, AIIMS, New Delhi, India for conduction of the study.

Informed Consent Written informed consent for publication was obtained from participants.

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