Prevalence of Loss of Smell and/or Taste and other Otorhinolaryngology Symptoms in COVID-19 Patients

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ABSTRACT

Background

Loss of smell and/or taste have been described in COVID-19 patients. Studies have not been conducted to evaluate the loss of smell and/or taste in the context of Nepal.

Objective

To investigate the prevalence of Ear, Nose and Throat related symptoms and assess smell and taste disorders in laboratory-confirmed SARS-CoV-2 patients.

Method

This prospective cross-sectional study evaluated patients from September 2020 to March 2021 with preceding COVID-19 diagnosis from a tertiary centre in Kathmandu. COVID-19 positive patients visiting out-patient department, quarantined or admitted were included. Patients were given questionnaire consisting of demographic data, history of smoking and evaluation of presenting symptoms. Loss of smell and taste were subjectively tested and followed up via telephone for ten weeks to evaluate for recovery time and degree of recovery.

Result

A total of 226 patients participated in the study, 18-92 years old (mean age, 36.77 ± 15.23 years; 53.5% males, 69% non-smokers). Majority of the patients had Myalgia (n = 128, 56.6%) as their presenting symptoms followed by fever (n = 122, 53.9%), loss of smell (n = 117, 51.7%), cough (n = 107, 47.34) and sore throat (n = 102, 45.1%). Loss of sense of smell and taste was reported in 51.8% and 42% respectively. The association between loss of sense of smell and taste was statistically significant ($p < .001$). All patients had some degree of recovery with 64.1% recovery of smell and 64.2% recovery of taste within 14 days of onset of symptoms. The mean recovery time for sense of smell and taste was 14.34 ± 9.82 days and 15.03 ± 10.06 days, respectively.

Conclusion

Olfactory and gustatory dysfunctions are cardinal features of COVID-19. They recover spontaneously along with other symptoms within few weeks. The absence of smell or taste in times of pandemic can be suggestive of potential COVID-19 infection and be used as a screening tool for early diagnosis and reduce transmission of the infection.

KEY WORDS

COVID-19, SARS-CoV-2, Loss of smell, Loss of taste

INTRODUCTION

SARS-CoV-2, the etiological agent of a global pandemic of coronavirus disease 2019 (COVID-19) was initially identified in late 2019 in China.[1,2] The clinical presentation of SARS-CoV-2 namely, fever, cough, tiredness, and difficulty breathing have been well described in the literature.[1,2] Lately, ear, nose, and throat (ENT) symptoms, including loss of smell and/or loss of taste (STL) have been described.[2,3]

The World Health Organization has pointed STL as a potential screening symptom for COVID-19. Subsequently, Otolaryngologic and Rhinologic Societies have suggested to take into account newly acquired sudden STL as a potential COVID-19 infection.[3-11] Screening for STL could help in early detection, testing, and guiding quarantine instructions.[1,2,4]

With the increase of publications concerning STL pertaining to the pandemic, we planned to undertake a study in our hospital. The objective of the study was to investigate the prevalence of ENT related symptoms and determine the frequency, severity and recovery of STL in laboratory-confirmed SARS-CoV-2 patients.

METHODS

This descriptive, cross-sectional, hospital based study was conducted at Kathmandu Medical College Teaching Hospital, located in capital city Kathmandu, tertiary referral center for all kinds of disease including COVID-19. The study was conducted from September 2020 to March 2021. Convenience sampling method was done. The inclusion criteria were all patients ≥ 18 years, any gender, providing consent, diagnosed with COVID-19 confirmed with Polymerase chain reaction (PCR) positive testing for the SARS-CoV-2 viral genome at Kathmandu Medical College Teaching Hospital and patients clinically able to fulfill the questionnaire. Patients who were less than 18 years at the time of study, no confirmed positive PCR test results, failure to complete the whole questionnaire, patients unable to answer (intubated, admitted in the intensive care unit, under mechanical ventilation), history of olfactory and gustatory disorders before COVID-19 outbreak, recent head injury, brain or nose surgery or unreachable by telephone were excluded from the study. Data was not collected from deceased patients. Written informed consent was obtained from all the participants (if possible) or family members/relatives and confidentiality of information was maintained. Ethical clearance and approval of the protocol to be followed were obtained from the Institutional Review Committee of Kathmandu Medical College Teaching Hospital. The approval number for our study is 0710202002.

A questionnaire survey was administered to these patients and interviewed through telephone after admission during the isolation days. Patients were contacted via telephone to evaluate smell and taste impairment due to COVID-19 and data was collected in the proforma. All the data collected were entered in Microsoft Excel. Questionnaire consisted of demographic data of patients, history of smoking and evaluation of symptoms at presentation such as need to blow nose, nasal obstruction, sneezing, running nose, cough, post nasal discharge, ear fullness, dizziness, facial pain, fever, sore throat, headache, myalgia, difficulty breathing and diarrhoea. Patients were also assessed for loss of sense of smell and taste and its frequency, severity and recovery. Patients with complaints of smell loss and taste loss were further inquired separately via telephone to investigate the recovery of smell and taste. In cases of STL, the degree of recovery was assessed subjectively by asking patients to compare current sense of smell and taste with patients' own chemosensory functions before COVID-19 infection. We followed-up patients for 10 weeks to evaluate recovery. The degree of recovery was classified under 'none' for no recovery, 'partial recovery' for some degree of recovery, however, not the same as pre-COVID-19 senses and 'complete recovery' for regain of smell and taste with functionality just the same as before.

Descriptive statistics are presented as mean, standard deviation, minimum and maximum for continuous data value and frequency for categorical. Normality testing was done using the Kolmogorov-Smirnov test. For comparison of continuous data between groups, independent t-tests was used. For comparison of categorical data between groups, a chi-square test was used. Statistical analysis was performed on SPSS Statistics version 20.0. For all statistical analysis, significance was accepted at $p < .05$.

RESULTS

A total of 236 patients participated in the study. Out of these participants ten did not meet the inclusion criteria (eight were less than 18 years of age and two were unreachable via telephone), thus excluded from the study. So, 226 patients with confirmed polymerase chain reaction (PCR) testing positive for SARS-CoV-2 and answering all the questions were included in the study as shown in Figure 1. The patients' age ranged from 18 to 92 years (36.77 ± 15.23 years), 53.5% were males (n = 121) and 69% (n = 156) were non-smokers. The mean time for duration of symptoms was 4.84 ± 4.38 days.

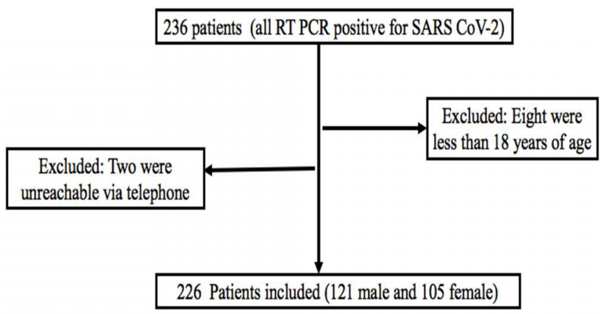

Figure 1. Flow diagram of patient selection

Table 1. Demography and clinical presentation of patients with SARS-CoV-2 in the study population

Characteristics		Number (%)
Age	≤40 years	153 (67.6)
	>40 years	73 (32.3)
Sex	Male	121 (53.54)
	Female	105 (46.46)
History of smoking	Yes	70 (30.97)
	No	156 (69.02)
Onset of symptoms	≤7 days	188 (83.18)
	>7 days	38 (16.81)
Myalgia	Yes	128 (56.63)
	No	98 (43.37)
Fever	Yes	122 (53.98)
	No	104 (46.01)
Loss of sense of smell	Yes	117 (51.76)
	No	109 (48.24)
Cough	Yes	107 (47.34)
	No	119 (52.66)
Sore throat	Yes	102 (45.13)
	No	124 (54.87)
Loss of sense of taste	Yes	95 (42.03)
	No	131 (57.96)
Headache	Yes	87 (38.49)
	No	139 (61.51)
Running nose	Yes	69 (30.53)
	No	157 (69.47)
Nasal obstruction	Yes	52 (23)
	No	174 (77)
Need to blow nose	Yes	51 (22.56)
	No	175 (77.44)
Sneezing	Yes	39 (17.25)
	No	187 (82.75)
Difficulty breathing	Yes	28 (12.38)
	No	198 (87.62)
Ear fullness	Yes	26 (11.5)
	No	200 (88.5)
Diarrhoea	Yes	22 (9.73)
	No	204 (90.27)
Post nasal discharge	Yes	20 (8.84)
	No	206 (91.16)
Dizziness	Yes	20 (8.84)
	No	206 (91.16)
Facial pain/ pressure	Yes	18 (7.96)
	No	208 (92.03)

The demographic profile and clinical symptoms of patients are reported in Table 1.

The majority of the patients (56.6%) had myalgia as their presenting symptoms followed by fever, loss of smell, cough and sore throat. Loss of sense of smell was reported in 51.80%. The mean age of loss of sense of smell was 36.77 ± 14.62 years. Loss of sense of taste was reported in 42%. The mean age of presentation of loss of sense of taste was 35.22 ± 13.69 years. Loss of smell and taste occurred simultaneously in 32.3%.

Association of presenting symptoms with gender, age and history of smoking

The presenting physical symptoms of patients were not statistically significant with gender (all p > .05). Headache, myalgia and difficulty breathing were found to be statistically significant with age. (p = .028, p = .000 and p = .008, respectively). History of smoking and myalgia were found to be associated (p = .007). (Table 2)

Comparison of groups with loss of smell and loss of taste

The association between loss of sense of smell and loss of sense of taste was statistically significant (p < .001). Patient with altered smell were more likely to have nasal obstruction (p = .001), sneezing (p < .001), runny nose (p = .003) ear fullness (p = .021), postnasal discharge (p = .029) and facial pain (p = .021) (Table 3). However, patients with dysguesia were more likely to have headache (p = .040). A total of 49 out of 95 (51.57%) patients with loss of sense of taste had headache. Other symptoms were not associated with loss of sense of smell or taste (all p > .05). (fig. 2).

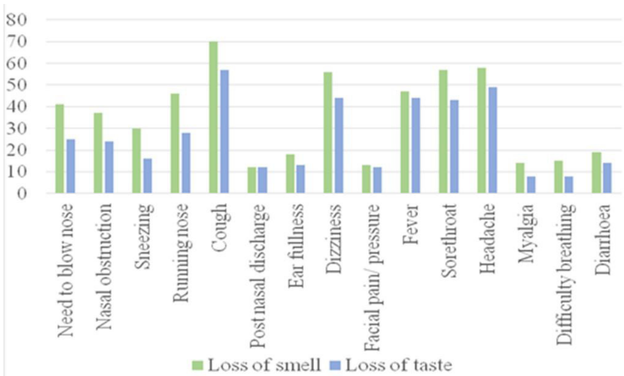

Figure 1. Presenting symptoms of SARS-CoV-2 in loss of smell and loss of taste groups

Recovery status of loss of sense of smell and taste

Our research identified 64.1% of patients who recovered from loss of smell within 14 days. On arranging duration of recovery into groups, more number of patients recovered within 10-14 days (31.62%). The average time for recovery of sense of smell was 14.34 ± 9.82 days. About 64% of patients with loss of taste sensations recovered within 14 days. Most number of patients recovered within 10-14 days (41.05%). The average time for recovery of sense of taste was 15.03 ± 10.06 days.

Degree of recovery of smell and taste

All the patients having loss of smell and taste had some degree of recovery. None of the patients were found to not have recovered some sense of smell and taste.

Table 2. Association of presenting symptoms with gender, age and history of smoking

Variables		Gender			Age group			Smoking history		
		Male	Female	p value	≤ 40 years	> 40 years	p value	Yes	No	p value
Myalgia	Yes	72 (31.8)	56 (24.7)	.351	75 (33.1)	53 (23.4)	.001	49 (21.6)	79 (34.9)	.007
	No	49 (21.6)	49 (21.6)		78 (34.5)	20 (8.8)		21 (9.2)	77 (34)	
Fever	Yes	65 (28.7)	57 (25.2)	.932	82 (36.2)	40 (17.6)	.866	37 (16.3)	85 (37.6)	.820
	No	56 (24.7)	48 (21.2)		71 (31.4)	33 (14.6)		33 (14.6)	71 (31.4)	
Loss of sense of smell	Yes	61 (26.9)	56 (24.7)	.661	78 (34.5)	39 (17.2)	.731	39 (17.2)	78 (34.5)	.427
	No	60 (26.5)	49 (21.6)		75 (33.1)	34 (15)		31 (13.7)	78 (34.5)	
Cough	Yes	55 (24.3)	52 (23)	.541	68 (30)	39 (17.2)	.206	31 (13.7)	76 (33.6)	.537
	No	66 (29.2)	53 (23.4)		85 (37.6)	34 (15)		39 (17.2)	80 (35.3)	
Sore throat	Yes	57 (25.2)	45 (19.9)	.522	66 (29.2)	36 (15.9)	.383	35 (15.4)	67 (29.6)	.325
	No	64 (28.3)	60 (26.5)		87 (38.4)	37 (16.3)		35 (15.4)	89 (39.3)	
Loss of sense of taste	Yes	48 (21.2)	47 (20.7)	.439	68 (30)	27 (11.9)	.288	26 (11.5)	69 (30.5)	.318
	No	73 (32.3)	58 (25.6)		85 (37.6)	46 (20.3)		44 (19.4)	87 (38.4)	
Headache	Yes	49 (21.6)	38 (16.8)	.507	53 (23.4)	34 (15)	.085	33 (14.6)	54 (23.8)	.074
	No	72 (31.8)	67 (29.6)		100 (44.2)	39 (17.2)		37 (16.3)	102 (45.1)	
Running nose	Yes	37 (16.3)	32 (14.1)	.987	50 (22.1)	19 (8.4)	.310	23 (10.1)	46 (20.3)	.611
	No	84 (37.1)	73 (32.3)		103 (45.5)	54 (23.8)		47 (20.7)	110 (48.6)	
Nasal obstruction	Yes	31 (13.7)	21 (9.2)	.317	36 (15.9)	16 (7)	.788	13 (5.7)	39 (17.2)	.288
	No	90 (39.8)	84 (37.1)		117 (51.7)	57 (25.2)		57 (25.2)	117 (51.7)	
Need to blow nose	Yes	29 (12.8)	22 (9.7)	.589	35 (15.4)	16 (7)	.872	15 (6.6)	36 (15.9)	.784
	No	92 (40.7)	83 (36.7)		118 (52.2)	57 (25.2)		55 (24.3)	120 (53)	
Sneezing	Yes	20 (8.8)	19 (8.4)	.756	28 (12.38)	11 (4.8)	.548	10 (4.4)	29 (12.8)	.429
	No	101 (44.6)	86 (38)		125 (55.3)	62 (27.4)		60 (26.5)	127 (56.1)	
Difficulty breathing	Yes	15 (6.6)	13 (5.7)	.997	14 (6.1)	14 (6.1)	.032	11 (4.8)	17 (17.5)	.309
	No	106 (46.9)	92 (40.7)		139 (61.5)	59 (26.1)		59 (26.1)	139 (61.5)	
Ear fullness	Yes	13 (5.7)	13 (5.7)	.700	18 (7.9)	8 (3.5)	.859	10 (4.4)	16 (7)	.380
	No	108 (47.7)	92 (40.7)		135 (59.7)	65 (28.7)		60 (26.5)	140 (61.9)	
Diarrhoea	Yes	14 (6.1)	8 (3.5)	.318	14 (6.2)	8 (3.5)	.668	7 (3)	15 (6.6)	.928
	No	107 (47.3)	97 (42.9)		139 (61.5)	65 (28.7)		63 (27.8)	141 (62.3)	
Post nasal discharge	Yes	9 (3.9)	11 (4.8)	.423	14 (6.1)	6 (2.6)	.818	7 (3)	13 (5.7)	.683
	No	112 (49.5)	94 (41.5)		139 (61.5)	67 (29.6)		63 (27.8)	143 (63.2)	
Dizziness	Yes	8 (3.5)	12 (5.3)	.203	8 (3.5)	12 (5.3)	.006	5 (2.2)	15 (6.6)	.545
	No	113 (50)	93 (41.1)		145 (64.1)	61 (26.9)		65 (28.7)	141 (62.3)	
Facial pain/ pressure	Yes	8 (3.5)	10 (4.4)	.420	10 (4.4)	8 (3.5)	.251	5 (2.2)	13 (5.7)	.760
	No	113 (50)	95 (42)		143 (63.2)	65 (28.7)		65 (28.7)	143 (63.2)	

Complete recovery of smell was found in 77.77%. Similarly, complete recovery of taste was found in 82.1%. The degree of recovery of smell was not significant statistically with the duration of recovery and age. Similarly, the degree of recovery of taste was not significant statistically with the duration of recovery and age (Table 4).

DISCUSSION

Coronaviruses, much studied about their effect on the respiratory system are also neuroinvasive, in particular the olfactory system. Hence, STL may be more pronounced in the COVID-19 patients than other respiratory viral infections.[12,13] With the help of spike protein (S), a type-1

Table 3. Association of loss of smell and taste with Demography and Presenting Symptoms

Characteristics		Loss of smell	p value	Loss of taste	p value
Age	≤40 years	153	.732	153	.290
	>40 years	73		73	
Sex	Male	121	.663	121	.441
	Female	105		105	
History of smoking	Yes	70	.429	70	.320
	No	156		156	
Onset of symptoms	≤7 days	188	.058	188	.148
	>7 days	38		38	
Myalgia	Yes	128	.318	128	.387
	No	98		98	
Fever	Yes	122	.170	122	.539
	No	104		104	
Cough	Yes	107	.872	107	.793
	No	119		119	
Sore throat	Yes	102	.264	102	.973
	No	124		124	
Headache	Yes	87	.594	87	.040
	No	139		139	
Running nose	Yes	69	.003	69	.770
	No	157		157	
Nasal obstruction	Yes	52	.001	52	.495
	No	174		174	
Need to blow nose	Yes	51	.400	51	.253
	No	175		175	
Sneezing	Yes	39	.000	39	.889
	No	187		187	
Difficulty breathing	Yes	28	.158	28	.617
	No	198		198	
Ear fullness	Yes	26	.021	26	.196
	No	200		200	
Diarrhoea	Yes	22	.785	22	.213
	No	204		204	
Post nasal discharge	Yes	20	.029	20	.848
	No	206		206	
Dizziness	Yes	20	.217	20	.089
	No	206		206	
Facial pain/ pressure	Yes	18	.021	18	.830
	No	208		208	

glycosylated transmembrane protein SARS-CoV-2 binds to cells via a specific cellular receptor angiotensin-converting enzyme 2 (ACE2) receptor, followed by protease-dependent S protein priming mediated by viral spike protein, Transmembrane Protease Serine 2 (TMPRSS2) cellular protease.[12]

The most common presentations of COVID-19 in our study were myalgia, fever, loss of smell, and cough in descending order of frequency. Huang et al. reported

Table 4. Comparison of the degree of recovery of smell and taste with the duration of recovery and age.

Recovery	Duration of recovery Mean ± SD	p value	Age Mean ± SD	p value
Degree of smell recovery				
Partial recovery (n = 26, 22.2%)	15.23 ± 11.42 days	.622	37.54 ± 14.19 years	.726
Complete recovery (n = 91, 77.8%)	14.08 ± 9.31 days		36.56 ± 14.81 years	
Degree of taste recovery				
Partial recovery (n=17, 17.9%)	14.24 ± 13.26 days	.427	34.06 ± 12.26 years	.782
Complete recovery (n=78, 82.1%)	15.21 ± 9.39 days		35.47 ± 14.05 years	

myalgia, fever, and cough as the three most common presenting symptoms, based on the evaluation of 41 COVID-19 patients in Wuhan, China, this study was one of the first few scientific papers based on COVID-19.[14] Similar clinical presentations were notable in other initial studies conducted in China.[14-16] Because not much was known about olfactory and gustatory manifestations with regards to COVID-19 infections so they had not been reported in the initial studies.

In our study, 51.8% of patients presented with loss of smell, and 42% of patients complained of loss of taste. Loss of smell and loss of taste was the third and sixth most common presenting symptoms respectively. In our study, thirty-two percent of the patients had both loss of sensation of smell and taste. Our observation was comparable to results from Vaira et al. which reported a loss of sensation of both smell and taste on objective evaluation for STL in forty-two percent COVID-19 patients.[11] Agyeman et al. conducted a systematic review including 8438 patients from twenty-four studies across 13 countries and showed 41.0% of patients presented with olfactory dysfunction and 38.2% presented with gustatory dysfunction.[17] Samaranayake et al. conducted a meta-analysis from eight studies including 11,054 COVID-19 patients, concluded that anosmia and dysgeusia were prevalent among 74.9% and 81.3% of the cases respectively.[18] The mean age of loss of sense of smell in our study was 36.7 years compared to 35.2 years in loss of taste. Similar observation has been made in other studies, STL being more common among patients in their 4th decade.[1,10] There were no significant age and gender differences for loss of smell and taste in our study.

However, in terms of frequency, male patients were more affected, which could be explained by the gender-based differences i.e. poor health-seeking behavior in women of Nepal.[19] However, there have been confounding results with regards to gender and STL. Samaranayake et al. concluded combined loss of smell and taste were more common in males, in contrary.[20] Lee et al. suggested strong association between loss of smell and taste in young females.[13]

The most plausible explanation for the anosmia in

COVID-19 would be damage to the olfactory bulb and nerve due to invasion and multiplication of SARS-CoV-2 and the entry of virus being through the olfactory bulb, the only part of the CNS which is not protected by dura.[13,21] In experiments done on mice that were transgenic for the SARS-CoV receptor (human ACE2) showed that the virus entered the brain primarily via the olfactory bulb.[22] Injury to the olfactory bulb was evidenced by micro bleeding or abnormal enhancement in patients with anosmia on MR Imaging.[23] Olfactory bulb atrophy post-COVID-19 infection could also be the cause of failure of recovery of loss of smell. Chiu et al. measured the olfactory bulb volume in a patient with persistent anosmia and had noticed a significant decrease in volume on consecutive MR imaging.[24] However, according to a recent study by Brann et al. human olfactory epithelial supporting cells, the sustentacular cells were found to express ACE2 and TMPRSS2 on single cell sequencing.[25] So the anosmia could be attributed to the injury to the sustentacular cell rather than the olfactory sensory neuron. Ageusia may be secondary to olfactory dysfunction. In a study done by Xu et al. wide and highly enriched expression of angiotensin-converting enzyme 2 receptor on epithelial cells of the oral mucosa and the epithelial cells of the tongue, enabling viral infection and injury resulting in ageusia.[26]

There was a significant positive association between loss of sense of smell and loss of sense of taste in our study. Similar association has been described in other studies.[1,27]

In our study, none of the patients had persistent loss of smell and taste. Out of 226 patients, 64.1% of patients recovered from loss of smell within 14 days. At 14-day follow up in another study, 67.1% of respondents had return of smell function, the number of which increased to 71.8% on 30-day follow-up.[28] Our study estimated slightly higher rate of recovery of smell (88.8%) within 25 days. Our results showed that 64.2% of patients recovered loss of taste within 14 days. This is lesser compared to study conducted by Reiter et al. on recovery of smell and taste after subjective smell and taste changes in COVID-19 infection in which 73.1% of respondents had improvements within 14 days.[28]

Coronavirus, Rhinovirus, parainfluenza virus, and Epstein-Barr virus can cause olfactory dysfunction.[6] An important implication of our results is on comparing the prevalence of olfactory dysfunction post viral infections, anosmia is much common in SARS CoV-2 infection as compared to other viruses causing upper respiratory tract infection. However, the rate of recovery of smell post COVID was higher in our study as compared to only 30% recovery following other viral anosmia.[29] This might infer that STL is transient in most of the COVID-19 cases and reversible. Additionally, specific treatment for the STL need not be required, as evidenced by self-recovery reported in all our patients.

To our knowledge this is the first study to assess the frequency and outcome of loss of smell and taste in COVID-19 patients in the context of Nepal. Prospective design, large sample size and evaluation of all real time SARS-CoV-2 PCR confirmed patients are the strengths of our study. However, results were derived from the subjective responses of individual patients. We could not conduct an objective smell assessment test such as the University of Pennsylvania smell Identification Test to confirm smell dysfunction. These tests are expensive, not easily available in our context and warrant prolonged contact between the Otorhinolaryngologist and the patient, increasing the risk of spread of infection substantially. Although our patients showed improvement in symptoms of STL, assessment of complete recovery in follow-up more than 70 days were not available.

CONCLUSION

ENT symptoms are concurrent with COVID-19 infections. Loss of smell and taste are common symptoms in COVID-19 positive individuals. New onset of loss of smell and/or taste during COVID-19 pandemic should be considered potential SARS-CoV-2 infection until proven otherwise. Considering anosmia and ageusia as a screening symptom and testing for potential COVID-19 disease and isolation can substantially lower the risk of transmission of COVID-19. However, long term, multicentric, detailed studies are needed to understand olfactory and gustatory dysfunction, in terms of its prevalence, pathogenesis, role in disease progression and severity, and prognostic value.

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