

# PROGRESS OF ORONASAL MANIFESTATIONS IN COVID-19 PATIENTS DURING THE INFECTION

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## **Abstract:**

**Background:** Coronavirus disease 2019 (COVID-19) is a pandemic affect the world in end of 2019 which is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is rapidly spreading from its origin in Wuhan City of Hubei Province of China to the rest of the world. **Objectives:** The main objective of this study is to highlight the oro-nasal manifestations that could be reported in mild to moderate cases of COVID-19 patients. **Subjects and methods:** The study design was a cross-sectional trial based on a questionnaire survey. The questionnaire contained demographic data regarding patient gender, age and level of education. The questionnaire was assessed by a group of dentists' students. We asked 100 patients about oro-nasal manifestations during the COVID period. This was done written by answer a question paper. **Results:** 100% of patients suffered from complete loss of test, 65% of patients suffered from severe ulceration. 32.6 % patients suffered from glossitis. 43.5% of patients suffered from gingivitis. Also 82.6% of patients expressed halitosis. 87% of patients suffered from complete loss of smell however, 87 % of patients suffered from headache. 82.6 % of patients suffered from nasal congestion and finally, 21.7 % of patients expressed rhinorrhea. **Conclusions:** It was proven that mild-to-moderate cases of COVID-19 infection were associated with oro-nasal manifestations, with variable incidence. The most frequent oral manifestation was complete loss of taste, while the least expressed symptom was halitosis. The most frequent nasal manifestations were complete loss of smell and headache, while the least expressed symptom was rhinorrhea.

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## **INTRODUCTION AND REVIEW OF LITERATURE:**

Coronavirus disease 2019 (COVID-19) is a transmissible disease that started to spread globally by the end of 2019. A coronavirus strain – identified as; severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2) – is responsible for developing this respiratory infection. <sup>[1]</sup> Coronaviruses are single stranded RNA, enveloped, positive- sense, diverse viruses. Their diameter ranges from 60 nm to 140 nm. They are given the prefix corona, because their surfaces are jabbed, giving them a crown appearance. <sup>[2]</sup>

The World Health Organization (WHO), On February 11th, 2020, called the new disease - brought about by SARS-CoV-2 virus - CoV disease (COVID-19). One month later, it was declared as a pandemic.

As the beginning of 21st century, two highly infectious viruses have emerged: the Middle East Respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-Co V). SARS-CoV-2 virus, the causative agent for the COVID-19, has emerged by the end of 2019, and by March 2020, it was declared a pandemic. <sup>[3]</sup>

According to the WHO, the total cases are 619,161,228 as of October 2022. The WHO claims that the worldwide total deaths from Covid-19 is over 15 million. <sup>[3,4,5]</sup> It is no secret, that COVID-19 has overburdened the

healthcare system and caused massive financial crisis worldwide, despite the fact, its mortality is much lower than SARS-CoV and MERS-CoV. The fact is SARS-CoV-2 virus is more transmissible than the other viruses. <sup>[6]</sup>

It is widely known that COVID-19 mainly causes respiratory tract illness with symptoms ranging from mild to severe. <sup>[7]</sup> The most common symptoms are cough, fever, dyspnea, tiredness, loss of taste and smell, and shortness of breath. Less frequent symptoms are diarrhea, nausea, skin discoloration, nasal congestion, runny nose, and sore throat.

Older age group (65 years or older) is at higher risk of developing severe SARS-CoV-2 infection because of higher proportion of established co-morbidities. However, younger adults are also being hospitalized with severe illness, albeit with much lower frequency [8].

In a study by Zhang et al., SARS-CoV-2 infection was less likely in smokers, but the likelihood of the severity of disease upon infection in smokers may be higher<sup>[9]</sup>. Data from USA suggests that obesity may be considered as an independent risk factor for hospitalization and severe disease <sup>[10]</sup>.

Children are less likely to develop symptomatic infection and are less prone to severe disease <sup>[11]</sup>. Furthermore, there have been reports of taste alterations and olfactory disturbances documented during the earlier course of the disease <sup>[12]</sup>. Additionally,

cutaneous manifestations such as erythematous rashes and urticaria have also been reported in infected patients [13].

COVID-19 has also been associated with the involvement of the cardiovascular system [14-16]. Moreover, neurological manifestations such as headache, altered conscious state, dizziness, and acute cerebrovascular disease have also been exhibited by patients [17]. Regarding liver injury in COVID-19, multiple reasons such as drug-related hepatotoxicity and immune-mediated damage like cytokine storm have been suggested to play a role [18]. On studying the development of venous and arterial thrombotic events, most of the venous thromboembolic events were Pulmonary Embolisms (PEs) [19].

Moreover, there have also been reports of an increase in the number of children presenting with a disease termed Multisystem Inflammatory Syndrome in Children (MIS-C), thought to be a result of SARS-CoV-2 induced inflammation. Lastly, ophthalmological involvement is infrequent but it has been documented nevertheless, majorly as ocular pain, redness, and follicular conjunctivitis.

In a study by Kamel et al., carried on Egyptian people who recovered from covid-19 to discuss the relationship between oral health and severity of covid and effect of oral health and covid on recovery period. Study done on 377

people and showed that people with bad oral hygiene the bacterial count colonizing teeth was proven to be raised twofold to tenfold, thus introducing more bacteria into the bloodstream, resulting in bacteremia. It was observed that the severity of COVID-19 symptoms significantly increased in patients with poor oral health status.

Moreover, symptoms of severity significantly decreased in those with good oral health status. It shows that delayed recovery period (up to six weeks) was found on people with bad oral hygiene and severe symptoms. while fast recovery period (2 weeks) found on people with good oral health and mild symptoms.[20] Chen et al. [21] referred to xerostomia in COVID-19 patients. They reported that, dry mouth was present in 46.3% overall, 22.2% of males and 24.1% of females. The prevalence of xerostomia associated with COVID-19 seems unlikely to vary by country, as it ranged from 46% to 56% in Italy, China. [22,23]

In another review by Aziz et al. [24], the prevalence of ageusia/dysgeusia was estimated to be 49.8% in five studies. Amorim dos Santos et al. [25] revealed that the prevalence of dysgeusia, hypogeusia, and ageusia are 38%, 35%, and 24%, respectively, in 33 studies between March and June 2020.

The latest review of Cirillo et al., including 67 eligible studies (27,687 COVID-19 cases, 16 countries, and multi-national cooperation),

indicated that the overall reported prevalence of gustatory dysfunction shows geographical differences ranging from 5.6% to 96%. The prevalence and the characteristics of gustatory

dysfunction associated with COVID-19 may depend on or relate to country or ethnicity, age, gender, and disease severity. In COVID-19 infection, the most reported symptom was fever. Cough was the second most common manifestation [26-28].

Dyspnea and fatigue are reported in many patients. Dysgeusia is the first oral manifestation of covid 19 followed by oral ulcers, cheilitis, and tongue lesions (before hospitalization), while perioral pressure ulcers, macroglossia, blisters, and oral candidiasis (during hospitalization). One of most common oronasal manifestations of COVID-19 were sore throat accompanied with pharyngeal erythema, nasal congestion, rhinorrhea, and headache [29-32].

Meticulous checkup of the oral cavity in respiratory medicine is usually ignored. However, it can help in clinical diagnosis and in providing advice and guidance to the patients. In addition, dentists who detect atypical oral lesions should seek appropriate guidance and professional medical advice.

## **OBJECTIVES**

The major aim of this study is to draw attention

to the oral and olfactory signs that patients with mild to moderate COVID-19 instances may experience. Additionally, to raise awareness among dentists of these oral symptoms to facilitate early diagnosis and maintain patients' overall health and welfare.

## **SUBJECTS AND METHODS:**

### **Study design:**

Based on a questionnaire survey, the study was created as a cross-sectional trial. The patients who are included were chosen from the Al-Ahram Canadian University Hospital. The COVID-19 test results for each subject were all positive. Demographic information about the patient's gender, age, and level of education was included in the questionnaire. The oronasal symptoms during the COVID-19 infection period were discussed with one hundred patients. Written answers to a question paper were used.

### **Exclusion criteria:**

The following exclusion criteria have been taken into account: non-Egyptians, those between the ages of 18 and 50, those who did not complete the entire questionnaire, those without a confirmed positive PCR test result, patients who reported to have poor oral hygiene or who had any of the oral symptoms that were being looked into prior to the epidemic, patients with chronic illnesses, smokers, those who had a serious case of Covid-19 infection,

and patients who needed to be hospitalized.

Inclusion criteria:

The following inclusion requirements have been considered: Egyptian, adult > 18 and 50 years old, laboratory-confirmed COVID-19 infection (PCR), non-smokers, medically healthy patients, patients with mild-to-moderate symptoms without severe respiratory failure, patients with reported good oral hygiene, and patients who had not previously experienced any oral manifestations.

Questionnaire tool:<sup>[33]</sup>

Personal information	
Name	
Age	
Marital status	
Qualifications	

Oral symptoms	Yes	No
Loss of taste sensation		
Ulcers		
Glossitis		
Any gingival disease		
Halitosis		

Nasal symptoms	Yes	No
Loss of smell		
Headache		
Nasal congestion		
Rhinorrhea		

Tests to confirm covid infection:

Test	Yes	No
PCR		
CRP		
Ferritin		
d-dimer		
Chest x-ray		

### Statistical analysis:

Information entered using IBM SPSS Statistics for Windows, version 22.0. (IBM Corp., Armonk, USA). The 2 test was used to compare the incidence of the researched parameters between the groups. Statistical significance was defined as a p-value 0.05. The GraphPad 7 tool was used to analyze the data. The Mann-Whitney test was used to compare the two groups (oral manifestations and nasal

manifestations).

### **RESULTS:**

In this study data was collected from 100 patient, 92 patient were included while eight patients were excluded because they are not Egyptians. In this study, we mainly included patients with mild to- moderate symptoms, without severe respiratory failure, who were not hospitalized.

#### Effect of mild covid 19 infections on oral health

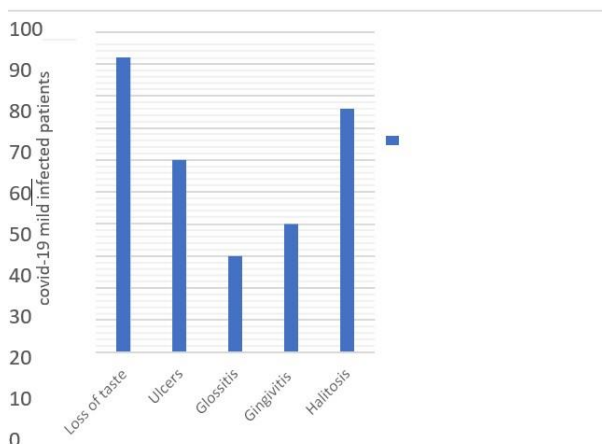
Hundred percent of patients suffered from complete loss of test, 65% of patients suffered from severe ulceration. 32.6 % patients suffered from glossitis. 43.5% of patients suffered from gingivitis. Also 82.6% of patients expressed halitosis.

There were statistically significant differences ( $p \leq 0.05$ ) between the respondents' answers regarding each symptom, (Table 1, graph 1). Comparing the incidence of the oral manifestation expressed, there was a significant difference between them with a significant high incidence of complete loss of taste however, significant low incidence of glossitis at  $p$  value  $\leq 0.05$ .

Oral manifestation	Incidence	No	%	P value
Loss of taste	Yes	2	100%	<0.05*
	No		0%	
Ulcers	Yes	0	65.2%	<0.05*
	No	2	34.8%	
Glossitis	yes	0	32.6 %	<0.05*
	No	2	67.4%*	
Gingivitis	Yes	0	43.5%	<0.05*
	No	2	56.5%	
Halitosis	Yes	6	82.6%	<0.05*
	No	6	17.4%	

Table 1:

Showing incidence and percentage of each oral manifestation either in covid-19 mild infected patients.\*Significance difference when the  $p$  value is  $\leq 0.05$



**Graph 1:** Showing the collaboration between Incidence of different oral manifestation in covid-19 mild infected patients.

### Effect of mild covid 19 infections on olfactory health

Eighty seven percent of patients suffered from complete loss of smell however, 87 % of patients suffered from headache. 82.6 % of patients suffered from nasal congestion and finally ,21.7 % of patients expressed rhinorrhea. Comparing the incidence of the nasal manifestation expressed, there was a significant difference between them with a significant low incidence of rhinorrhea at p value  $\leq 0.05$ . (Table2 and graph 2)

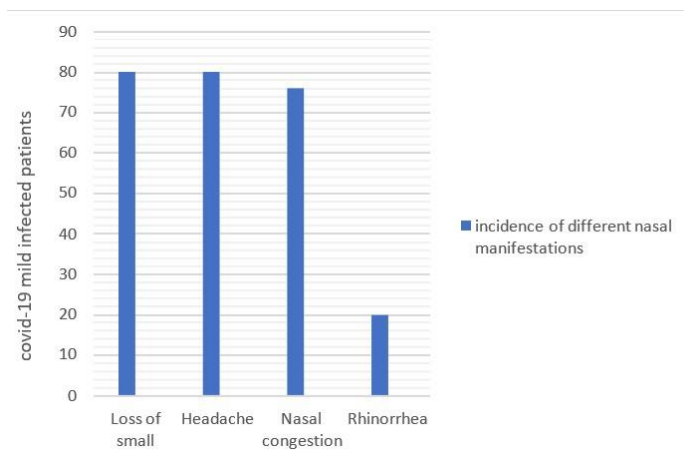
Nasal manifestations	Incidence	No	%	P value
Loss of smell	Yes	8	7%	<0.05*
	No	1	3%	

Headache	yes	8	7%	<0.05*
	No	2	13	
Nasal congestion	Yes	6	2.6 %	<0.05*
	No	6	7.45%	
Rhinorrhea	Yes	0	1.7%	<0.05*
	No	2	8.3%	

**Table 2:**

showing incidence and percentage of each nasal manifestation in covid-19 mildinfected patients.

\*Significancedifference when the pvalue is  $\leq 0.05$



**Graph 2:**

Showing the correlation between incidence of different nasal manifestations in covid-19 mildinfected patients.

Data were analyzed using the GraphPad 7 program, Two groups were compared by Mann-Whitney test and the results were considered significant when ( $P \leq .05$ ). The interpretation of the statistical results of nasal and oral manifestations showed that median of oral = 60 while median of nasal =78 and there was no significant difference between the two group when ( $P < 0.05$ ) . (Table 3)

Nasal manifestations vs. Oral manifestations	
P value	0.7857
Significantly different? ( $P < 0.05$ )	No
Sum of ranks in column A,B	23.50 , 21.50
Mann-Whitney U	8.500
Median of column A	60.00
Median of column B	78.00

Table 3: Nasal - oral data among the studied groups

### **DISCUSSION:**

Covid -19 pathogenicity is a serious threat to public health owing to its rapid transmission among the public, and virulence. The clinical characteristics remain to be unclear: the infected individual may exhibit no symptoms at all, some individuals show mild symptoms,

and others appear with severe symptoms with multiorgan failure [3-5].

The primary sites of infection are the nasopharyngeal and oropharyngeal issues. They are the source of infection transmission and the site for sample collection. The literature focuses mainly on the lower respiratory tract infection owing to potentially fatal nature. Our study highlighted the oral and olfactory manifestations that could be reported in mild to moderate cases of COVID-19 patients.[32]

In this study data was collected from 100 patient, 92 patient were included, eight patients were excluded, because they are not Egyptians. Hospitalized patients were excluded to avoid the variable of different drug usage. The study excluded subjects below 50 years old, since they are considered more susceptible to severe Covid 19 symptoms by the WHO. [34]

In this survey, hundred percent of patients suffered from complete loss of test, and 87% of patients suffered from complete loss of smell. Smell and taste dysfunctions in COVID-19 patients were sparsely mentioned in many literatures and there is still a paucity of peer-reviewed literature to support a causal association between anosmia (loss of smell) and COVID-19 [35].

Menni et al. (not peer reviewed article) observed that loss of smell and taste were encountered in 59% of COVID-19 positive



patients in comparison to 18% of those with negatively- tested COVID-19 negative test. It was suggested that fever, persistent cough, loss of taste and smell, fatigue, and GIT symptoms are prognostic for positive Covid 19 test. Anosmia was unclear if it is developed before the other symptoms or after <sup>[36]</sup>.

After performing smell and taste tests on 72 patients with positive covid 19 test and with no history of function loss, Varia et al. found 73.6% of the Covid positive patients experienced loss of smell and taste, while 14.4% had unrelated olfactory dysfunctions <sup>[37]</sup>.

The first peer reviewed study that reported 58.6% olfactory dysfunction was done by Lechien. However, they utilized a questionnaire focusing on social and psychological impact of smell dysfunction specifically in Covid 19 pandemic <sup>[38]</sup>.

Kaye et al. report on 237 US patients with COVID-19 and found that 73% reported anosmia, and that loss of sense of smell was the initial symptom in 26.6%. While Mao et al. found out anosmia in 5.1% of their studied cases. However, later studies show much higher incidence <sup>[39, 40]</sup>

Furthermore, 65% of COVID-19 patients reported the appearance of ulcers in their oral cavities. This is in accordance with several cases, in which blisters and oral ulcers occurred during COVID-19 infection. It has been demonstrated that psychological upsets, such

as anxiety and stress, contribute to the development and progression of oral lesions like recurrent aphthous ulcers, and this applies to COVID-19 patients. It has also been proven that psychological distress stimulates the immunoregulatory mechanism by elevating the leukocyte count at inflammatory sites. In addition, ACE2 is detected in the oral cavity and appears in high amounts in epithelial cells. It is elevated in the tongue, gingival and buccal mucosa. These findings demonstrate that the oral mucosa may be a target for COVID-19 infection <sup>[41, 42]</sup>

In the present study, 82.6% of COVID-19 patients complained of halitosis. It has been reported that oral halitosis caused by respiratory tract infections may reach up to 10%.<sup>23</sup>. This could be due to the passage of sinus or nasal secretions into the oropharynx. The pungent gases produced by different respiratory pathogens are retained in the exhaled breath, stimulate olfactory receptors, and are released through the mouth or the nose, causing malodor. In addition, halitosis is also among the symptoms related to *Helicobacter pylori* infection, which is the major pathogenic cause of ulcerative alterations in the gastric mucosa. Moreover, gastroesophageal reflux disease is usually associated with halitosis <sup>[43, 44]</sup>.

In this study, 32.6 % patients suffered from glossitis. 43.5% of patients suffered from

gingivitis. It has been reported that in addition to potential direct viral infection, the cytokines such as gamma interferon, interleukins, prostaglandin E2 and TNF, and pro-inflammatory signaling molecules induced by the infection can impact for gingivitis and glossitis. These mediators fight against various microorganisms, but when the immunologic response becomes hyperactive, it can damage various tissues.<sup>[45]</sup>

Also in this questionnaire, 87 % of patients suffered from headache. 82.6 % of patients suffered from nasal congestion and finally, 21.7 % of patients expressed rhinorrhea. This is in accordance with several clinical studies, which reported these symptoms as the most prevalent ones in mild and moderate cases of COVID-19 infection.<sup>[38]</sup>

Therefore, we should pay more attention to olfactory and/or gustatory symptoms in the suspicious COVID-19 patients with or without the main COVID-19 symptoms because asymptomatic COVID-19 infection (and/or transmission) is a major public health issue at present.

### **CONCLUSIONS:**

From this survey it was concluded that:

The most common oral manifestation for the subjects, whereas halitosis was the least common symptom.

Additionally, it was established that mild-to-

moderate COVID-19 infections were occasionally linked to nasal symptoms. The participants that were included reported experiencing headaches and total loss of smell the most frequently, while rhinorrhea was the least common symptom.

Based on the foregoing, it is important to underline the value of dental examinations for people with infectious diseases and the part a dentist plays in helping difficult situations like COVID-19 patients as a member of a multidisciplinary team.

Moreover, it is necessary to follow the clinical course and the long-term results of olfactory and/or gustatory dysfunctions in the cured COVID-19 patients.

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