



SIGNIFICANCE OF ORAL PRESENTATION IN COVID -19 PATIENTS

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ABSTRACT

The importance of oral manifestations in SARS-CoV-2 patients is still controversial. The aim of this study was to determine the oral manifestation of the hospitalized patients for COVID-19. A total of 50 patients met the inclusion criteria and gave their signed informed consent. A questionnaire of 17 questions regarding the oral and systemic health condition was administered to these patients during the convalescence. A descriptive statistic was performed. Data were analyzed to assess the statistical significance. A statistically significant increase of about 48% of reporting xerostomia during hospitalization was observed. Meanwhile, a decrease of oral hygiene was observed during the hospitalization, even if a non-statistically significant difference was shown between the two study time points (before and after hospitalization). During the hospitalization period, 98% of patients reported impaired taste, 28% burning sensation, and 34% difficulty in swallowing. The onset of the oral manifestations varied considerably among the cases due to lack of reference time points. The importance of good oral hygiene could be an interesting aspect to evaluate a relationship between SARS-CoV-2 and oral manifestations. Further studies are necessary to better understand the symptoms of this new virus in order to faster detect its presence in humans.

KEYWORDS : SARS-CoV-2; COVID-19; xerostomia, hypogeusia, chemosensory alterations.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-chain RNA virus that is the cause of novel coronavirus disease known as COVID-19. It is the seventh coronavirus known to infect humans.^{1,2} It belongs to the family of Coronaviridae, of the order Nidovirales, comprising large, single, plus-stranded RNA as their genome.^{3,4} The new coronavirus SARS-CoV-2 has, like other coronaviruses, with high probability, a zoonotic origin.⁵ The main transmission routes described are direct, as caused by coughing, sneezing, droplets of saliva expelled during the phonation, or indirect by contact with the main body mucous membranes such as oral, ocular, and nasal.^{6,8} The main symptoms of COVID-19 are fever, tiredness, and dry cough. Some patients may experience soreness and muscle pain, nasal congestion, runny nose, sore throat, or diarrhea, but in severe cases, the infection can cause pneumonia, severe acute respiratory syndrome, kidney failure, and even death.⁶ Although there are many studies in the literature on clinical signs in positive SARS-CoV-2 patients, the majority of them have not verified the oral health status of the patients.¹⁰ Possible oral-related symptoms include: hypogeusia, xerostomia, and chemosensory alterations.¹¹ Interestingly, xerostomia has been found mainly among COVID-19 patients, due to the neuroinvasive and neurotropic potential of SARS-CoV-2.

Pathogenesis

It has been stated that COVID-19 acute infection, along with associated therapeutic measures, could probably contribute to adverse outcomes concerning oral health. Current research shows that coronavirus invades human cells via the receptor angiotensin-converting enzyme 2 (ACE2) through scRNA-seq data analyses. The study identified the organs that are at risk and are vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections (e.g., lung; Zou et al. 2020).¹² Therefore, cells with ACE2 receptor distribution may become host cells for the virus and cause inflammatory response in related organs and tissues, such as the tongue mucosa and salivary glands.^{13,14} Badran et al. suggested that the periodontal pocket could be a reservoir for this virus.¹⁵ Dziejczak and Wojtyczka, in 2020 stated that the impaired immune system and/or susceptible oral mucosa can lead to various opportunistic fungal infections, unspecific oral ulcerations, recurrent oral herpes simplex virus (HSV-1) infection, dysgeusia, fixed drug eruptions, xerostomia linked

to decreased salivary flow, ulcerations and gingivitis.¹⁶

Pathogenesis of taste disorders in Covid-19 patients



1. Peripheral nervous system is affected by the new coronavirus.
2. As gustatory buds are innervated by cranial nerves, related functions may be impaired resulting in taste disorders.^{17,18}
3. SARS-CoV-2 may bind essential salivary mucin components, such as sialic acid, consequently accelerating taste particle degradation and disturbing gustatory sensation.^{19,22}
4. The tongue presents a high expression of ACE2 and its interaction with SARS CoV- 2 may affect normal gustatory functions through dopamine and serotonin synthesis pathway coregulation.^{23,24}
5. ACE inhibitors and ACE2 blockers are frequently associated with impairment of taste sensation.^{25,26} These drugs play a role in taste disorders by G protein-coupled and sodium channel inactivation.^{21,22}
6. The findings might also suggest the inability of ACE2 to degrade this protein during COVID-19 infection, resulting in disorderly taste responses.²⁷⁻²⁹ Therefore, taste disorders may be common symptoms in patients with COVID-19 and should be considered in the scope of the disease's onset and progression.

The oral signs and symptoms related to COVID-19 are taste disorders, unspecific oral ulcerations, desquamative gingivitis, petechiae, and coinfections such as candidiasis.³⁰ However, it is still uncertain whether these manifestations could be a typically clinical pattern resulting from the direct SARS-CoV-2 infection or a systemic consequence, given the possibility of coinfections, impaired immune system, and adverse reactions of medical treatment.^{16,31} Interestingly, in the present pandemic by SARS-CoV-2, olfactory and gustatory disorders have become extensively noticed as common symptoms of COVID-19.

Table 1: Most common oral lesions seen in SARS CoV-2 patients and affected sites

Oral mucosal lesions	Affected sites
White and erythematous plaques	Tongue
Irregular ulcers	Palate
Small blisters	Lip
Petechiae	Gingiva
Desquamative gingivitis	Buccal mucosa

Study Design and Sample Selection

A total of 50 patients were enrolled in this observational study conducted in a period of one month (from Jan 2021 to Feb 2021). The survey was completed by 50 patients who met, during the described period, the inclusion and exclusion criteria. The average age of the participants was 45.56 years. Of these, 64% were males and 36% females. A specific questionnaire of 17 questions was submitted to these patients detected by SARS-CoV-2 hospitalized at SMS Medical Hospital, Jaipur with the aim to collect information related to health status, oral hygiene habits, and symptoms in the oral cavity before and during the disease manifestation. The inclusion criteria were patients of both sex and of any age hospitalized for COVID-19 at the above mentioned hospital able to give their consent to participate in the study. The exclusion criteria were patients of both sex and any age hospitalized for COVID-19 at above mentioned hospital in need of intensive care and/or who were unable to give their consent to participate in the study. All the questionnaires were given to the patients during the doctor routine visits in that department. Then, all the papers were collected in a separate box with all the recommendations to reduce the contagion. Data collection took place in the time period from 2 Jan to 8 Feb 2021.

Statistical Analysis

Some of the answers were codified as dichotomous variables, namely as Yes/No responses, or in general as categorical variables. Given the nature of our survey we computed descriptive statistics for most of the questions. For each question, we computed the percentage of the respondents that gave a particular answer with respect to the number of total responses to the question. Answers obtained prior and during the disease manifestation were compared through the use of t-Test, to assess the statistical significance. All statistical comparisons were conducted with a significance level of $p < 0.05$. Statistical analyses were performed using the t-Test: two sample assuming equal variances.

Results

The results demonstrated that most of the patients (70%) had more than 20 teeth. Moreover, the majority of participants (66%) were nonsmokers. The 52% of them reported that they brushed their teeth twice a day, before hospitalization. The patients also reported that during the hospitalization period, the attention to oral hygiene decreased. Regarding the presence of oral manifestations 22% of patients reported xerostomia before hospitalization, while during hospitalization the percentage increased to 70%. The difference between the two study time points was statistically significant ($p = 0.00000019$). In addition, during the hospitalization period, 98% of patients reported impaired taste, 28% burning sensation, and 34% difficulty in swallowing. Finally, by comparing these data and the onset of some manifestations between sex and age, no statistically significant results emerged. All statistical comparisons were conducted with a significance level of $p < 0.05$. Statistical analyses were performed using the t-Test: two sample assuming equal variances.

DISCUSSION

Recent studies depicts a relevant role of the oral cavity and its mucosae in the transmission and in the pathogenicity of SARS-CoV-2.²⁸ It has been demonstrated that there is an increased gravity of COVID-19 in periodontopathic patients.³¹

The main aim of this study was to understand the correlation between SARS CoV-2 and oral manifestations of hospitalized patients. The total of 50 patients was included in our study, 64% were males and 36% females comprising of 66% non-smokers and 34% smokers. Most of the individuals 70% in our study had more than 20 teeth and they used to go to the dentist regularly, demonstrating the importance given to the oral health condition. Regarding the oral manifestations, 22% of patients reported xerostomia before hospitalization which subsequently increased to 70% during the period of hospitalization. These data are relevant because xerostomia has also been found in a relatively high proportion of COVID-19 patients from Chinese researchers.³² Although, xerostomia can also be induced by different drug therapies such as: antidepressants, antipsychotics, anticholinergics, antihypertensives, antihistamines, and sedatives. Therefore, the onset of this symptom can be associated with the drug therapy administered for the treatment of COVID-19 and also with the infectious and inflammatory processes activated by the virus itself.

Regarding other oral symptoms, 20% of patients reported burning sensation in mouth prior hospitalization which increased to 28% post hospitalization. 20% patients complained of difficulty in swallowing before hospitalization which increased to 34% post hospitalization. 92% patients complained of altered taste before hospitalization which increased to 98% post hospitalization. Indeed, dysgeusia can be described as one of the early symptoms of COVID-19 infection. Clinically, these data may allow easier identification of pre-symptomatic or asymptomatic patients. Moreover, the diagnosis of this oral manifestation may significantly reduce disease transmission, especially when diagnostic tests are not readily available and/or unpredictable.³³ It is almost known that such pathologies are aggravated by factors such as smoking. An interesting result that emerged from our study is that approximately 66% of the participants were nonsmokers. In the literature, there are several studies that analyzed the relationship between COVID-19 and smoking. According to the World Health Organization (WHO), no studies examined tobacco use and the risk of infection or the risk of hospitalization with COVID-19 among smokers.³⁴ In fact, the majority of the studies in the literature are observational reports, and they reported the prevalence of smoking amongst hospitalized COVID-19 patients.³⁴

Although this study reports interesting data of 50 COVID-19 hospitalized patients, it has its own limitations. Firstly, the small sample size, only 50 patients were enrolled because of difficulty in enrolling patients with the above mentioned criteria during that period and the difficulty in having personnel available to administrate the questionnaire. The questionnaires probably should have been done in a more specific way to better understand the occurrence of oral symptoms. Stress might play an important role in the appearance of these oral conditions. Cause-effect relationship between coronavirus infection and the appearance of oral lesions cannot be established. 95% of the patients were given the following drugs: lopinavir/ritonavir and/or hydroxychloroquine, in combination with other specific drugs for the various systemic pathologies they presented. Different types of therapies including chlorhexine mouthwash, nystatin, oral fluconazole, topical or systemic corticosteroids, systemic antibiotics, systemic acyclovir, artificial saliva, and photobiomodulation therapy (PBMT) were prescribed for oral lesions.

CONCLUSION

Oral symptoms are not frequently described in COVID-19 clinical studies. This study illustrates the close link between SARS-CoV-2 and oral manifestations. There is no scientific

evidence in the literature that certifies which oral symptoms SARS-CoV-2 can actually cause. The presence of xerostomia in our patients suggests a symptom given by the virus, but it must always be correlated with the patient's therapy. In addition, it may be essential to carry out the measurement of the salivary flow before and after the COVID-19 diagnosis to demonstrate a close correlation of it with the virus. Furthermore, dysgeusia is reported in 98% of cases post hospitalization which suggests that this symptom may be a warning signal for the patients. The multiple clinical aspects suggest coinfections, immunity impairment, and adverse reactions rather than a genuine oral mucosa infection primarily caused by SARS-CoV-2. Further studies are necessary to better understand the symptoms of this new virus in order to faster detect its presence in humans; probably, a multidisciplinary team following the COVID-19 patients could be of key importance.

Questionnaire

S.NO	QUESTIONS	BEFORE HOSPITALIZATION	DURING HOSPITALIZATION
1	Age		
2	Sex		
3	Place of origin		
4	How many teeth do you have in your mouth?		
5	When did you last go to the dentist?		
6	Are you wearing any prosthesis?		
7	Do you suffer from Diabetes/ cardiovascular disease?		
S.N	QUESTIONS	BEFORE HOSPITALIZATION	DURING HOSPITALIZATION
8	Smoker/ Non smoker		
9	No. of times you brush your teeth		
10	Bleeding gums		
11	Problem in chewing		
12	Problem in swallowing		
13	Burning sensation		
14	Halitosis		
15	Tooth problems/ pain		
16	Taste alterations		
17	Xerostomia		

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