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EVALUATION OF ORAL CHANGES IN PATIENTS INFECTED WITH SARS-COV-2: SEVERE VERSUS CRITICAL COVID-19

ANÁLISE DAS ALTERAÇÕES EM CAVIDADE BUCAL EM PACIENTES INFECTADOS POR SARS-COV-2: COVID GRAVE X COVID CRÍTICA

ANÁLISIS DE CAMBIOS EM LA CAVIDAD ORAL EN PACIENTES INFECTADOS POR SARS-COV-2: COVID GRAVE X COVID CRÍTICO

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ABSTRACT

Individuals infected with SARS-CoV-2 can develop a wide range of symptoms, with reported oral manifestations including xerostomia, sialadenitis, vesiculobullous lesions, ulcerative lesions, and dysgeusia. This study aimed to evaluate the oral changes in COVID-19 patients admitted to wards and intensive care units (ICUs) at two COVID-19 care units in Pernambuco, Brazil. This was an analytical, cross-sectional study involving 30 adult patients infected with SARS-CoV-2 of both sexes. Sociodemographic characteristics, symptoms, biomedical maintenance variables, and changes in the hard and soft tissues of the oral cavity were examined. Data were collected using a form containing sociodemographic information and medical history. An intraoral examination was also performed using the CPO-D and CPI indices and a physical examination to diagnose oral mucosal lesions. The data obtained were subjected to specific statistical tests and analyzed using SPSS software. The mean age of the patients was 64.47 ± 2.74 years, with 56.7% being male. The individuals exhibited poor oral hygiene, with 63.3% showing a high caries rate (DMFT = 22.5), severe periodontal disease, and 70% presenting oral lesions at the time of the examination. Based on the findings of this study, it was concluded that oral lesions were common

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among COVID-19 patients, regardless of their symptom severity. It was also observed that most of the patients had poor oral hygiene, periodontal issues, and tooth loss.

Keywords: Mouth Diseases. COVID 19. SARS-CoV-2. Intensive Care Units. Patients' Rooms.

RESUMO

As pessoas infectadas com SARS-CoV-2 podem desenvolver sintomas variados e as possíveis manifestações orais relatadas que podem ser observadas são xerostomia, sialoadenite, lesões vesículo bolhosas, lesões ulceradas e disgeusia. O objetivo deste estudo foi avaliar comparativamente as alterações bucais de pessoas infectadas com COVID-19 em enfermarias e unidades de terapia intensiva, em duas unidades de atendimento a paciente COVID em Pernambuco, Brasil. Este foi um estudo analítico com desenho transversal envolvendo 30 pacientes adultos infectados com SARS-CoV-2 de ambos os sexos. Foram observados condições sociodemográficas, sintomas, variáveis de manutenção biomédica, bem como alterações nos tecidos duros e moles da cavidade oral. Para a coleta de dados foi utilizado um formulário com informações sociodemográficas e histórico médico. Também foi realizado exame intraoral com os instrumentos CPO-D e CPI, bem como diagnóstico de lesões na mucosa oral pelo exame físico. Os dados obtidos nesta pesquisa foram submetidos a testes estatísticos específicos analisados no SPSS. Os pacientes analisados tinham média de idade de 64,47±2,74 anos, sendo 56,7% do sexo masculino. Os indivíduos apresentavam condições de higiene bucal precárias, com 63,3% apresentando alto índice de cárie (CPO-D= 22,5), com problemas periodontais graves, além de 70% apresentarem lesões orais no momento do exame. De acordo com os achados do presente estudo, foi possível concluir que as lesões orais foram frequentes em pacientes portadores de COVID-19 em diversos níveis sintomatológicos. Observou-se também que a maioria dos pacientes analisados apresenta uma má higiene oral, com problemas periodontais e perdas dentárias.

Palavras-chave: Doenças da Boca. COVID 19. SARS-CoV-2. Unidades de Terapia Intensiva. Quartos de Pacientes.

RESUMEN

Las personas infectadas con SARS-CoV-2 pueden desarrollar síntomas variados y las posibles manifestaciones bucales reportadas que se pueden observar son xerostomía, sialoadenitis, lesiones vesiculares ampollosas, lesiones ulceradas y disgeusia. El objetivo de este estudio fue evaluar comparativamente los cambios orales de personas infectadas con COVID-19 en salas y unidades de cuidados intensivos, en dos unidades de atención a pacientes COVID en Pernambuco, Brasil. Se trató de un estudio analítico con diseño transversal en el que participaron 30 pacientes adultos infectados con SARS-CoV-2 de ambos sexos. Se observaron condiciones sociodemográficas, síntomas, variables biomédicas de mantenimiento, así como cambios en los tejidos duros y blandos de la cavidad bucal. Para la recolección de datos se utilizó un formulario con información sociodemográfica e historia clínica. También se realizó un examen intraoral con los instrumentos CPO-D y CPI, así como diagnóstico de lesiones en la mucosa oral mediante examen físico. Los datos obtenidos en esta investigación fueron sometidos a pruebas estadísticas específicas analizadas en SPSS. Los pacientes analizados tenían una edad media de 64,47±2,74 años, de los cuales el 56,7% eran varones. Los individuos presentaban malas condiciones de higiene bucal, presentando el 63,3% un alto índice de caries (CPOD= 22,5), con problemas

periodontales graves, además el 70% presentaba lesiones bucales al momento del examen. Según los hallazgos del presente estudio, se pudo concluir que las lesiones bucales fueron frecuentes en pacientes con COVID-19 en diferentes niveles sintomatológicos. También se observó que la mayoría de los pacientes analizados presentan una mala higiene bucal, con problemas periodontales y pérdida de dientes.

Palabras clave: Enfermedades de la Boca. COVID 19. SARS-CoV-2. Unidades de Cuidados Intensivos. Habitaciones de Pacientes.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease that primarily affects the respiratory system and is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus belonging to the coronavirus family. The nomenclature “Coronavirus Disease (COVID-19)” was established by the World Health Organization (WHO), which became known as “SARS-CoV-2” by the International Committee on Taxonomy of Viruses (Gorbalenya *et al.*, 2020).

The WHO recognized COVID-19 as a pandemic disease in December 2019 when most countries reported significant numbers of infected people and deaths (WHO, 2020). Typical clinical symptoms of patients with COVID-19 were fever, cough, shortness of breath, myalgia, and weakness in the presence of an abnormal chest CT, while less prevalent symptoms were sputum formation, headache, hemoptysis, and diarrhea. A change in or loss of the sense of taste and smell was often observed (Guan *et al.*, 2020; Huang *et al.*, 2020; Lechien al., 2020; Vinayachandran, Balasubramanian, 2020).

SARS-CoV-2 enters human cells via the angiotensin-converting enzyme two receptor (ACE2), with current evidence indicating that ACE2 acts as the primary host cell receptor for the virus (Zou *et al.*, 2020). The virus binds to ACE2 using the spike-like protein on its surface, and the receptor will serve as a cell portal for entry of the virus into the cell to cause COVID-19 infection (Ciaglia *et al.*, 2020). Therefore, organs with high ACE2 expression, such as the lung, can become targets during SARS-CoV-2 infection, which then causes inflammatory reactions in related organs and tissues such as salivary glands and the tongue. This fact may explain the loss

of taste and oral ulceration as a result of the destruction of oral keratinocytes and fibroblasts (Zhou *et al.,* 2020). Otherwise, a high viral load in saliva and nasal secretion may be a pathogenic factor involved in the development of oral changes associated with COVID-19 infection, indicating a direct effect of the virus on oral tissues (Cruz Tapia *et al.,* 2020). On the other hand, these effects may be attributed to the indirect influence of the virus on the immune system, contributing to other opportunistic infections such as recurrent herpes simplex virus (HSV-1) infection and oral ulcerations (Brandao *et al.,* 2020; Dziedzic Wojtyczka, 2020).

COVID-19 can be transmitted directly or indirectly. Indirect transmission occurs through saliva, while direct transmission occurs through the inhalation of droplets emitted by coughing or sneezing or direct contact with oral, nasal, and ocular mucous membranes (Peng*et al.,* 2020; Speth, *et al.,* 2020). The oral cavity has been described as a mirror that reflects the underlying health status. Thus, careful examination of the mouth will aid in the early diagnosis and treatment since some oral symptoms (e.g., mouth ulcers, bleeding gums, dry mouth, oral discomfort, halitosis, burning sensation, or difficulty swallowing) may be associated with certain systemic disorders (Chi *et al.,* 2010). Within this context, several studies consider oral transmission to be one of the main routes of infection with COVID-19 (Gu *et al.,* 2020; Hindson, 2020; Yeo *et al.,* 2020).

Although many studies have addressed the validity of saliva for the diagnosis of COVID-19 (Fernandes *et al.,* 2020; Pedrosa *et al.,* 2020; Sabino-Silva *et al.,* 2020; To *et al.,* 2020), as well as precautions and implications for dental practice during the COVID-19 pandemic (Coulthard, 2020; Ge *et al.,* 2020; Sabino-Silva *et al.,* 2020; Spagnuolo *et al.,* 2020), there is a gap in knowledge about the oral manifestations related to COVID-19, as well as about the impact of the disease on the oral cavity and on the patient's quality of life. Therefore, the aim of this study was to investigate the oral manifestations associated with COVID-19 infection and to describe the oral signs and symptoms of patients with COVID-19 hospitalized in wards (severe COVID-19) and in intensive care units (ICUs) (critical COVID-19).

METHODOLOGY

The present study was conducted following the Declaration of Helsinki (revised 2012) and was approved by the local Ethics Committees on Research Involving Humans (approval number 4.386.409) and of Sociedade Pernambucana de Combate ao Câncer – SPCC (approval

number 4.469.039). All participants or legal representatives of the selected individuals signed the free informed consent form. This article was prepared following the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology).

This was an analytical, cross-sectional study. A convenience sample of thirty adult patients of both sexes with a positive diagnosis of COVID-19 who were hospitalized in the Specialized Emergency Care Unit of Goiana (UPAE GOIANA) and the Provisional Hospital Recife 1, Aurora Unit, State of Pernambuco, Brazil, between September 2020 and February 2021, participated in the study. Patients with incomplete and/or erroneous medical records were excluded.

A form was used to collect sociodemographic data, the results of medical examinations performed for the confirmation of COVID-19 infection, hematological and biochemical parameters, clinical symptoms, and medications used by the patients. All COVID-19 cases were confirmed twice in hospitalized patients by a positive real-time reverse transcription polymerase chain reaction (PCR) result for SARS-CoV-2 in nasopharyngeal swabs.

For the analysis of oral health, an intraoral examination was performed by a single previously calibrated dentist (one of the researchers) using the codes and criteria recommended by the WHO (Who, 2013). As visible plaque index, we used the Index of Oral Cleanliness (IOC) proposed by Bearn et al. 1996 based on the evaluation and distribution of plaque. The index of decayed, missing and filled teeth (DMFT) was used for the permanent dentition. A DMFT ≤ 7 was classified as low and an index ≥ 8 was classified as high (Klein; Palmer, 1937). The patient's periodontal condition was evaluated using the Community Periodontal Index (CPI) developed by the Who (1997) (Dhingra; Vandana, 2011), which assesses the presence of bleeding, calculus, and periodontal pockets. Oral mucosal lesions were diagnosed by anamnesis and intraoral examination. The patients were attended at the hospital bed.

The absolute and relative frequencies of the variables are given in tables. Numerical variables were reported as measures of central tendency and dispersion. The chi-squared test or Fisher's exact test was used for categorical variables and the Mann-Whitney test for numerical variables. All tests were applied adopting a 95% confidence interval and maximum error of 5%. The analyses were performed using the SPSS 23.0 software (SPSS Inc. Chicago, IL, USA).

RESULTS

Thirty adults and older adults ranging in age from 33 to 94 year (mean 64.47 ± 2.74 years) participated in the study; 56.7% were male and 73.3% were hospitalized in an ICU (critical patients). Most of the participants (84.4%) were admitted within the first week of symptom onset (mean of 5 days). Regarding outcome, 80% of these patients were discharged, while 20% died or were transferred to chronic treatment hospitals (Table 1).

Table 1

Characterization of the sample.

Variable	N	%
Age (years)		
18-59	9	26.7
60 or more	22	73.3
Sex		
Male	17	56.7
Female	13	43.3
Hospital unit		
ICU (critical)	22	26.7
Ward (severe)	8	73.3
Interval between symptom onset and admission (weeks)		
1 to 2	25	83.4
2 to 3	4	13.3
3 or more	1	3.3
Outcome		
Discharge	24	80
Transfer	3	10
Death	3	10
Total	30	100

Source: Personal archive.

Regarding the health conditions of the patients, 66.7% of the sample had hypertension, 46.7% had diabetes, and 70% had other comorbidities. In addition, 80% of the patients required oxygen therapy, and only 13.3% needed prone positioning. Oxygen saturation was the most frequently altered vital sign, with a mean saturation of 94%. The mean glucose concentration was 259 mg/dl. The hematological parameters were outside the reference range in most of the participants, with an altered leukocyte count of 53.3%, hemoglobin levels below the expected in

60%, and altered C-reactive protein of 70%. Alterations on chest X-rays were observed in 36.7% of the patients; 63.3% of the patients exhibited loss of smell and 66.7% had a loss of taste. The visible plaque index indicated the presence of precarious oral hygiene in 93.3% of the sample, with 63.3% showing a high caries index (DMFT = 22.5). Oral lesions were detected in 70% of the sample during examination (Table 2).

Table 2

Health condition of the sample.

Variable	**N**	**%**	**Mean**
Hypertension			-
Yes	20	66.7	
No	10	33.3	
Diabetes			-
Yes	14	46.7	
No	16	53.3	
Other comorbidities			-
Yes	21	70	
No	9	30	
Oxygen therapy			-
Yes	24	80	
No	6	20	
Prone positioning			-
Yes	4	13.3	
No	26	86.7	
Heart rate	-	-	86 bpm
Respiratory rate	-	-	24 bpm
Blood pressure	-	-	138 x 80 mmHg
Oxygen saturation	-	-	94%
Temperature	-	-	35.65ºC
Glucose	-	-	250.85 mg/dL
Hemoglobin			12.15 g/dl
Normal	9	30	
Altered	18	60	
Not obtained	3	10	
Hematocrit			36.459%
Normal	6	20	
Altered	11	36.7	
Not obtained	13	43.3	
Leukocytes			98,814.26 mm^3
Normal	11	36.7	

Altered	16	53.3	
Not obtained	3	10	
Platelets			
Normal	19	63.3	283,826.09 mm^3
Altered	4	13.3	
Not obtained	7	23.3	
C-reactive protein			
Normal	0	0	49.94 mg/dL
Altered	21	70	
Not obtained	9	30	
D-dimer			
Normal	0	0	5.59 µd/mL
Altered	5	16.7	
Not obtained	25	83.3	
Chest X-ray			
Normal	2	6.7	
Altered	11	36.7	-
Not performed	17	56.7	
Loss of smell			
Yes	19	63.3	
No	1	3.3	-
No data	10	33.3	
Loss of taste			
Yes	20	66.7	
No	3	10	-
No data	7	23.3	
Visible plaque index (oral hygiene)			
Adequate	2	6.7	-
Inadequate	28	93.3	
DMFT			
Low caries index	0	0	
High caries index	19	63.3	-
Edentulous	11	36.7	
Oral lesions			
Yes	21	70	-
No	9	30	
Total	30	100	

Source: Personal archive.

The oral lesions detected included pseudomembranous candidiasis, geographic tongue, lipoma, erythema multiforme, ulceration on the palate and dorsum of the tongue, vesiculobullous lesions, macules, and petechiae (Figures 1 and 2).

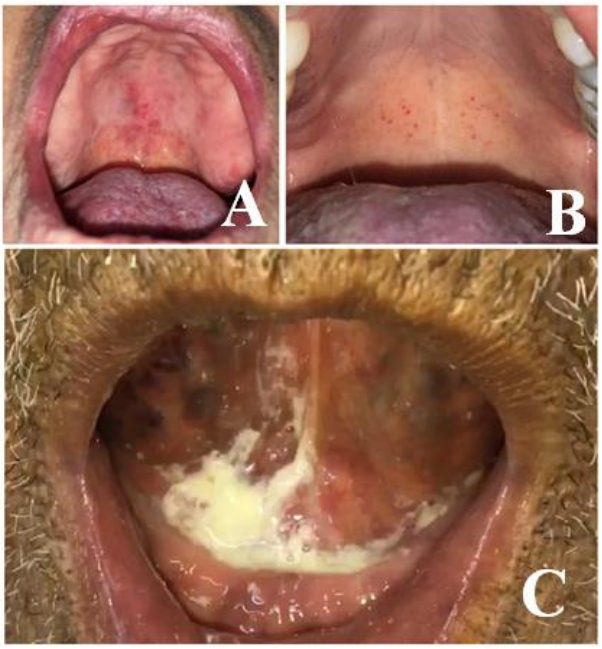
Figure 1

a) Vesiculobullous lesion on the palate; b) ulcerated lesion on the dorsum of the tongue.

Source: Personal archive.

Figure 2

a) Erythematous lesions on the palate; b) petechiae on the palate; c) oral candidiasis.



Source: Personal archive.

The periodontal condition was investigated using the CPI. In the present sample, 10% of the patients had pockets measuring ≥ 6 mm in the first sextant and 70% had the third and fourth sextants excluded because of the absence of teeth. The presence of isolated bleeding was low and was more associated with dental calculus or deep pockets. There were few healthy sextants (Table 3).

Table 3

Community Periodontal Index (CPI) of the sample.

Condition	**Sextant (%)**					
	16/17	**11**	**26/27**	**36/17**	**31**	**46/47**
Excluded	63.3	56.7	70	70	30	66.7
Healthy	6.7	6.7	6.7	6.7	6.7	6.7
Bleeding	0	6.7	0	0	0	6.7
Calculus	0	16.7	3.3	10	33.3	0
Pocket 4-5 mm	20	13.3	13.3	13.3	23.3	13.3
Pocket ≥ 6 mm	10	0	6.7	0	6.7	6.7

Source: Personal archive.

The antibiotics most frequently used by the patients were ceftriaxone (80%) combined with azithromycin (73.3%). Tazocin (32.3%), meropenem (23.3%), vancomycin (10%), and polymyxin (6.7%) were also administered.

Table 4 shows the correlation analysis of hospital unit with sex, age, duration of symptoms, outcome, hypertension, diabetes, other comorbidities, oxygen therapy, prone positioning, hemoglobin, hematocrit, leukocytes, platelets, C-reactive protein, D-dimer, loss of taste and smell, and oral lesions. The prevalence of critical patients (ICU) was higher among patients aged 60 years or older (53.3%), male patients (43.3%), patients admitted to the ICU (46.7%), and patients with a mean symptom duration of 5 days. Most patients were discharged (56.7%), were hypertensive (46.7%), and were not diabetic (40%) but had other comorbidities (56.7%). Furthermore, 80% of severe (ward) and critical (ICU) patients required oxygen therapy. Loss of taste and smell was reported by 46.7% and 65.0% of critical patients. Regarding blood parameters, the application of Pearson's chi-squared test, Fisher's exact test, or the Mann-Whitney test revealed no significant associations ($p>0.05$).

Table 4

Distribution of ward and ICU patients according to demographic data, health conditions, and hematological parameters.

	Hospital unit					
	Ward		**ICU**		**Total (%)**	**p**
Variable	**N**	**%**	**N**	**%**		
Age (years)	0.901					
18 to 59	2	6.7	6	20.0	8 (26.7)	
≥ 60	6	20.0	16	53.3	22 (73.3)	
Sex	0.657					
Male	4	13.3	13	43.3	17 (56.7)	
Female	4	13.3	9	30.0	13 (43.3)	

Symptom duration	0.109					
1 week	5	16.7	20	66.7	25 (83.3)	
1-2 weeks	2	6.7	2	6.7	4 (13.3)	
> 2 weeks	1	3.3	0	0	1 (3.3)	
Outcome	0.539					
Discharge	7	23.3	17	56.7	24 (80)	
Transfer for chronic treatment	1	3.3	2	6.7	3 (10)	
Death	0	0	3	10.0	3 (10)	
Hypertension	0.559					
Yes	6	20.0	14	46.7	20 (66.7)	
No	2	6.7	8	26.7	10 (33.3)	
Diabetes	0.151					
Yes	2	6.7	10	33.3	14 (46.7)	
No	6	20.0	12	40.0	16 (53.3)	
Other comorbidities	0.149					
Yes	4	13.3	17	56.7	21 (70)	
No	4	13.3	5	16.7	9 (30)	
Oxygen therapy	0.148					
Yes	5	16.7	19	63.3	24 (80)	
No	3	10.0	3	10.0	6 (20)	
Hemoglobin	0.451					
Normal	2	6.7	7	23.3	9 (30)	
Altered	6	20	12	40	18 (60)	
Hematocrit	0.211					
Normal	0	0	6	20	6 (20)	
Altered	3	10	8	26.7	11 (36.7)	
Leukocytes	0.531					
Normal	3	10	8	26.7	11 (36.7)	
Altered	5	16.7	11	36.7	16 (53.3)	
Platelets	0.146					
Normal	7	30.4	12	52.2	19 (82.6)	
Altered	0	0	4	17.4	4 (17.4)	
C-reactive protein	0.589					
Normal	0	0	0	0	0	
Altered	5	16.7	16	53.3	21 (70)	
D-dimer	0.593					
Normal	0	0	0	0	0	
Altered	2	6.7	3	10	5 (16.7)	
Prone positioning	0.195					
Yes	0	0	4	13.3	4 (13.3)	
No	8	26.7	18	60	26 (86.7)	

Loss of smell	0.162					
Yes	6	30.0	13	65.0	19 (95)	
No	1	5.0	0	0	1 (5)	
Loss of taste	0.907					
Yes	6	30.0	14	46.7	20 (87.0)	
No	1	4.3	2	8.7	3 (13.0)	
Oral lesions	0.394					
Yes	7	23.3	14	46.6	22 (70)	
No	1	3.3	8	26.7	9 (30)	

Source: Personal archive.

DISCUSSION

Various extrapulmonary manifestations of COVID-19 have been reported in the literature, suggesting that the hematological, cardiovascular, renal, gastrointestinal, hepatobiliary, endocrinological, and neurological systems, as well as eyes and skin, may be involved (Gupta *et al.*, 2020; Lenti *et al.*, 2020). Several studies have drawn attention to the oral cavity as the primary portal of entry of the virus into the body. Furthermore, the oral cavity is involved in viral transmission and pathogenicity and acts as a protective or aggravating factor of viral infection and progression (Pedrosa; Sipert; Nogueira, 2020).

Clinical evidence demonstrates that the oral mucosa is a primary site of entry for SARS-CoV-2 and is possibly susceptible to infection with the novel coronavirus (2019-nCoV), mainly because of the high expression of ACE2 which causes a hyperinflammatory state in the mouth after infection with SARS-CoV-2. This receptor is found on mucous membranes throughout the oral cavity, especially on the tongue (Xu *et al.*, 2020; Wang *et al.*, 2020).

So far, no efficient and safe pharmacological agent against COVID-19 exists and the drugs used are associated with various adverse events, including oral lesions (De Melo Filho *et al.*, 2012; Godinho *et al.*, 2020; Mehra *et al.*, 2020; National Center for Biotechnology Information, 2020). Furthermore, acute COVID-19 infection along with therapeutic measures associated with poor oral hygiene can potentially contribute to adverse oral health-related outcomes, likely causing opportunistic fungal infections, recurrent oral HSV-1 infection, loss of taste, xerostomia linked to decreased salivary flow, ulcerations, and gingivitis as a result of an impaired immune system and/or susceptible oral mucosa (Dziedzica, Wojtyczka, 2020). Oral lesions may also be a direct result of infection with SARS-CoV-2 or may be related to stress or a general immunosuppressive state caused by prolonged disease and hospitalization (Novak *et al.*, 2021).

These lesions may also be associated with a weakened immune system or treatment with antibiotics that can cause oral dysbiosis.

Among the 30 patients evaluated in the present study, 70% had oral lesions. The visible plaque index indicated poor oral hygiene conditions in 93.3% of the sample; a high caries index (DMFT = 22.5) was observed in 63.3% of cases and an unsatisfactory periodontal condition in 90.9%.

Abnormal coagulation associated with COVID-19 is caused by endothelial injury, immobilization of the patient, and an increase in circulating prothrombotic factors (Singhania *et al.,* 2020), events that can contribute to the formation of necrotic ulcers such as those found in the present study.

Kaya et al. (2020) reviewed the literature on cutaneous manifestations associated with COVID-19 and reported a frequency of skin lesions ranging from 1.8 to 20.4%. De Sousa et al. (2020) suggested the frequency of oral mucosal lesions to be comparable to the frequency of cutaneous lesions, assuming that both have a similar underlying pathology. In contrast to the literature, we found no cutaneous alterations but oral lesions were present in 70% of the patients. These lesions exhibited the classic and well-defined characteristics of pseudomembranous candidiasis, geographic tongue, lipoma, erythema multiforme, ulceration, vesiculobullous lesions, macules, and petechiae.

In the present study, oral lesions were found in 21 patients, including 7 severe cases and 14 critical cases. The mean age of patients admitted to wards was 68 years and there were three women and four men. The characteristics of these lesions raised the diagnostic hypothesis of lingual lipoma, ulcerated lesion on the palate, petechiae on the palate, and oral candidiasis in the region of the tongue, buccal mucosa, buccal gingiva and palate, with the last being the most frequent. The mean age of critical cases was 72 years, a higher mean age than that of patients admitted to wards. These patients exhibited oral changes such as candidiasis on the tongue, cheek mucosa, oral vestibule, retromolar region, sublingual and palate, geographic tongue, petechiae on the palate, ulceration in the retromolar region, palate and dorsum of the tongue, vesiculobullous lesions on the palate, and erythematous lesions on the palate. These findings can be compared to those reported by other authors such as Jimenez-Cauhe et al. (2020), Carreras-Presas et al. (2020), Dos Santos et al. (2020), and Soares et al. (2020) who demonstrated lesions in patients with COVID-19.

Studies have shown that psychological distress stimulates the immunoregulatory mechanism by elevating the leukocyte count at sites of inflammation (Redwine *et al.*, 2003) and that anxiety and concerns related to disease and hospitalization are risk factors for psychological distress in patients (Biadsee *et al.*, 2020). This fact would explain the presence of altered leukocyte counts in the majority of patients.

The results of the present study corroborate the literature regarding the uncertainty whether the aforementioned oral manifestations are the direct result of viral infection or are due to deterioration of systemic health, side effects of the drugs used, and/or immune system impairment. COVID-19 is a relatively new disease and information in the literature is still limited. Although we included cases for whom detailed medical reports and laboratory tests were available, we cannot completely rule out the possibility of a secondary cause. In addition, the sample size was small, a fact that poses a risk of bias. However, we observed that petechiae, candidiasis, herpes, and ulcers were the most prevalent lesions.

CONCLUSION

The present findings showed that oral lesions are frequent in COVID-19 patients with varying degrees of symptoms. Furthermore, most of the patients analyzed had poor oral hygiene, including periodontal problems and tooth loss.

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REFERENCES

BEARN, D. R. et al. Index of Oral Cleanliness (IOC). A new oral hygiene index for use in clinical audit. **British Journal of Orthodontics**, v. 23, n. 2, p. 145-151, 1996.

BIADSEE, Ameen et al. Olfactory and oral manifestations of COVID-19: sex-related symptoms — a potential pathway to early diagnosis. **Otolaryngology–Head and Neck Surgery**, v. 163, n. 4, p. 722-728, 2020.

BRANDÃO, Thaís Bianca et al. Oral lesions in patients with SARS-CoV-2 infection: Could the oral cavity be a target organ?. **Oral surgery, oral medicine, oral pathology and oral radiology**, v. 131, n. 2, p. e45-e51, 2021.

CARRERAS-PRESAS, Carmen Martín et al. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. **Oral diseases**, 2020.

CHI, Angela C. et al. Oral manifestations of systemic disease. **American family physician**, v. 82, n. 11, p. 1381-1388, 2010.

CIAGLIA, Elena; VECCHIONE, Carmine; PUCA, Annibale Alessandro. COVID-19 infection and circulating ECA2 levels: protective role in women and children. **Frontiers in pediatrics**, v. 8, p. 206, 2020.

COULTHARD, Paul. Dentistry and coronavirus (COVID-19)-moral decision-making. **British Dental Journal**, v. 228, n. 7, p. 503-505, 2020.

CRUZ TAPIA, Roberto Onneret al. Oral mucosal lesions in patients with SARS-CoV-2 infection. Report of four cases. Are they a true sign of COVID-19 disease?. **Special Care in Dentistry**, v. 40, n. 6, p. 555-560, 2020.

DE MELO FILHO, Mário Rodrigues et al. Palate hyperpigmentation caused by prolonged use of the anti-malarial chloroquine. **Head and neck pathology**, v. 6, n. 1, p. 48-50, 2012.

DE SOUSA, Fernando Augusto Cervantes Garcia; PARADELLA, Thaís Cachuté. Considerations on oral manifestations of COVID-19. **Journal of Medical Virology**, 2020.

DHINGRA, Kunaal; VANDANA, Kharidhi Laxman. Indices for measuring periodontitis: a literature review. **International dental journal**, v. 61, n. 2, p. 76-84, 2011.

DOS SANTOS, Juliana Amorim et al. Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations?. **International Journal of Infectious Diseases**, v. 97, p. 326-328, 2020.

DZIEDZIC, Arkadiusz; WOJTYCZKA, Robert. The impact of coronavirus infectious disease 19 (COVID-19) on oral health. **Oral diseases**, v. 27, p. 703-706, 2021.

FERNANDES, L. L. et al. Saliva in the diagnosis of COVID-19: a review and new research directions. **Journal of Dental Research**, v. 99, n. 13, p. 1435-1443, 2020.

GE, Zi-yu et al. Possible aerosol transmission of COVID-19 and special precautions in

dentistry. **Journal of Zhejiang University-SCIENCE B**, v. 21, n. 5, p. 361-368, 2020.

GODINHO, Géssica Vasconcelos et al. Extensive hard palate hyperpigmentation associated with chloroquine use. **British journal of clinical pharmacology**, v. 86, n. 11, p. 2325-2327, 2020.

GORBALENYA, Alexander E. et al. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. **Nat. Microbiol**, v. 5, n. 4, p. 536-544, 2020.

GU, Jinyang; HAN, Bing; WANG, Jian. COVID-19: gastrointestinal manifestations and potential fecal–oral transmission. **Gastroenterology**, v. 158, n. 6, p. 1518-1519, 2020.

GUAN, Wei-jie et al. Clinical characteristics of coronavirus disease 2019 in China. **New England journal of medicine**, v. 382, n. 18, p. 1708-1720, 2020.

GUPTA, Aakriti et al. Extrapulmonary manifestations of COVID-19. **Nature medicine**, v. 26, n. 7, p. 1017-1032, 2020.

HINDSON, Jordan. COVID-19: faecal–oral transmission?. **Nature Reviews Gastroenterology & Hepatology**, v. 17, n. 5, p. 259-259, 2020.

HUANG, Chaolin et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. **The Lancet**, v. 395, n. 10223, p. 497-506, 2020.

JIMENEZ-CAUHE, Juan et al. Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings. **Clinicaland experimental dermatology**, 2020.

KAYA, Gürkan; KAYA, Aysin; SAURAT, Jean-Hilaire. Clinical and histopathological features and potential pathological mechanisms of skin lesions in COVID-19: review of the literature. **Dermatopathology**, v. 7, n. 1, p. 3-16, 2020.

KLEIN, Henry; PALMER, Carroll E.; KRAMER, Morton. Studies on dental caries. II. The use of the normal probability curve for expressing the age distribution of eruption of the permanent teeth. **Growth**, v. 1, n. 385-394, p. 20, 1937.

LECHIEN, Jerome R. et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. **European Archives of Oto-Rhino-Laryngology**, v. 277, n. 8, p. 2251-2261, 2020.

LENTI, Marco Vincenzo et al. Impact of COVID-19 on liver function: results from an internal medicine unit in Northern Italy. **Internal and emergency medicine**, v. 15, n. 8, p. 1399-1407, 2020.

MEHRA, Mandeep R. et al. RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. **The Lancet**, 2020.

NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION. Pub ChemDatabase. **Ritonavir**. 2020.

NOVAK, Natalijia et al. SARS-CoV-2, COVID-19, skin and immunology–What do we know so far?. **Allergy**, v. 76, n. 3, p. 698-713, 2021.

PEDROSA, Marlus da Silva; SIPERT, Carla Renata; NOGUEIRA, Fernando Neves. Salivary glands, saliva and oral findings in COVID-19 infection. **Pesquisa Brasileira em Odontopediatria e Clínica Integrada**, v. 20, 2020.

PENG, Xian et al. Transmission routes of 2019-nCoV and controls in dental practice**. International journal of oral science**, v. 12, n. 1, p. 1-6, 2020.

REDWINE, Laura et al. Acute psychological stress: effects on chemotaxis and cellular adhesion molecule expression. **Psychosomatic medicine**, v. 65, n. 4, p. 598-603, 2003.

SABINO-SILVA, Robinson; JARDIM, Ana Carolina Gomes; SIQUEIRA, Walter L. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. **Clinical oral investigations**, v. 24, n. 4, p. 1619-1621, 2020.

SINGHANIA, Namrata et al. Current overview on hypercoagulability in COVID-19. **American Journal of Cardiovascular Drugs**, v. 20, n. 5, p. 393-403, 2020.

SOARES, Ciro Dantas et al. Letter to Editor: Oral lesions in a patient with Covid-19. **Medicina oral, patologia oral y cirugia bucal**, v. 25, n. 4, p. e563, 2020.

SPAGNUOLO, Gianrico et al. COVID-19 outbreak: an overview on dentistry. **International Journal of Environmental Research and Public Health**, v. 17, n. 6, p. 2094, 2020.

SPETH, Marlene M. et al. <? covid19?> Olfactory dysfunction and sinonasal symptomatology in COVID-19: prevalence, severity, timing, and associated characteristics. **Otolaryngology–Head and Neck Surgery**, v. 163, n. 1, p. 114-120, 2020.

TO, Kelvin Kai-Wang et al. Consistent detection of 2019 novel coronavirus in saliva. **Clinical Infectious Diseases**, v. 71, n. 15, p. 841-843, 2020.

VINAYACHANDRAN, Divya; BALASUBRAMANIAN, Saravanakarthikeyan. Salivary diagnostics in COVID-19: Future research implications. **Journal of dental sciences**, v. 15, n. 3, p. 364, 2020.

WANG, Chenxing et al. Does infection of 2019 novel coronavirus cause acute and/or chronic sialadenitis?. **Medical hypotheses**, v. 140, p. 109789, 2020.

WORLD HEALTH ORGANIZATION (WHO) et al. WHO health emergency dashboard—WHO (COVID-19) homepage. Vol. 2020. Webpage. **World Health Organization**, 2020.

WORLD HEALTH ORGANIZATION (WHO). Oral health surveys: basic methods. World Health Organization, 2nd ed. Geneva: World Health Organization, 2013; 127p.

XU, Hao et al. High expression of ECA2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. **International journal of oral science**, v. 12, n. 1, p. 1-5, 2020.

YEO, Charleen; KAUSHAL, Sanghvi; YEO, Danson. Enteric involvement of coronaviruses: is faecal–oral transmission of SARS-CoV-2 possible?. **The lancet Gastroenterology &**

hepatology, v. 5, n. 4, p. 335-337, 2020.

ZHOU, Peng et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. **Nature**, v. 579, n. 7798, p. 270-273, 2020.

ZOU, Xin et al. Single-cell RNA-seq data analysis on the receptor ECA2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. **Frontiers of medicine**, p. 1-8, 2020.