Clinical Signs and Symptoms Associated with COVID-19: A Cross Sectional Study

Signos y Síntomas Clínicos Asociados a COVID-19: Un Estudio Transversal

Norma Samanta Romero Castro[1]; Israel Colín Hernández[2]; María Estela Godoy Reyes[3]; Margarita Hernández Hernández[4]; Alicia García Verónica[1]; Sergio Paredes-Solis[5] & Salvador Reyes Fernández[1,6]

ABSTRACT: Covid-19 is a viral disease that has spread throughout the world, becoming a pandemic. Dysgeusia and anosmia are some of its most frequent symptoms. The aim of the study was to determine the frequent signs and symptoms associated with COVID-19 patients. A cross-secional study from 370 patients with acute respiratory illness admitted by emergency services of a hospital in Acapulco. An institutional survey was applied to all patients as a data collection instrument, and a SARS-CoV-2 test, by RT-PCR processed by a certified laboratory. Statistical analysis was performed using the STATA V13 program. The numerical variables without normality were reported in medians, 25th and 75th percentiles, and the Mann Withney U test was performed for differences between groups. The categorical variables were presented in percentages and differences between groups with Chi-square test. A generalized linear models (GLM) analysis was carried out to determine the most frequent symptoms and signs associated with COVID-19. Clinical signs and symptoms associated to COVID-19 in the bivariate análisis were dysgeusia, odynophagia, anosmia, arthralgia, myalgia, conjunctivitis, and age older than 40 years. In the final multivariate model only age older than 40 years (OR) 2.2; CI 95 % 1.3,3.8) and dysgeusia (OR 2.1; CI95 % 1.2,3.6) kept significance. Dysgeusia, odynophagia, anosmia, arthralgia, myalgia and conjunctivitis are clinical signs and symptoms that can appear in the early stages of the disease, so they could be important for an early diagnosis.

KEY WORDS: COVID-19. dysgeusia. odynophagia. anosmia. arthralgia. myalgia.

INTRODUCTION

The pandemic that is currently being faced throughout the world has its origin in the Chinese city of Wuhan in the Hubei province. At the end of December 2019 (Meng *et al*., 2020), a group of people who had in common being workers or frequent consumers of a market in this city where wild animal meat is sold (Odeh *et al*., 2020), including bats, developed acute respiratory síndrome (Gaitán Cepeda *et al*., 2020). These patients were diagnosed with atypical pneumonia of possible viral origin. Subsequently, a type of coronavirus was isolated

from the material obtained from bronchial washes of these patients (Gaitán Cepeda *et al*.). Authors suggest that it is a zoonosis and that this coronavirus comes from the bat (Sabino-Silva *et al*., 2020). In January 2020, the World Health Organization (WHO) determined that it was a global public health emergency (Meng *et al*.), and in March of this year declared it a true pandemic (Saddik *et al*., 2020). At the end of February 2020, it was officially announced by the Chinese Center for Disease Control and Prevention that the causative agent of this emerging

[1] Professor, Speciality in Implantology and Oral Rehabilitation, UAGRO-CA-133, School of Dentistry, Autonomous University of Guerrero, Acapulco, Guerrero, Mexico.
[2] Head of Stomatology service, Acapulco Naval Hospital, Acapulco, Guerrero, Mexico.
[3] Head of Pediatric dentistry service, Acapulco Naval Hospital, Acapulco, Guerrero, Mexico.
[4] Head of Public health service, Acapulco Naval Hospital, Acapulco, Guerrero, Mexico.
[5] Professor, Center for Research in Tropical Diseases (CIET), UAGRO-CA-25, Autonomous University of Guerrero, Acapulco, Guerrero, Mexico.
[6] Acapulco General Hospital, Secretaria de Salud, Acapulco, Guerrero, México.

disease called COVID-19 was a new coronavirus called SARSCoV-2 for its acronym in English (Severe acute respiratory syndrome coronavirus-2) and in the same month it had already expanded to 34 countries, reaching more than 80,000 laboratory-confirmed cases and more than 2,500 deaths (Meng *et al*.).

Human coronaviruses (HCoV) were for a long time considered harmless pathogens that cause the common cold, however in 2003 (Smales & Samaranyake, 2003; Saddik *et al*.) and 2012 (Kharma *et al*., 2015), two variants of coronavirus emerged that caused major epidemics. The severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV) respectively (Saddik *et al*.).

Recent research concludes that this virus is zoonotic from some species of bat, and that the transmission initially took place from animal to human, to later be transmitted from human to human by drops of saliva and direct contact. The virus is currently known to be present in the feces, urine, and saliva of infected people (Smales & Samaranyake; Meng *et al*.). Its incubation period ranges from 5 to 6 days and it can last up to 14 days (Meng *et al*.).

Fortunately, most people who become infected with this virus are asymptomatic or develop mild signs or symptoms such as fever, dry cough, fatigue, muscle pain, diarrhea, and vomiting. Still others develop acute respiratory failure, arrhythmias, and shock, for which they must be transferred to an intensive care unit. These serious and sometimes fatal conditions tend to occur in older people or those with pre-existing systemic diseases such as diabetes mellitus, high blood pressure and other cardiovascular diseases, which worsens the prognosis (Meng *et al*.).

The diagnosis is based on four aspects: The history of contact with potentially infected people, signs and symptoms, imaging studies, and laboratory tests.

The main way to control the spread of COVID-19 is to prevent person-to-person transmission, which can be achieved through a combination of public health measures, including the rapid identification and isolation of infected people (Pissurno *et al*., 2020).

Hand hygiene remains the most appropriate measure to reduce the risk of transmission. SARSCoV-2 can remain active on surfaces from a few hours to several days, depending on the type of surface, temperature or humidity of the environment.

The recommended measures for dental clinical practice are aimed at different infection control methods such as physical barriers, area management and general asepsis, antisepsis and sterilization measures (Meng *et al*.).

Angiotensin-converting enzyme 2 (ACE2) has been reported to be the major host cell receptor for 2019-nCoV and plays a crucial role in virus entry into the cell to cause eventual infection. Recent work has shown that ACE2 is expressed in the oral mucosa, especially in the mucus of the tongue, so the oral cavity may be a high-risk site for infectious susceptibility to COVID-19 (Dos Santos *et al*., 2020).
The genome of the COVID-19 virus has been detected in saliva in most patients with this disease, indicating possible infection of the salivary glands (To *et al*., 2020).

Because Covid-19 is an emerging disease, there are not many publications of an association of oral lesions to the disease. One of those publications is the one that reported the case of a 45-year-old female who presented an irregular ulceration in the oral mucosa, however, the authors concluded that it is only a possible incidental finding (Chaux-Bodard *et al*., 2020). Another article reports three cases of oral mucosa ulcerations and blisters in one positive and two COVID-19 suspects but they suppose that many intraoral findings can often go unnoticed due to the lack of an intraoral examination during hospital admission (Sinadinos & Shelswell, 2020). Other researchers have published isolated cases of lesions of the oral mucosa in patients with the disease (Dos Santos *et al*.). Olfactory and gustatory disorders have also been reported as prevalent symptoms in COVID-19 (Barón-Sánchez *et al*., 2020; Abalo-Lojo *et al*., 2020; Levinson *et al*., 2020; Russell *et al*., 2020).

The objective of this research was to determine the frequent signs and symptoms associated with COVID-19 positive patients.

MATERIAL AND METHOD

We carried out a cross-secional study from 370 patients with acute respiratory illness admitted by emergency services of a hospital in Acapulco, Mexico, from April 13th to August 29th, 2020. All patients had a SARS-CoV-2 test, by real-time polymerase chain reaction processed by a certified laboratory, 227 tested positive, 135 negative and 8 cases had unsuitable

samples, leaving 362 useful observations. From patients clinical files we collected clinical signs and symptoms related to acute respiratory illness. Clinical signs and symptoms included in analysis were age, fever, headache, dry cough, fatigue, dysgeusia, odynophagia, anosmia,rhinorrhea, conjunctivitis, polypnea, dyspnea, perioral cyanosis, chest pain, arthralgia, myalgia, general discomfort, diarrhea, and abdominal pain.

The statistical analysis of the data was carried out in the STATA V13 program, simple frequencies of the data are presented, the numerical variable age when not having normality was reported in medians, 25th and 75th percentiles and the Mann Withney U test was applied for difference between groups. The categorical variables were presented in percentages and the differences between groups with the Chi-square test. An generalized linear models (GLM) analysis was carried out to determine the most frequent symptoms and signs associated with COVID-19.

RESULTS

Patients average age was 45 years old (range 33-61); 226 (62 %) were male and 136(38 %) female, the sociodemographic variables are shown in Table I.

Symptoms such as cough, fever, headache and general discomfort were presented by most of the patients since they were admitted for some type of acute respiratory infection, however, Table II shows that there were no significant differences between the positive and negative COVID-19 groups.

Symptoms such as chest pain, rhinorrhea, polypnea, dyspnea, perioral cyanosis, and some gastric symptoms such as diarrhea, abdominal pain, and vomiting were not presented by most of the patients, and there were no significant differences between those who were positive for COVID-19 and those who were negative.

Some patients (65), 18 % reported history of arterial systemic hypertension, 68(19 %) diabetes mellitus type 2 (DM2) and 33(9 %) obesity. Table III shows the systemic condition of the patients.

The most frequent symptoms in positive COVID-19 patients and with significant differences from negative patients were: myalgia conjunctivitis, arthralgia, anosmia, odynophagia, dysgeusia, and age over 40 years.

Other important findings are that of the 141 patients for whom data of anosmia and dysgeusia were obtained, 40 % (57) had both symptoms, and that of the

Table I. Sociodemographic characteristics of the study population.

Characteristic	Population n = 362 (100%)	COVID-19 positive n = 227 (63%)	COVID-19 negative n = 135 (37%)	p value
Age, years[a]	45 (33-61)	46 (34-62)	41 (31-58)	0.01
Sex[b]				
Female	136 (38)	85 (37)	52 (38)	
Male	226 (62)	142 (63)	84 (62)	0.95
Total n (%)	362 (100)	227 (100)	135 (100)	
Occupation[b]				
Employees from other areas	193 (53)	114 (50)	79 (58)	
Health area employees	57 (16)	41 (18)	16 (12)	
Merchant	12 (3)	9 (4)	3 (2)	
Home	70 (19)	45 (20)	25 (19)	0.12
Retired	20 (6)	15 (6.5)	5 (4)	
Unemployed	3 (1)	1 (0.5)	2 (1)	
Students	7 (2)	2 (1)	5 (4)	
Total n (%)	362 (100)	227 (100)	135 (100)	

[a]Median is shown (p25-p75), *p* value calculated by Mann Whitney statistical test; [b]n(%) are shown for categorical variables, *p* value calculated by Chi Square statistical test.

Table II. Frequent clinical signs and symptoms of the study population n(%) are shown for categorical variables; *p* value calculated by Chi Square statistical test.

Characteristic	Population n = 362 (100%)	COVID-19 positive n = 227 (63%)	COVID-19 negative n = 135 (37%)	*p* value
Fever				0.35
Yes	325 (90)	201 (89)	124 (92)	
No	37 (10)	26 (11)	11 (8)	
Total	362 (100)	227 (100)	135 (100)	
Cough				0.38
Yes	318 (88)	202 (89)	116 (86)	
No	44 (12)	25 (11)	19 (14)	
Total	362 (100)	227 (100)	135 (100)	
Headache				0.91
Yes	304 (84)	191 (84)	113 (84)	
No	58 (16)	36 (16)	22 (16)	
Total	362 (100)	227 (100)	135 (100)	
General				0.32
Yes	255 (70)	165 (73)	90 (67)	
No	106 (29)	61 (26)	45 (33)	
Total	361 (99)	226 (100)	135 (100)	

Table III. Study population systemic condition.

Characteristic	Population n = 362 (100 %)	COVID-19 positive n = 227 (63 %)	COVID-19 negative n = 135 (37 %)	*p* value
Hypertension				0.69
Yes	65 (18)	42 (20)	23 (17)	
No	296 (82)	184 (80)	112 (83)	
Total	361 (100)	226 (100)	135 (100)	
Obesity				0.79
Yes	33 (9)	20 (9)	13 (10)	
No	329 (91)	207 (91)	122 (90)	
Total	362 (100)	227 (100)	135 (100)	
Diabetes				0.00
Yes	68 (19)	52 (23))	16 (12)	
No	294 (81)	175 (77)	119 (88)	
Total	362 (100)	227 (100)	135 (100)	
Smoking				0.18
Yes	3 (1)	3 1	0 (0)	
No	359 (99)	224 (99)	135 (100)	
Total	362 (100)	227 (100)	135 (100)	

n(%) are shown for categorical variables; P value calculated by Chi Square statistical test.

52 COVID-19 positive patients with diabetes mellitus, 15.4 % (8) died during their hospital stay.

Table IV shows the results of the analysis of bivariate generalized linear models (GLM) of clinical signs and symptoms associated to COVID-19. In the final multivariate model only age older than 40 years (OR 2.2; CI95 % 1.3,3.8) and dysgeusia (OR 2.1; CI95 % 1.2,3.6) kept statistical significance.

Table IV. Clinical signs and symptoms associated to COVID-19

Characteristic	OR	95%CI	*p* value
Age older than 40 years	1.6	1.1, 2.5	0.03
Arthralgia	2.4	1.6, 3.7	0.00
Conjunctivitis	1.9	1.1, 3.6	0.03
Myalgia	1.9	1.3, 3.1	0.00
Odynophagia	1.6	1.1, 2.4	0.04
Anosmia	1.9	1.1, 3.4	0.01
Dysgeusia	2.2	1.2, 3.8	0.00

Generalized linear models bivariate analysis (GLM); OR = odds ratio.

Table V. Signs and symptoms with significant differences between groups.

Characteristic	Population	COVID-19 positive	COVID-19 negative	p value
	n = 362	n = 227	n = 135	
	(100%)	(63%)	(37%)	
Arthralgia				0.00
Yes	205 (57)	147 (65)	58 (43)	
No	156 (43)	80 (35)	76 (57)	
Total	361 (100)	227 (100)	134 (100)	
Myalgia				0.00
Yes	237 (65)	162 (71)	75 (56)	
No	125 (35)	65 (29)	60 (44)	
Total	362 (100)	227 (100)	135 (100)	
Odynophagia				0.04
Yes	225 (62)	150 (66)	75 (56)	
No	137 (38)	77 (34)	60 (44)	
Total	362 (100)	227 (100)	135 (100)	
Anosmia				0.01
Yes	89 (38)	62 (44)	27 (28)	
No	148 (62)	80 (56)	68 (72)	
Total	237 (100)	142 (100)	95 (100)	
Dysgeusia				0.00
Yes	93 (39)	66 (46)	27 (28)	
No	145 (61)	77 (54)	68 (72)	
Total	238 (100)	143 (100)	95 (100)	

n (%) are shown for categorical variables; P value calculated by Chi Square statistical test.

DISCUSSION

This cross-secional study carried out in patients with COVID-19 at a hospital in Acapulco, México, shows important results regarding the most frequent signs and symptoms that were found in the institutional admission COVID-19 format, such as dysgeusia, odynophagia, anosmia, arthralgia, myalgia, conjunctivitis, age older tan 40 years and comorbidity with diabetes mellitus. Two of the symptoms that showed significant differences between positive for COVID-19 and those negative were dysgeusia and anosmia (Table V). Of the patients who tested positive for COVID-19, 46 % had dysgeusia, 44 % had anosmia, and 40 % had both. This agrees with Abalo-Lojo *et al*. who reported high percentages of these signs. Of the total of their sample, 58.8 % had anosmia, and 56.5 % had dysgeusia. Other authors such as Levinson *et al*. in a sample of 42 patients with COVID-19 reported 35.7 % anosmia and 33.3 % dysgeusia.

However, there are reports of much higher percentages of presentation of these disorders in COVID-19 patients such as that of Ormianer, who reported that 67 % of their patients had olfactory disorders and 52 % taste alteration (Biadsee *et al*., 2020).

Other authors report different percentages of anosmia in their COVID-19 patients, such as Klopfenstein *et al*. (2020) who found 47 % of this disorder.

Salmon *et al*. (2020) reported in their study of 55 patients, that 92 % of all patients with olfactory alterations were positive for SARSCov-2.

Although the cause of these taste and olfactory alterations is not clear, it is thought that the virus damages the taste and olfactory cells by binding to the angiotensin-converting enzyme 2 receptor, which is expressed both in the mucosa of the tongue and in the olfactory mucosa (Abalo-Lojo *et al*.; Lozada-Nur *et al*., 2020).

Patients often find it difficult to distinguish between smell and taste disturbances. Therefore, in patients who refer to these alterations in a combined way in COVID-19, there is the possibility of an underlying olfactory alteration being the primary etiology. The perceived taste disturbance could be secondary to anosmia, rather than any actual disturbance with the taste system. We must pay attention to the cases of

patients who reported having taste alterations without alterations in smell. This could be the first report of any oral manifestation associated with COVID-19 (Vinayachandran & Balasubramanian, 2021).

Our results lead us to affirm, like Abalo-Lojo *et al*., that these two symptoms are essential for the early diagnosis of COVID-19 because they usually appear in the first days of the disease.

In this regard, Levinson *et al*. reported that both symptoms began approximately on the third day after the onset of the disease, and that most of these patients recovered both senses about a week after being detected. Another relevant data reported by Ormianer is that within their studied patients, 38.3 % presented smell alterations and 38.2 % presented taste alterations as initial symptoms (Biadsee *et al*.).

With the data obtained in this research on taste and smell alterations, we intend to contribute to the evidence that Russell *et al*. consider necessary to affirm this association.

Our patients presented other signs and symptoms similar to those reported by most authors, such as fever, cough, headache and general attack, chest pain, rhinorrhea, polypnea, dyspnea, perioral cyanosis, and some gastrointestinal symptoms such as diarrhea, pain abdominal pain and vomiting (Meng *et al*.; Abalo-Lojo *et al*.; Biadsee *et al*.; Klopfenstein *et al*.). However, none of the aforementioned signs or symptoms showed significant differences between the groups that were positive and negative for COVID-19.

Other symptoms frequently associated with COVID-19, such as odynophagia, arthralgia and myalgia, also showed significant differences between the groups that were positive and negative for COVID-19. In our studies we found 66 % percentage of odynophagia, against 30 % of Abalo-Lojo *et al*., 43 % of Klopfenstein *et al.* and 26 % of Ormianer (Biadsee *et al*.).

Regarding arthralgia, we found 75 %, against 72 % reported by Klopfestein *et al*., and Myalgias with 71 % in our study, against 74 %, 46.6 % and 47 % reported by Klopfestein *et al*., Abalo-Lojo *et al*. and Ormianer respectively (Biadsee *et al*.).

Within the systemic conditions presented by the patients, only diabetes mellitus showed significant differences between the groups, with a greater number of diabetics in proportion among the positive than among the negative cases, being 23 % of the total COVID-19 positive patients diabetics. These data coincide with the global consensus regarding the association between COVID-19 and diabetes mellitus (Rubino *et al*., 2020). This association is bidirectional as stated by Rubino *et al*., who afirm that diabetes increased risk of getting COVID-19, and that COVID-19 can lead to new-onset diabetes and/or serious metabolic complications of pre-existing diabetes. In our study 8 patients (15.4 %) of the total diabetic and COVID-19 positive patients (52 patients) died during their hospital stay.

The sample size was determined by the number of patients who came to the study hospital for consultation with respiratorydisorders, until the moment when the cases of covid-19 decreased significantly in this hospital and throughout Mexico. We waited until then, in order to achieve the largest possible sample size. It is evident that this study can be expanded and reconsidered with a much larger sample depending on the new cases from the cut-off.

We consider that our sample size is a strength of this study since it is very competitive compared to other similar studies. Some of its limitations are that a large amount of missing or non-obtained data is presented. Another aspect that we did not consider in this research, and that it would be important to incorporate in future studies, is the time of installation of the symptoms, as well as their duration.

There is no consensus on whether the oral manifestations of isolated cases or small series of recently published COVID-19 patients are incidental findings, or if they are associated in a secondary way with other symptoms such as fever, and the weakening suffered by these patients, or as a direct consequence of virus infection on the oral mucosa (Dos Santos *et al*.; Chaux-Bodard *et al*.; Sinadinos & Shelswell; Carreras-Presas *et al*., 2021). We agree with various researchers such as Martín Carreras-Presas *et al*. who affirm regarding the possibility that intraoral injuries could be going unnoticed due to the lack of detailed intraoral examinations, because when patients are hospitalized by COVID-19, care is focused to the serious aspects of the disease (Carreras-Presas *et al*.).

CONCLUSIONS

Arthralgia, dysgeusia, anosmia, myalgia, conjunctivitis and age older than 40 years are clinical

signs and symptoms associated with COVID-19. These signs could appear in the early stages of the disease so they could be important data for obtaining an early diagnosis.

In the final multivariate model only age older than 40 years and dysgeusia kept statistical significance. Most likely, if the sample had been larger, all the signs and symptoms of the bivariate analysis would have remained associated.

ETHICS APPROVAL

This research was approved by the hospital committee for bioethics and biosafety (constitutive act number 02/20-extraordinary sesión of June 23th, 2020) of the study hospital. The present study did not put the integrity and life of the patients at risk, since the procedures had diagnostic purposes for admission to the hospital (survey), the doctors in charge of the survey put on the protective equipment used by the study hospital for patients at risk of COVID-19.

ROMERO, C. N. S.; COLIN, H. I.; GODOY, R. M. E.; HERNÁNDEZ, H. M.; GARCÍA, V. A.; PAREDES-SOLÍS, S. & REYES, F. S. Signos y síntomas clínicos asociados a COVID-19: Un estudio transversal. *Int. J. Odontostomat., 16(1)*:112-119, 2022.

RESUMEN: El Covid-19 es una enfermedad viral que se ha extendido por todo el mundo, convirtiéndose en una pandemia. La disgeusia y la anosmia son algunos de sus síntomas más frecuentes. El objetivo del estudio fue determinar los signos y síntomas frecuentes asociados con los pacientes con COVID-19. Estudio transversal de 370 pacientes con enfermedad respiratoria aguda ingresados por los servicios de emergencia de un hospital de Acapulco. A todos los pacientes se les aplicó una encuesta institucional como instrumento de recolección de datos, y una prueba de SARS-CoV-2, por RT-PCR procesada por un laboratorio certificado. El análisis estadístico se realizó utilizando el programa STATA V13. Las variables numéricas sin normalidad se reportaron en medianas, percentiles 25 y 75, y se realizó la prueba U de Mann Withney para diferencias entre grupos. Las variables categóricas se presentaron en porcentajes y diferencias entre grupos con la prueba de Chi-cuadrado. Se realizó un análisis de modelos lineales generalizados (GLM) para determinar los síntomas y signos más frecuentes asociados a la COVID-19. Los signos y síntomas clínicos asociados a COVID-19 en el análisis bivariado fueron disgeusia, odinofagia, anosmia, artralgia, mialgia, conjuntivitis y edad mayor de 40 años. En el modelo multivariado final solo la edad mayor de 40 años (OR) 2,2; IC 95 % 1,3,3,8)

y la disgeusia (OR 2,1; IC95 % 1,2,3,6) mantuvieron significanca estadística. Disgeusia, odinofagia, anosmia, artralgias, mialgias y conjuntivitis son signos y síntomas clínicos que pueden aparecer en etapas tempranas de la enfermedad, por lo que podrían ser importantes para un diagnóstico precoz.

PALABRAS CLAVE: COVID-19. disgeusia, odinofagia, anosmia, artralgia, mialgia.

REFERENCES

Abalo-Lojo, J. M.; Pouso-Diz, J. M. & Gonzalez, F. Taste and Smell Dysfunction in COVID-19 Patients. *Ann. Otol. Rhinol. Laryngol., 129(10)*:1041-2, 2020.

Barón-Sánchez, J.; Santiago, C.; Goizueta-San Martín, G.; Arca, R. & Fernández, R. Smell and taste disorders in Spanish patients with mild COVID-19. *Neurologia (Engl. Ed.), 35(9)*:633-8, 2020.

Biadsee, A.; Biadsee, A.; Kassem, F.; Dagan, O.; Masarwa, S. & Ormianer, Z. Olfactory and Oral Manifestations of COVID-19: Sex-Related Symptoms-A Potential Pathway to Early Diagnosis. *Otolaryngol. Head Neck Surg., 163(4)*:722-728, 2020.

Carreras-Presas, C. M.; Amaro Sánchez, J.; López-Sánchez, A. F.; Jané-Salas, E. & Somacarrera Pérez, M. L. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Dis., 27 Suppl. 3*:710-2, 2021.

Chaux-Bodard, A. G.; Deneuve, S. & Desoutter, A. Oral manifestation of Covid-19 as an inaugural symptom? *J. Oral Med. Oral Surg., 26*:18, 2020.

Dos Santos, J. A.; Normando, A. G. C.; da Silva, R. L. C.; De Paula, R. M.; Cembranel, A. C.; Santos-Silva, A. R. & Guerra, E. N. S. Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations? *Int. J. Infect. Dis., 97*:326-8, 2020.

Gaitán Cepeda, L. A.; Leyva-Huerta, E. R.; Cruz-González, R.; Carmona Ruíz, D.; Rodríguez, M. E. & Gómez Arenas, A. COVID-19 y el cirujano dentista. Una revisión integral. *Rev. Odontol. Mex., 23(4)*:207-15, 2019.

Kharma, M. Y.; Alalwani, M. S.; Amer, M. F.; Tarakji, B. & Aws, G. Assessment of the awareness level of dental students toward Middle East Respiratory Syndrome-coronavirus. *J. Int. Soc. Prev. Community Dent., 5(3)*:163-9, 2015.

Klopfenstein, T.; Kadiane-Oussou, N. J.; Toko, L.; Royer, P. Y.; Lepiller, Q.; Gendrin, V. & Zayet, S. Features of anosmia in COVID-19. *Med. Mal. Infect., 50(5)*:436-9, 2020.

Levinson, R.; Elbaz, M.; Ben-Ami, R.; Shasha, D.; Levinson, T.; Choshen, G.; Petrov, K.; Gadoth, A. & Paran, Y. Time course of anosmia and dysgeusia in patients with mild SARS-CoV-2 infection. *Infect. Dis. (Lond.), 52(8)*:600-2, 2020.

Lozada-Nur, F.; Chainani-Wu, N.; Fortuna, G. & Sroussi, H. Dysgeusia in COVID-19: possible mechanisms and implications. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol., 130(3)*:344-6, 2020.

Meng, L.; Hua, F. & Bian, Z. Coronavirus disease 2019 (COVID-19): emerging and future challenges for dental and oral medicine. *J. Dent. Res., 99(5)*:481-7, 2020.

Odeh, N. D.; Babkair, H.; Abu-Hammad, S.; Borzangy, S.; Abu-Hammad, A. & Abu-Hammad, O. COVID-19: Present and Future Challenges for Dental Practice. *Int. J. Environ. Res. Public Health, 17(9)*:3151, 2020.

Pissurno, N. S. C. A.; de Castro Lichs, G. G.; Dos Santos, E. J. L.; Fernandes Druzian, A.; do Valle Leone de Oliveira, S. M. & Mi-

randa Paniago, A. M. Anosmia in the course of COVID-19: A case report. *Medicine (Baltimore), 99(31)*:e21280, 2020.

Rubino, F.; Amiel, S. A.; Zimmet, P.; Alberti, G.; Bornstein, S.; Eckel, R. H.; Mingrone, G.; Boehm, B.; Cooper, M. E.; Chai, Z.; *et al*. New-Onset Diabetes in Covid-19. *N. Engl. J. Med., 383(8)*:789-90, 2020.

Russell, B.; Moss, C.; Rigg, A.; Hopkins, C.; Papa, S. & Van Hemelrijck, M. Anosmia and ageusia are emerging as symptoms in patients with COVID-19: What does the current evidence say? *Ecancermedicalscience, 14*:ed98, 2020.

Sabino-Silva, R.; Jardim, A. C. G. & Siqueira, W. L. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. *Clin. Oral Investig., 24(4)*:1619-21, 2020.

Saddik, B.; Hussein, A.; Sharif-Askari, F. S.; Kheder, W.; Temsah, M. H.; Koutaich, R. A.; Haddad, E. S.; Al-Roub, N. M.; Marhoon, F. A.; Hamid, Q.; *et al*. Increased levels of anxiety among medical and non-medical university students during the COVID-19 pandemic in the United Arab Emirates. *Risk Manag. Healthc. Policy, 13*:2395-406, 2020.

Salmon, D.; Bartier, S.; Hautefort, C.; Nguyen, Y.; Nevoux, J.; Hamel, A. L.; Camhi, Y.; Canouï-Poitrine, F.; Verillaud, B.; Slama, D.; *et al*. Self-reported loss of smell without nasal obstruction to identify COVID-19. The multicenter Coranosmia cohort study. *J. Infect., 81(4)*:614-20, 2020.

Sinadinos, A. & Shelswell, J. Oral ulceration and blistering in patients with COVID-19. *Evid. Based Dent., 21(2)*:49, 2020.

Smales, F. C. & Samaranyake, L. P. Maintaining dental education and specialist dental care during an outbreak of a new coronavirus infection. Part 1: a deadly viral epidemic begins. *Br. Dent. J., 195(10)*:557-61, 2003.

To, K. K. W.; Tsang, O. T. Y.; Yip, C. C. Y.; Chan, K. H.; Wu, T. C.; Chan, J. M. C.; Leung, W. S.; Chik, T. S. H.; Choi, C. Y. C.; Kandamby, D. H.; *et al*. Consistent detection of 2019 novel coronavirus in saliva. *Clin. Infect. Dis., 71(15)*:841-3, 2020.

Vinayachandran, D. & Balasubramanian, S. Is gustatory impairment the first report of an oral manifestation in COVID-19? *Oral Dis., 27 Suppl. 3*:748-9, 2021.

Corresponding autor:
Salvador Reyes Fernández
Av. Ruiz Cortines s-n
Col. Infonavit Alta Progreso
Acapulco
Guerrero
MÉXICO

E-mail: 10640@uaro.mx

Norma Samanta Romero Castro   orcid.org/0000-0003-3468-6437
Israel Colin Hernández   orcid.org/0000-0001-5020-7841
María Estela Godoy Reyes   orcid.org/0000-0002-1106-2333
Margarita Hernández Hernández   orcid.org/0000-0003-3895-3176
Alicia García Verónica   orcid.org/0000-0002-5318-5155
Sergio Paredes-Solís   orcid.org/0000-0002-3015-3038
Salvador Reyes Fernández   orcid.org/0000-0002-4144-4113