



## EVALUATION OF THE ORAL SYMPTOMS IN COVID 19 PATIENTS IN KAMRUP METRO- A CROSS-SECTIONAL STUDY

<b>Dr Rubi Kataki</b>	Professor, Department Of Conservative Dentistry And Endodontics, Regional Dental College, Guwahati, Assam
<b>Dr Pranamee Barua</b>	Reader, Department of Pediatric And Preventive Dentistry, Regional Dental College, Guwahati, Assam.
<b>Dr Debosmita Roy*</b>	Post Graduate Trainee, Department of Conservative Dentistry And Endodontics, Regional Dental College, Guwahati, Assam. *Corresponding Author
<b>Dr Prasanta Kumar Rabha</b>	Lecturer, Department of Oral And Maxillofacial Surgery, Regional Dental College, Guwahati, Assam.

**ABSTRACT** The novel coronavirus are found to affect the ACE2 receptors in the epithelial cells of the lining of the respiratory tract. Since live virus have been found in the saliva of infected patients, and ACE2 receptors are present in epithelial lining of salivary glands and tongue, there are chances that the virus might affect the oral cavity and hence might have oral manifestation. The aim of the study was to determine and evaluate the presence of oral symptoms in the patients infected with the 2019 Novel Coronavirus (Covid 19). **MATERIALS AND METHODS:** In this cross sectional descriptive study, a set of questionnaires was formulated and the patients who have come to covid screening centers in Kamrup Metro region were interviewed for both oral symptoms and general symptoms. A total of 467 patients were evaluated. The samples were divided according to covid positive or negative. Group 1: Covid positive (+ve); Group 2: Covid negative (-ve). Out of which Group 1 had 287 patients whereas Group 2 had 180 patients. **RESULTS:** Upon statistical analysis, significant differences were found with respect to **fever, cough, breathing difficulty, sore throat, arthralgia, and asthenia** where covid positive patients found to have a high prevalence of these symptoms. On evaluation of the of the oral symptoms in both covid positive and negative patients significant differences were found viz., burning sensation, swollen gums, changes in taste sensation, pain in the TMJ and bleeding gums with covid positive patients having more predilection of having all these symptoms. On evaluation of the gender predilection between positive patients with symptoms, positive patients without symptoms and negative patients with symptoms, there found to be no significant difference. **CONCLUSION** oral symptoms of burning sensation, changes in taste sensation, bleeding gums and pain in the TMJ are found to be more prevalent with patients having corona virus infection.

**KEYWORDS :** ACE2 receptor, altered taste sensation, covid 19 oral ulcers

### I. INTRODUCTION:

In the last two decades, several epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 to 2003, and H1N1 influenza in 2009, have been recorded. In 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in Saudi Arabia.

On December 31, 2019 an epidemic of cases with unexplained low respiratory infections was detected in Wuhan, the largest metropolitan area in China. As it was unable to identify the causative agent, these first cases were classified as "pneumonia of unknown etiology." The aetiology of the disease is now attributed to a novel virus belonging to the coronavirus (CoV) family. At first, the new virus was called 2019-nCoV. Subsequently, the International Committee on Taxonomy of Viruses (ICTV) termed it the SARS-CoV-2 virus as it is very similar to the one that caused the SARS outbreak (SARS-CoVs)(Cascella et al., 2020).

The main clinical manifestations are respiratory in nature with a mean incubation period of five days (range: 0–24 days). A higher risk of infection was found in patients with certain comorbidities like hypertension, diabetes, and ischemic heart disease. Common clinical features include fever, cough, headache, diarrhoea, fatigue, headache, and myalgia.(Henry et al., 2020) One of the important mechanisms for ARDS is the cytokine storm, uncontrolled systemic inflammatory response occurring from the release of large amounts of proinflammatory cytokines and chemokines. SARS-CoV-2 binds to the host cell's membrane via the Angiotensin-Converting Enzyme 2 (ACE2) receptor (Wu et al., 2020). ACE 2 receptor is found in the lung, liver, kidney, gastrointestinal (GI) and even on the epithelial surfaces of sweat glands and on the endothelia of dermal papillary vessels.(Iranmanesh et al., 2021)

Xu et al. reported that ACE2 is abundantly expressed in the epithelial cells of the oral mucosa, with higher expression in the tongue, in comparison to the buccal and gingival tissues.(H. Xu et al., 2020) SARS-CoV-2 has been detected from saliva of the patients and it has been also demonstrated that reverse transcriptase-polymerase chain

reaction (RT-PCR) from saliva can even be a more sensitive test in comparison with nasopharyngeal test. These findings suggest that the oral cavity has high susceptibility to COVID-19 infection.

Some authors in Italy reported cases of dermatologic implication in patients affected by SARSCoV-2 infection(Recalcati, 2020). Some reports have also been describing dermatologic involvement, involvement of hands and feet in teenagers to vasculitis, rash, urticaria and varicella-like lesions(Estébanez et al., 2020). In one case report, the authors reported the presence of oral white lesions in the dorsum of the tongue without any cutaneous manifestation which resolved upon resolution of symptoms of covid.(Amorim dos Santos et al., 2020) Galván Casas et al. (2020) provided a description of the cutaneous manifestations of COVID-19 in an impressive 375 case series, and with that, they had documented for the first time the oral manifestations of the disease. The report includes an atlas of these manifestations as a downloadable supplement that includes apparently 150 different cases and among those, three cases with intra-oral manifestations that vary from ulcers in the palatal mucosa, to localized erythema in the palate and the margins of gingiva.(Casas et al., 2020)

Based on the fact that the 2019 novel coronavirus has the capability to infect the salivary glands' epithelial cells and epithelial cells of the tongue and that live virus particles can be present in the saliva, and that taste and olfactory symptoms are widely related to various viral infection, the chances of having other manifestation like ulcers, altered taste sensations, glossodynia, altered smell sensations, etc are very probable.

The present study is taken up to elucidate the various oral symptoms that can be present alongwith typical clinical symptoms of covid19 virus infection. The study hypothesized that there is presence of oral symptoms in conjunction to typical clinical symptoms of coronavirus infection. The aim of the study was to determine and evaluate the presence of oral symptoms in the patients infected with the 2019 Novel Coronavirus (Covid 19).

### II. MATERIALS AND METHODOLOGY

A set of questionnaires was formulated and the patients who have come

to covid screening centers in Kamrup Metro region were interviewed for both oral symptoms and general symptoms.

**Samples:** A total of 467 patients were evaluated. The samples were divided according to covid positive or negative. Group 1: Covid positive (+ve); Group 2: Covid negative (-ve). Out of which Group 1 had 287 patients whereas Group 2 had 180 patients.

**Study Design: Cross Sectional Descriptive study design**

**Statistical methods:**

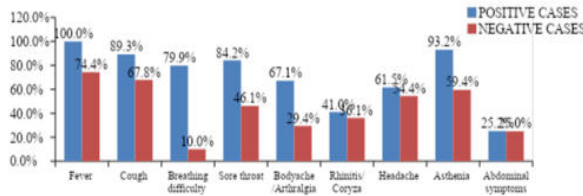
The association of the oral and general symptoms with covid positive cases was analysed using pearsons chi square test. The likelihood of symptoms in covid positive cases compared to covid negative cases was analysed using odds ratio with 95% confidence interval. All Statistics have been computed using IBM SPSS version 20 and Microsoft Excel.

**III. RESULTS:**

**TABLE 1: Prevalence of General symptoms in COVID patients**

	Fever	Cough	Breathing difficulty	Sore throat	Bodyache /Arthralgia	Rhinitis/ Coryza	Headache	Asthenia	Abdominal symptoms
POSITIVE CASES (234 excluding 53 cases without symptoms)	234 (100%)	209 (89.3%)	187 (79.9%)	197 (84.2%)	157 (67.1%)	96 (41%)	144(61.5%)	218 (93.2%)	59 (25.2%)
NEGATIVE CASES (180)	134 (74.4%)	122 (67.8%)	18 (10%)	83 (46.1%)	53 (29.4%)	65 (36.1%)	98 (54.4%)	107 (59.4%)	45(25%)
TOTAL (414)	368	331	205	280	210	161	242	325	104
Pearsons Chi square P value	p < 0.001, HS	p < 0.001, HS	p < 0.001, HS	p < 0.001, HS	p < 0.001, HS	0.309, NS	0.146, NS	p < 0.001, HS	0.960, NS
Odds Ratio (Exp/Control)	NA	3.97	35.81	6.22	4.89	1.23	1.34	9.30	1.01
95% Confidence Interval		[2.364 , 6.681]	[19.997 , 64.121]	[3.938 , 9.831]	[3.208 , 7.442]	[0.825 , 1.837]	[0.903 , 1.986]	[5.161 , 16.743]	[0.646 , 1.583]
P-value		p < 0.001, HS	p < 0.001, HS	p < 0.001, HS	p < 0.001, HS	0.154, NS	0.073, NS	p < 0.001, HS	0.480, NS

\*NS – Not Significant, S – Significant, HS – Highly Significant. Level of significance 0.05



**Graph 1: Bar Chart Showing Prevalence Of General Symptoms In COVID Patients**

Out of 287 covid positive cases 53 cases had no clinical symptoms whereas 234 (+ve) cases had cases had typical symptoms of covid

which included fever(100%), cough (89.3%), breathing difficulty(79.9%), sore throat (84.2%), arthralgia (67.1%), Rhinitis (41%), headache (61.5%),Asthenia (93.2%) and abdominal symptoms (25.2%).

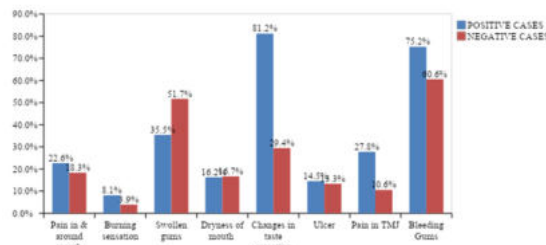
Out of 180 covid negative cases, the symptoms included fever (74.4%), cough (67.8%), breathing difficulty (10%), sore throat (46.1%), arthralgia (29.4%),Rhinitis(36.1%), headache (54.4%),Asthenia (59.4%)and abdominal symptoms (25%).

Upon statistical analysis, significant differences werefound with respect to *fever, cough, breathing difficulty, sore throat, arthralgia, and asthenia* where covid positive patients found to have a high prevalence of these symptoms as shown in table 1 and graph 1.

**Table 2: Prevalence Of Oral Symptoms In Covid Patients**

ORAL SYMPTOMS	Pain in & around mouth	Burning sensation	Swollen gums	Dryness of mouth	Changes in taste sensation	Ulcer	Pain in TMJ	Bleeding Gums
POSITIVE CASES (234 excluding 53 cases without symptoms)	53 (22.6%)	19 (8.1%)	83 (35.5%)	38 (16.2%)	190 (81.2%)	34 (14.5%)	65 (27.8%)	176 (75.2%)
NEGATIVE CASES (180)	33 (18.3%)	7 (3.9%)	93 (51.7%)	30 (16.7%)	53 (29.4%)	24 (13.3%)	19 (10.6%)	109 (60.6%)
TOTAL (414)	86	26	176	68	243	58	84	285
Pearson's Chi square P value	0.28, NS	0.07, NS	p < 0.001, HS	0.90, NS	p < 0.001, HS	0.728, NS	p < 0.001, HS	0.001, S
Odds Ratio (P/N)	1.30	2.18	0.514	0.969	10.34	1.10	3.25	1.97
95% Confidence Interval	[0.802 , 2.121]	[1.897 , 5.315]	[0.346 , 0.764]	[0.574 , 1.637]	[3.136 , 7.024]	[0.629 , 1.940]	[1.871 , 5.676]	[1.297 , 3.012]
P-value	0.14, NS	0.04, S	p < 0.001, HS	0.45, NS	p < 0.001, HS	0.364, NS	p < 0.001, HS	p < 0.001, HS

\*NS – Not Significant, S – Significant, HS – Highly Significant. Level of significance 0.05



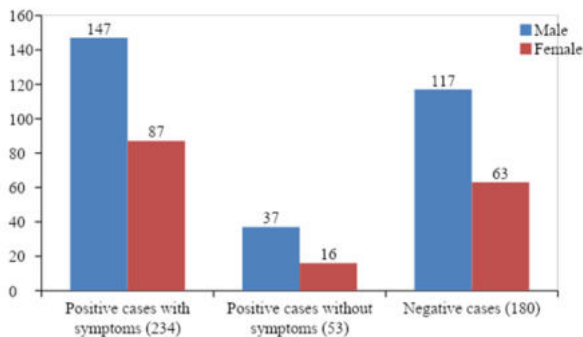
**Graph 2: Bar Chart Showing Prevalence of Oral Symptoms in COVID Patients**

On evaluation of the of the oral symptoms in both covid positive and negative patients significant differences were found with respect to oral symptoms , viz., burning sensation, swollen gums , changes in taste sensation, pain in the TMJ and bleeding gums with positive patients having more predilection of having all these symptoms. But the oral symptoms of swollen gums is found to be more prevalent in negative patients.

**TABLE 3: Gender predilection**

		Male		Female		Total	Pearsons Chi Square test
		Count	% of column total	Count	% of column total		
Positive cases with symptoms	Count	147	48.8%	87	52.4%	234	0.618, NS
	% of row total	62.8%	-	37.2%	-	100.0%	
Positive cases without symptoms	Count	37	12.3%	16	9.6%	53	-
	% of row total	69.8%	-	30.2%	-	100.0%	
Negative cases	Count	117	38.9%	63	38.0%	180	-
	% of row total	65.0%	-	35.0%	-	100.0%	
TOTAL		301	100.0%	166	100.0%	467	

\*NS – Not Significant, S – Significant, HS – Highly Significant. Level of significance 0.05



**Graph 3: Bar Chart Showing Gender Predilection**

On evaluation of the gender predilection between positive patients with symptoms, positive patients without symptoms and negative patients with symptoms , there found to be no significant difference.

**Table 4: Symptoms With The Higher Prevalence And Odds In Covid Positive Patients**

Categories	Symptoms	% of positive cases with this symptom	(Positive / Negative) Odds Ratio & Significance
ORAL SYMPTOMS	Changes in Taste Sensation	81.2%	10.34, p < 0.001 (HS)
	Bleeding Gums	75.2%	1.97, p < 0.001 (HS)
	Pain in TMJ	27.8%	3.25, p < 0.001 (HS)
GENERAL SYMPTOMS	Fever	100%	In all positive cases
	Breathing difficulty	79.9%	35.81, p < 0.001 (HS)
	Asthenia	93.2%	9.30, p < 0.001 (HS)

\*NS – Not Significant, S – Significant, HS – Highly Significant. Level of significance 0.05

From the above data, it was found that with respect to oral symptoms in covid positive patients, the highest odds are in the order – Change in taste sensation (81.2%), Bleeding gums(75.2%) and Pain in TMJ ( 27.8%). And with respect to general symptoms, the highest odds are on the order – fever (100%), breathing difficulty (79.9%) and asthenia ( 93.2%) of the covid positive patients.

**IV. DISCUSSION**

According the present study, out of 287 covid positive cases 53 patients had no clinical symptoms whereas 234 patients had clinical symptoms which included fever(100%), cough (89.3%), breathing

difficulty(79.9%), sore throat (84.2%), arthralgia (67.1%), Rhinitis (41%), headache (61.5%),Asthenia (93.2%) and abdominal symptoms ( 25.2%). In case of covid negative patients, there were 180 patients which included the following symptoms- fever (74.4%), cough (67.8%), breathing difficulty (10%), sore throat (46.1%), arthralgia (29.4%), Rhinitis (36.1%), headache (54.4%),Asthenia (59.4%) and abdominal symptoms (25%). From the results it was evident that a statistically higher percentage of positive patients had **fever, cough, breathing difficulty, sore throat, arthralgia, and asthenia**. The results are in conjunction with other studies (Guo et al., 2020). Till now, no study has compared the prevalence of symptoms in relation to covid positive and negative patients.

When we studied the prevalence of oral symptoms in covid positive and negative patients, it was found that a statistically significant difference was present with more predilection of **burning sensation, changes in taste sensation, pain in the TMJ and bleeding gums** with positive patients. During infection from most viruses, the first step is to attach to the surface and recognize the cell surface receptor of the host cell for invasion.(Maginnis, 2018; Mostafa et al., 2018) With similar external subdomain of receptor-binding domain (RBD), 2019-nCoV spike share same host-cell receptor— angiotensin-converting enzyme II (ACE2)—with SARS-CoV spike, but in a higher affinity than SARS-CoV spike.(Hofmann et al., 2005; Li et al., 2003; X. Xu et al., 2020; Zhou et al., 2020) Several studies have shown that salivary gland and tongue express ACE2 receptor, suggesting oral cavity as host for 2019-nCoV to invade. The increase in bleeding gums might be because of the suppression and a persistent inflammatory status might trigger the coagulation cascade which is associated with increased levels of fibrinogen degradation products (e.g., D-dimer) and might aggravate prior underlying untreated moderate or severe periodontitis.(Vieira, 2021)

Furin has been implicated in virus infection by cleaving viral envelope glycoproteins and enhancing infection with host cells.(Izaguirre, 2019) Furin expression was detected by immunostaining in human tongue epithelia.(López de Cicco et al., 2004) Combined with the presence of ACE II receptors present in the tongue , this might be the reason for altered taste sensation. And also, because of the disruption of the salivary gland cells (has ACE II receptor), there might be decreased salivation (xerostomia) which could lead to burning sensation in and around the mouth. Moreover due to this , the susceptibility to other oral infections might increase like ulcer and erosion, aphthous lesions, candidiasis, etc.

It is well established the importance of psychosocial factors in development and maintenance of Temporomandibular Disorders (TMD) (De La Torre Canales et al., 2018; Manfredini et al., 2017; Osiewicz et al., 2019) There is a significant relationship between painful TMD, depression, and anxiety.(Boscatto et al., 2013; Kindler et al., 2012) All psychological issues involved in emergency and threatening situations like the ones faced with COVID-19 pandemic are able to trigger sympathetic activity and further release of adrenocortical steroids which lead to muscle vasoconstriction and increased peripheral vascular resistance.(Almeida-Leite et al., 2020) Feelings of warmth and cold, palpitations, tachycardia, nausea, abdominal pain, diarrhea, and constipation can all be the consequences of autonomic stress responses.(Low, 2011) Thus, this might be the reason for aggravating a pre existing masticatory muscle disorder and might have led to increased prevalence of pain in relation to covid positive patients.

In the present study, with regard to gender predilection, there was no significant difference in relation to symptoms in both covid positive and negative cases. It is also highlighted from the study that the patients who are covid positive have higher odds in the order of changes in taste sensation> bleeding gums> pain in TMJ. No other study has been reported till now regarding pain in TMJ as a symptom of covid 19. Therefore, further research in regard to this aspect is warranted.

The limitations of the present study are the limited number of samples (487). Hence further studies with a large number of samples are needed. As the present study is a cross sectional study, the symptoms present on the day of screening were taken into consideration. The time of onset of oral and general symptoms has not been taken into consideration. The time of onset of symptoms is one of the important factors in the pathogenesis of any disease. Moreover, the present study has not undertaken the consideration of food habits and lifestyle of the

patients which might affect the immune system. Hence, future studies incorporating these facts should be considered.

## V. CONCLUSION:

Within the limitations of the study, it can be concluded that oral symptoms of burning sensation, changes in taste sensation, bleeding gums and pain in the TMJ are found to be more prevalent with patients having corona virus infection. In the light of the present study, it can be said that pain in temporomandibular joint might be a new symptom in these patients which may be related to the stress and anxiety caused by this disease.

## REFERENCES:

- Almeida-Leite, C. M., Stuginski-Barbosa, J., & Conti, P. C. R. (2020). How psychosocial and economic impacts of COVID-19 pandemic can interfere on bruxism and temporomandibular disorders? *Journal of Applied Oral Science: Revista FOB*, 28, e20200263.
- Amorim dos Santos, J., Normando, A. G. C., Carvalho da Silva, R. L., De Paula, R. M., Cembranel, A. C., Santos-Silva, A. R., & Guerra, E. N. S. (2020). Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations? *International Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases*, 97–, 326328.
- Boscato, N., Almeida, R. C., Koller, C. D., Presta, A. A., & Goettems, M. L. (2013). Influence of anxiety on temporomandibular disorders—an epidemiological survey with elders and adults in Southern Brazil. *Journal of Oral Rehabilitation*, 40–(9), 643649.
- Casas, C. G., Galván Casas, C., Catalá, A., Carretero Hernández, G., Rodríguez-Jiménez, P., Fernández-Nieto, D., Rodríguez-Villa Lario, A., Navarro Fernández, I., Ruiz-Villaverde, R., Falkenhain-López, D., Llamas Velasco, M., García-Gavín, J., Baniandrés, O., González-Cruz, C., Morillas-Lahuerta, V., Cubiró, X., Figueras Nart, I., Selda-Enriquez, G., Romani, J., ... García-Doval, I. (2020). Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *British Journal of Dermatology*–(Vol. 183, Issue 1, pp. 7177). <https://doi.org/10.1111/bjd.19163>
- Casella, M., Rajnik, M., Cuomo, A., Dulebohn, S. C., & Di Napoli, R. (2020). Features, Evaluation and Treatment Coronavirus (COVID-19). In *StatPearls*. StatPearls Publishing.
- De La Torre Canales, G., Cámara-Souza, M. B., Muñoz Lora, V. R. M., Guarda-Nardini, L., Conti, P. C. R., Rodrigues Garcia, R. M., Del Bel Cury, A. A., & Manfredini, D. (2018). Prevalence of psychosocial impairment in temporomandibular disorder patients: A systematic review. *Journal of Oral Rehabilitation*, 45–(11), 881889.
- Estébanez, A., Pérez-Santiago, L., Silva, E., Guillen-Climent, S., García-Vázquez, A., & Ramón, M. D. (2020). Cutaneous manifestations in COVID-19: a new contribution. *Journal of the European Academy of Dermatology and Venereology: JEADV*. <https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.16474>
- Guo, Y.-R., Cao, Q.-D., Hong, Z.-S., Tan, Y.-Y., Chen, S.-D., Jin, H.-J., Tan, K.-S., Wang, D.-Y., & Yan, Y. (2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. *Military Medical Research*, 7(1), 11.
- Henry, D., Ackerman, M., Sancelme, E., Finon, A., & Esteve, E. (2020). Urticarial eruption in COVID-19 infection. *Journal of the European Academy of Dermatology and Venereology: JEADV*. <https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.16472>
- Hofmann, H., Pyrc, K., van der Hoek, L., Geier, M., Berkhout, B., & Pöhlmann, S. (2005). Human coronavirus NL63 employs the severe acute respiratory syndrome coronavirus receptor for cellular entry. *Proceedings of the National Academy of Sciences of the United States of America*, 102–(22), 79887993.
- Iranmanesh, B., Khalili, M., Amiri, R., Zartab, H., & Aflatoonian, M. (2021). Oral manifestations of COVID-19 disease: A review article. *Dermatologic Therapy*, 34(1), e14578.
- Izaguirre, G. (2019). The Proteolytic Regulation of Virus Cell Entry by Furin and Other Proprotein Convertases. *Viruses*, 11(9). <https://doi.org/10.3390/v11090837>
- Kindler, S., Samietz, S., Houshmand, M., Grabe, H. J., Bernhardt, O., Biffar, R., Kocher, T., Meyer, G., Völzke, H., Metelmann, H.-R., & Schwahn, C. (2012). Depressive and anxiety symptoms as risk factors for temporomandibular joint pain: a prospective cohort study in the general population. *The Journal of Pain: Official Journal of the American Pain Society*, 13–(12), 11881197.
- Li, W., Moore, M. J., Vasilieva, N., Sui, J., Wong, S. K., Berne, M. A., Somasundaram, M., Sullivan, J. L., Luzuriaga, K., Greenough, T. C., Choe, H., & Farzan, M. (2003). Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*, 426–(6965), 450454.
- López de Cicco, R., Watson, J. C., Bassi, D. E., Litwin, S., & Klein-Szanto, A. J. (2004). Simultaneous expression of furin and vascular endothelial growth factor in human oral tongue squamous cell carcinoma progression. *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research*, 10–(13), 44804488.
- Low, P. A. (2011). *Primer on the autonomic nervous system*. <https://books.google.com/books?hl=en&lr=&id=NI8twzARIC&oi=fnd&pg=PP1&dq=Ziegler+MG+Psychological+stress+and+the+autonomic+nervous+system+In+Robertson+D+Biaggioni+I+Burnstock+G+Low+P+A+editors+Primer+on+the+autonomic+nervous+system+2nd+ed&ots=zS4NuH9v0h&sig=0fKnblmdS6hPCMnrLX78SDM5Ew>
- Maginnis, M. S. (2018). Virus-Receptor Interactions: The Key to Cellular Invasion. *Journal of Molecular Biology*, 430–(17), 25902611.
- Manfredini, D., Lombardo, L., & Siciliani, G. (2017). Temporomandibular disorders and dental occlusion. A systematic review of association studies: end of an era? *Journal of Oral Rehabilitation*, 44–(11), 908923.
- Mostafa, A., Abdelwhab, E. M., Mettenleiter, T. C., & Pleschka, S. (2018). Zoonotic Potential of Influenza A Viruses: A Comprehensive Overview. *Viruses*, 10(9). <https://doi.org/10.3390/v10090497>
- Osiewicz, M., Manfredini, D., Biesiada, G., Czepiel, J., Garlicki, A., Aarab, G., Pytko-Polociński, J., & Lobbezoo, F. (2019). Prevalence of Function-Dependent Temporomandibular Joint and Masticatory Muscle Pain, and Predictors of Temporomandibular Disorders among Patients with Lyme Disease. *Journal of Clinical Medicine* (Vol. 8, Issue 7, p. 929). <https://doi.org/10.3390/jcm8070929>
- Recalcati, S. (2020). Cutaneous manifestations in COVID-19: a first perspective. *Journal of the European Academy of Dermatology and Venereology: JEADV*, 34(5). <https://doi.org/10.1111/jdv.16387>
- Vieira, A. R. (2021). Oral manifestations in coronavirus disease 2019 (COVID-19). *Oral Diseases*. <https://onlinelibrary.wiley.com/doi/abs/10.1111/odi.13463>
- Wu, A., Peng, Y., Huang, B., Ding, X., Wang, X., Niu, P., Meng, J., Zhu, Z., Zhang, Z., Wang, J., Sheng, J., Quan, L., Xia, Z., Tan, W., Cheng, G., & Jiang, T. (2020). Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. *Cell Host & Microbe*, 27–(3), 325328.
- Xu, H., Zhong, L., Deng, J., Peng, J., Dan, H., Zeng, X., Li, T., & Chen, Q. (2020). High

expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *International Journal of Oral Science*, 12(1), 8.

- Xu, X., Chen, P., Wang, J., Feng, J., Zhou, H., Li, X., Zhong, W., & Hao, P. (2020). Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Science China. Life Sciences*, 63–(3), 457460.
- Zhou, P., Yang, X.-L., Wang, X.-G., Hu, B., Zhang, L., Zhang, W., Si, H.-R., Zhu, Y., Li, B., Huang, C.-L., Chen, H.-D., Chen, J., Luo, Y., Guo, H., Jiang, R.-D., Liu, M.-Q., Chen, Y., Shen, X.-R., Wang, X., ... Shi, Z.-L. (2020). Addendum: A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, 588(7836), E6.