

The Relationship Between COVID-19 And Periodontitis Severity: A Retrospective Cohort Study

COVID-19 ile Periodontitis Şiddeti Arasındaki İlişki: Retrospektif Kohort Çalışması

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ABSTRACT

Objective: Coronavirus disease-2019 (COVID-19) is a severe acute respiratory infection. The severity of symptoms and mortality rate vary according to age, gender, and other existing systemic diseases. Periodontitis is a chronic inflammation, and it has relations to other systemic diseases. The aim of this study is to examine the relationship between periodontal disease and COVID-19 severity by retrospectively evaluating patient records and periodontal status.

Methods: 344 patients were included in the study. The severity of periodontal disease was determined as healthy, mild, moderate and severe according to National Health and Nutrition Examination Survey (NHANES) criteria. The COVID-19 severity was grouped as asymptomatic/mild, moderate and severe according to whether the patients required hospitalization and intensive care. Kruskal-Wallis test was used for independent samples between gender-age-periodontal status and gender-age- COVID-19 relationships.

Results: The mean age of all patients was 36±13; the mean age of those with systemic disease was 52±15, and the mean age of those without it was 32±9. The mean age of those with systemic disease was greater than that of those without it ($P<.001$). The relationship between systemic disease and periodontal status was corrected for age, and since no statistical significance was observed ($P>.05$) There was statistically significant relationship was observed between COVID-19 severity and periodontal status ($P=.029$).

Conclusion: Periodontitis and the severity of COVID-19 increases, regardless of systemic diseases and age.

Key words: COVID-19, Periodontal Diseases, SARS-CoV-2

ÖZ

Amaç: Koronavirüs hastalığı-2019 (COVID-19) ciddi bir akut solunum yolu enfeksiyonudur. Semptomların şiddeti ve ölüm oranı yaşa, cinsiyete ve diğer mevcut sistemik hastalıklara göre değişir. Periodontitis kronik bir inflamasyondur ve diğer sistemik hastalıklarla ilişkileri vardır. Bu çalışmanın amacı, COVID-19 hasta kayıtlarını ve periodontal durumu retrospektif olarak değerlendirerek periodontal hastalık ile COVID-19 şiddeti arasındaki ilişkiyi incelemektir.

Yöntemler: Çalışmaya 344 hasta dahil edildi. Periodontal hastalığın şiddeti Ulusal Sağlık ve Beslenme İnceleme Anketi (NHANES) kriterlerine göre sağlıklı, hafif, orta ve şiddetli olarak belirlendi. COVID-19 şiddeti, hastaların hastaneye yatırılması ve yoğun bakıma ihtiyacı duyup duymamasına göre asemptomatik/hafif, orta ve şiddetli olarak gruplandırıldı. Cinsiyet-yaş-periodontal durum ve cinsiyet-yaş-COVID-19 ilişkileri arasındaki bağımsız örnekler için Kruskal-Wallis testi kullanıldı.

Bulgular: Tüm hastaların yaş ortalaması 36±13; sistemik hastalığı olanların yaş ortalaması 52±15, olmayanların yaş ortalaması 32±9 idi. Sistemik hastalığı olanların yaş ortalaması, olmayanlardan daha büyüktü ($P<.001$). Sistemik hastalık ile periodontal durum arasındaki ilişki yaşa göre düzeltildi ve istatistiksel olarak anlamlı bir ilişki gözlenmediğinden ($P>.05$) COVID-19 şiddeti ile periodontal durum arasında istatistiksel olarak anlamlı bir ilişki gözlemlendi ($P=.029$).

Sonuç: Periodontitis ve COVID-19 şiddeti, sistemik hastalıklardan ve yaştan bağımsız olarak artmaktadır.

Anahtar kelimeler: COVID-19, Periodontal

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is a severe acute respiratory infection caused by respiratory syndrome coronavirus 2 (SARS-CoV-2) that emerged in Wuhan Province, China, in late 2019.¹ In COVID-19, contamination occurs through respiratory aerosols or body fluids. Symptoms such as fever, nasal congestion, sore throat, joint pain, headache, abdominal pain, skin rashes, diarrhea, cough and shortness

of breath are observed.² Although the severity of symptoms and mortality rate vary according to age, gender and other existing systemic diseases (diabetes, obesity, cardiovascular diseases, cancer, etc.), but other unidentified risk factors may also affect the severity of COVID-19.³

Periodontitis is a condition that affects both periodontal tissues and causes systemic inflammation; and it is caused due to the unbalance between the host immune system and oral bacteria.^{4,5} Periodontitis is thought to affect 45% to 50% of adults worldwide.⁶ Therefore, associations between periodontitis and other chronic non-communicable diseases such as diabetes, cardiovascular diseases, adverse pregnancy outcomes and Alzheimer's disease have been widely investigated.⁴

T helper 17 cells (Th17) are effective adaptive immune response cells showing functions by releasing IL-17 (IL-17A), IL-17F, IL-21, IL-22 and TNF- α cytokines. High Th17-mediated responses have been observed in SARS-CoV and MERS-CoV patients.⁷ Similarly Th17 cell population has been increased in patients with periodontitis compared to healthy individuals; and higher serum IL-17 levels have been observed in individuals with periodontitis.⁸ In addition, higher levels of IL-2, IL-7, IL-10, G-CSF, MCP1, MIP1A and TNF α have been observed in patients requiring intensive care due to COVID-19.^{7,9} These cytokines which are closely associated with periodontal disease might serve as a link between periodontal disease and COVID-19.

All this information suggests that there may be a relationship between COVID-19 and periodontal diseases and the severity of periodontal disease may be a determinant for the severity of COVID-19. The aim of this study is to examine the relationship between COVID-19 severity and periodontal disease retrospectively by evaluating the patient records and periodontal status.

METHODS

Study Design

The study was approved by Ataturk University School of Medicine's Ethics Committee and carried out in strict compliance with ethical guidelines of World Medical Association's Declaration of Helsinki (B.30.2.ATA.0.01.00/485; 25.11.2021). Prior to periodontal examination, each participant was informed about study methodology and written informed consent was obtained. Participants were enrolled among the patients applied to Ataturk University Department of Periodontology, between November 2021 and March 2022. Three hundred forty-four patients between the ages of 18-85, who were both diagnosed with periodontal disease and COVID-19 were included in the study. Systemic diseases such as diabetes, cardiovascular diseases, hypertension, asthma, chronic obstructive pulmonary disease (COPD) and epilepsy were recorded for all participants. Patients who did not have COVID-19, were pregnant, smoked, had any drug addiction, and did not agree to participate in the study were excluded from the study (Figure 1).

Determining COVID-19 Severity

The diagnosis of COVID-19 was determined by real time-polymerase chain reaction (Rt-PCR) test and the severity of the patients was questioned by taking verbal anamnesis and whether they required hospitalization and intensive care unit, which was further confirmed by comparing with the patients' health records. COVID-19 severity was grouped as follows:¹⁰

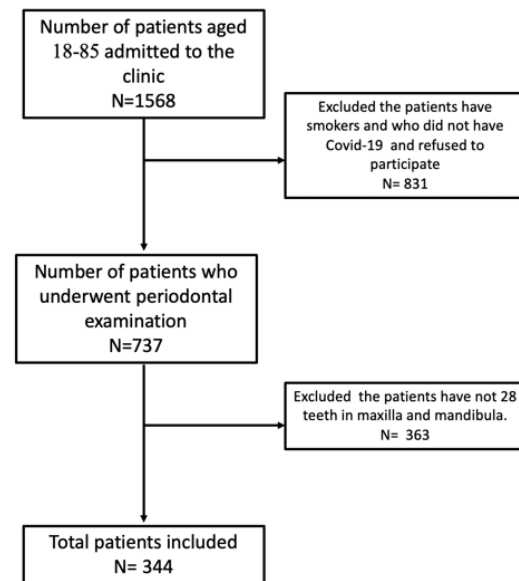


Figure 1. Flowchart of study sample. The patients were aged 18-85. Periodontal measurements were carried out according to NHANES III.

Asymptomatic/Mild group: Patients who had a positive Rt-PCR result but did not show symptoms of COVID-19, and patients who had symptoms such as fever, sore throat, muscle pain, joint pain and cough, but did not have respiratory distress, and whose chest radiography and/or lung tomography were normal.

Moderate group: Patients with symptoms such as fever, sore throat, muscle pain, joint pain and cough, respiratory rate <30 per minute, Oxygen saturation (SpO₂) >90% under normal conditions, and patients showing signs of mild-moderate pneumonia on chest radiography or tomography.

Severe group: Patients with symptoms such as fever, sore throat, muscle pain, joint pain and cough respiratory rate ≥30 per minute, SpO₂ ≤90% in room air, and findings of bilateral widespread pneumonia on chest radiography or tomography.

Periodontal Examination

Periodontal measurements were made according to NHANES III criteria.¹¹ One maxillary and one mandibular quadrant were included in each patient. Periodontal measurements were performed only on fully erupted teeth, and third molars were excluded. All measurements were made by a single clinician (YÖK). A maximum of 14 teeth were examined in each patient, including 7 teeth in the maxilla and 7 in the mandible. Patients were categorized according to their periodontal status:

1- Healthy patients (Gingivitis + healthy): Patients with no clinical attachment level (CAL) and probing depth (PD).

2-Mild periodontitis group: CAL between 3 and 4 mm in 2 or more interproximal areas, not on the same tooth; patients with 4 mm or more PD in 2 or more interproximal areas, not on the same tooth, or in a single area.

3- Moderate periodontitis group: CAL between 4 and 6 mm in 2 or more interproximal areas, not on the same tooth; patients with 5 mm or more PD in 2 or more interproximal areas, but not in the same tooth.

4- Severe periodontitis group: 6 mm or more CAL in 2 or more interproximal areas, not on the same tooth; patients with 5 mm or more PD in 2 or more interproximal areas, but not in the same tooth

Statistical Analysis

Based on the previous study results, the G* Power 3.1 Software Package's one-way ANOVA test was used to calculate the sample size.¹² Using an effect size of $f = 0.980$, it was determined that, with 80% power, each group should contain a minimum of 340 individuals, with a 95% confidence interval taking study Statistical analysis was performed using IBM SPSS Statistics v 20 (IBM SPSS Corp., Armonk, NY, USA). Kruskal-Wallis test was used for independent samples between age-periodontal status and age-COVID-19 relationships. All data are presented as mean, standard deviation, median, minimum-maximum, number and percentage. Statistical significance was determined as $P < .05$.

RESULTS

A total of 344 patients (204 men (59.3%) and 140 (40.7%) women) were evaluated. Of those who did not have a systemic disease, 166 (60.4%) were men and 109 (39.6%) were women. Of those with systemic disease, 38 (55.1%) were men and 31 (44.9%) were women. The average age of all patients was 36 ± 13 ; the average age of those without systemic disease was 32 ± 9 , those with systemic disease was 52 ± 15 . Patients with systemic disease had a higher mean age than patients without systemic disease ($P < .001$) (Table 1). While 275 (79.9%) of the patients were systemically healthy, 69 (20.1%) had at least one systemic disease. Sixty-five (18.9%) of the participants were periodontally healthy (healthy and gingivitis); 103 (29.9%) had mild, 97 (28.2%) moderate, and 79 (23%) severe periodontitis. 290 (84%) of the patients had mild COVID-19, 48 (14%) had moderate and 6 (2%) had severe COVID-19 (Table 2)

Table 1. Age and Systemic health status

	Systemic disease -				Systemic disease +				Z	P
	Mean	Standard Deviation	Median	Min-Max	Mean	Standard Deviation	Median	Min-Max		
Age	32	9	31	18-66	52	15	55	22-81	-9.298	<.001

* Statistical significance was determined $P < .05$

Systemic Disease - = Systematically healthy patients

Systemic Disease + = Patients having systemic disease

Table 2. Systemic disease, COVID-19 severity and periodontal status

		Systemic Disease		P
		Systemic Disease - (%)	Systemic Disease + (%)	
COVID-19 Severity	Asymptomatic/Mild group	258 (93.8%)	32 (46.4%)	<.001
	Moderate group	15 (5.5%)	33 (47.8%)	
	Severe group	2 (0.7%)	4 (5.8%)	
Periodontal Status	Healthy	62 (22.5%)	3 (4.3%)	.262
	Mild Periodontitis	94 (34.2%)	9 (13.0%)	
	Moderate Periodontitis	79 (28.7%)	18 (26.1%)	
	Severe Periodontitis	40 (14.5%)	39 (56.5%)	

* Statistical significance was determined $P < .05$

Systemic Disease - = Systematically healthy patients

Systemic Disease + = Patients having systemic disease

The association between periodontal state and COVID-19 severity was determined independent of age, gender, and systemic disease by statistically correcting these factors. According to the results of this evaluation, a statistically significant relationship was observed between COVID-19 severity and periodontal status ($P = .029$) (Table 3).

The probability of individuals with periodontitis having severe COVID-19 was found to be 1.24 times higher than those without periodontitis (Odd ratio (OR): 1.24; 95% Confidence Interval (CI): (1.17-1.31).

Table 3. Covid-19 Severity and Periodontitis Status

		Periodontal Status				Chi-Square	kappa value	P
		Healthy	Mild Periodontitis	Moderate Periodontitis	Severe Periodontitis			
COVID-19 Severity	Asymptomatic/Mild group	65	97	84	44	<0.001	0.046	.029
	Moderate group	0	5	12	31			
	Severe group	0	1	1	4			

* Statistical significance was determined $P < .05$

DISCUSSION

In this study, we aimed to retrospectively evaluate the relationship between COVID-19 and periodontal disease severity retrospectively, independent of systemic diseases, gender and age. Our results showed that there was a relationship between COVID-19 and periodontal disease severity, and that COVID-19 severity and periodontal disease severity increased in parallel.

Periodontitis has general inflammatory risk factors which effect the severity of COVID-19.^{13,14} The relationship between periodontal disease and COVID-19 severity has been explained through various mechanisms including the induction of angiotensin converting enzyme-2 (ACE2) overexpression by bronchial cells and alveolar epithelial cells, increase in IL-6 and IL-8 cytokine levels through aspiration of periodontal pathogens.¹⁵⁻¹⁷ Additionally, increase in the inflammatory release capacity of Th17 cells, one of the central cells in the formation of periodontal disease, during COVID-19 which results in cytokine storm development and enhanced inflammatory environment has been reported.^{18,19}

A previous study found that periodontitis was associated with serious complications caused by COVID-19, including intensive care unit admission, necessity of a ventilator, and death in more severe conditions.¹ Also according to the findings, patients with severe periodontitis had a higher likelihood of developing COVID-19-related issues compared to those with milder cases of the disease.¹ Another study suggests that there is a direct relationship between periodontitis and COVID-19-related outcomes.²⁰ In a study, periodontitis that the patient indicates, has been argued that the disease is a helpful marker to determine the risk of SARS-CoV-2 and claimed that these people show more symptoms at the beginning of COVID-19 disease.²¹ In our study, we found that the severity of COVID-19 was increased in people with severe periodontitis, following up the previous studies.

Aging is one of the important factors that increases the severity of both COVID-19 and periodontal disease.^{1,22,23} A study showed that older age may be associated with an increase in comorbidity of COVID-19.²⁴ Also, the relationship between the severity of COVID-19 and systemic diseases has been addressed in previous studies.^{25,26} A meta-analysis found that the patients with pre-existing chronic diseases have a higher risk of severe COVID-19 disease.²⁷ Another meta-analyses found that SARS-CoV-2 infected patients with a chronic illness have a more severe risk of covid disease and higher mortality rate.²⁸ In our study, COVID-19 severity was determined regardless of any systemic disease or age. Our results showed that there was a parallelism between periodontal disease and COVID-19 severity, independent of these two confounding factors.

The Covid-19 virus is more common in men. According to data collected at the start of the pandemic, men contributed about 60% of

all COVID-19 patients,^{29,30} 59 studies including 36,470 patients men had a higher risk than women in having infection, disease severity, intensive care unit (ICU) admission, and death. An additional investigation revealed that 1,875 (38%) of the 4,880 patients with respiratory symptoms or who had been in close contact with COVID-19 patients tested positive for SARS-CoV-2 infection; among those who tested positive, 40.43% were men. In line with these investigations, we also found that men had a higher rate of COVID-19.³¹ However, we did not include gender in our statistical analysis of the association between COVID-19 severity and periodontal disease.

Smoking is considered as a risk factor for both COVID-19 and periodontitis.^{32,33} We included non-smoking participants in our study. However, a previous study including smokers concluded that smoking does not affect the relationship between periodontal disease and COVID-19.¹² This may be related to the insufficient number of smoker participants in the study, and due to the increasing rate, which may misinterpret the relationship between these two diseases. To overcome this shortcoming, participants who smoke were not included in our study.

Severity of periodontitis was categorized according to NHANES III; and patients were grouped as severe, moderate, mild periodontitis and healthy. In our study, we aimed to compare individuals' periodontitis severity and its correlation with COVID-19 severity within appropriate criteria. In epidemiological studies with high participation conducted by a single physician, as in this study, the NHANES method provides advantages in terms of ease of application, shortening of examination time and precise application of measurements.^{34,35}

This study has some limitations. One of these is that cytokine levels were not measured and thus the relationship between COVID-19 and periodontal disease is not addressed biochemically. Another is that periodontal disease evaluation could not be performed during the time of COVID-19 due to the safety requirements.

In conclusion, our study showed that as the severity of periodontitis increases, the severity of COVID-19 increases, regardless of systemic diseases and age in this study. However, further clinical studies are needed to better explain the relationship between these two conditions.

Ethics Committee Approval: The study was approved by Ataturk University School of Medicine's Ethics Committee and carried out in strict compliance with ethical guidelines of World Medical Association's Declaration of Helsinki (B.30.2.ATA.0.01.00/485; 25.11.2021).

Informed Consent: Prior to periodontal examination, each participant was informed about study methodology and written informed consent was obtained.

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Hasta Onamı: Periodontal muayene öncesinde, her katılımcıya çalışma metodolojisi hakkında bilgi verilmiş ve yazılı onam alınmıştır.

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REFERENCES

1. Marouf N, Cai W, Said KN, et al. Association between periodontitis and severity of COVID-19 infection: A case-control study. *J Clin Periodontol*. 2021;48(4):483-491. doi:10.1111/jcpe.13435
2. Andrews M, Gao H, Datta S, Katz J. Increased odds for COVID-19 infection among individuals with periodontal disease. *Clin Oral Invest*. 2023;27(10):5925-5933. doi:10.1007/s00784-023-05204-x
3. Hamza A, Shah N, Azad A, Ghanshyam O, Khan Z. Impact of age, gender and comorbidities affecting the severity of COVID-19 infection in Kashmir. *J Family Med Primary Care*. 2022;11(4):1519-1524. doi:10.4103/jfmpc.jfmpc_278_21
4. Genco RJ, Sanz M. Clinical and public health implications of periodontal and systemic diseases: An overview. *Periodontol*. 2020;83(1):7-13. doi:10.1111/prd.12344
5. Sanz M, Beighton D, Curtis MA, et al. Role of microbial biofilms in the maintenance of oral health and in the development of dental caries and periodontal diseases. Consensus report of group 1 of the Joint EFP/ORCA workshop on the boundaries between caries and periodontal disease. *J Clin Periodontol*. 2017;44(S18). doi:10.1111/jcpe.12682
6. Vos T, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*. 2017;390(10100):1211-1259. doi:10.1016/s0140-6736(17)32154-2
7. Martonik D, Parfieniuk-Kowerda A, Rogalska M, Flisiak R. The role of TH17 response in COVID-19. *Cells*. 2021;10(6):1550. doi:10.3390/cells10061550
8. Carmona Loayza DA, Lafebre MF. Periodontal disease and COVID-19: Prognosis and potential pathways of association in their pathogenesis. *Can J Dent Hyg*. 2023;57(1):44-51.
9. Tang Y, Liu J, Zhang D, Xu Z, Ji J, Wen C. Cytokine Storm in COVID-19: The current evidence and treatment strategies. *Front Immunol*. 2020;11. doi:10.3389/fimmu.2020.01708
10. Can FK, Özkurt Z, Öztürk N, Sezen S. Effect of IL-6, IL-8/CXCL8, IP-10/CXCL 10 levels on the severity in COVID 19 infection. *Int J Clin Practice*. 2021;75(12). doi:10.1111/ijcp.14970

11. Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ. Prevalence of periodontitis in adults in the United States: 2009 and 2010. *J Dent Res.* 2012;91(10):914-920. doi:10.1177/0022034512457373
12. Anand PS, Jadhav P, Kamath KP, Kumar SR, Vijayalaxmi S, Anil S. A case-control study on the association between periodontitis and coronavirus disease (COVID-19). *J Periodontol.* 2021;93(4):584-590. doi:10.1002/jper.21-0272
13. Zhou Y, Wang W, Sun Y, et al. The prevalence and risk factors of psychological disturbances of frontline medical staff in china under the COVID-19 epidemic: Workload should be concerned. *J Affect Disord.* 2020;277:510-514. doi:10.1016/j.jad.2020.08.059
14. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intens Care Med.* 2020;46(5):846-848. doi:10.1007/s00134-020-05991-x
15. Herold T, Jurinovic V, Arnreich C, et al. Elevated levels of IL-6 and CRP predict the need for mechanical ventilation in COVID-19. *J Allerg Clin Immun.* 2020;146(1):128-136.e4. doi:10.1016/j.jaci.2020.05.008
16. Del Valle DM, Kim-Schulze S, Huang HH, et al. An inflammatory cytokine signature predicts COVID-19 severity and survival. *Nature Med.* 2020;26(10):1636-1643. doi:10.1038/s41591-020-1051-9
17. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020;395(10229):1033-1034. doi:10.1016/s0140-6736(20)30628-0
18. Cheng W, Hughes FJ, Taams LS. The presence, function and regulation of IL-17 and Th17 cells in periodontitis. *J Clin Periodontol.* 2014;41(6):541-549. doi:10.1111/jcpe.12238
19. Graves D. Cytokines that promote periodontal tissue destruction. *J Periodontol.* 2008;79(8S):1585-1591. doi:10.1902/jop.2008.080183
20. Koppolu P, Genady EM, Albdeirat LM, et al. Association between Severity of COVID-19, Periodontal Health and Disease in Riyadh Subpopulation. *Int J Mycobacteriol.* 2023;12(1):33-37. doi:10.4103/ijmy.ijmy_236_22
21. Anand PS, Jadhav P, Kamath KP, Kumar SR, Vijayalaxmi S, Anil S. A case-control study on the association between periodontitis and coronavirus disease (COVID-19). *J Periodontol.* 2021;93(4):584-590. doi:10.1002/jper.21-0272
22. Zhu L, Tang Z, Hu R, Gu M, Yang Y. Ageing and inflammation: What happens in periodontium? *Bioengineering.* 2023;10(11):1274. doi:10.3390/bioengineering10111274
23. Ebersole JL, Graves CL, Gonzalez OA, et al. Aging, inflammation, immunity and periodontal disease. *Periodontol 2000.* 2016;72(1):54-75. doi:10.1111/prd.12135
24. Endeshaw Y, Campbell K. Advanced age, comorbidity and the risk of mortality in COVID-19 infection. *J National Med Assoc.* 2022;114(5):512-517. doi:10.1016/j.jnma.2022.06.005
25. Matsuyama R, Nishiura H, Kutsuna S, Hayakawa K, Ohmagari N. Clinical determinants of the severity of Middle East respiratory syndrome (MERS): a systematic review and meta-analysis. *BMC Public Health.* 2016;16(1). doi:10.1186/s12889-016-3881-4
26. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *International Journal of Infectious Diseases.* 2016;49:129-133. doi:10.1016/j.ijid.2016.06.015
27. Treskova-Schwarzbach M, Haas L, Reda S, et al. Pre-existing health conditions and severe COVID-19 outcomes: an umbrella review approach and meta-analysis of global evidence. *BMC Med.* 2021;19(1). doi:10.1186/s12916-021-02058-6
28. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel Coronavirus-Infected pneumonia in Wuhan, China. *JAMA.* 2020;323(11):1061. doi:10.1001/jama.2020.1585
29. Li L, Huang T, Wang Y, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol.* 2020;92(6):577-583. doi:10.1002/jmv.25757
30. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *New England J Med.* 2020;382(18):1708-1720. doi:10.1056/nejmoa2002032
31. Liu R, Han H, Liu F, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. *Clinica Chimica Acta.* 2020;505:172-175. doi:10.1016/j.cca.2020.03.009
32. Hopkinson NS, Rossi N, El-Sayed_Moustafa J, et al. Current smoking and COVID-19 risk: results from a population symptom app in over 2.4 million people. *Thorax.* 2021;76(7):714-722. doi:10.1136/thoraxjnl-2020-216422
33. Haffajee AD, Socransky SS. Relationship of cigarette smoking to attachment level profiles. *J Clin Periodontol.* 2001;28(4):283-295. doi:10.1034/j.1600-051x.2001.028004283.x
34. Steffens JP, Wang X, Starr JR, Spolidorio LC, Van Dyke TE, Kantarci A. Associations between sex hormone levels and periodontitis in men: Results from NHANES III. *J Periodontol.* 2015;86(10):1116-1125. doi:10.1902/jop.2015.140530
35. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA. Accuracy of NHANES periodontal examination protocols. *J Dent Res.* 2010;89(11):1208-1213. doi:10.1177/0022034510377793