Association of Periodontitis severity in Covid19 Individuals: A Case Control Study

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Abstract

Introduction: Periodontitis is an inflammatory disease distressing the tissue that surrounds the teeth. When it progresses, its can damage PDL (periodontal ligament) and can worsen the condition and causes bone loss. Coronavirus pandemic provokes severe acute respiratory syndrome. The dissemination of Covid-19 around the globe has serious consequences, including increase in oral health disease such as periodontitis. It has brought various challenges for health sector including dental professionals. This article details about bidirectional causality of SARS Covid19 with other confounding factors.

Material and Method: It was a Case control study conducted at Bahria University and Dental College. The Sample size was 72 calculated by using Open Epi version 3, power of test will be 80%. Statistical analysis was done using SPSS version 23.0. Significance was tested using Chi square test and logistics regression model at P-value ≤ 0.05.

Results:
There were total 150 participants, 85 agreed to participate in the study, Covid positive individuals mean age was [34.92±1.99] and Covid negative individuals mean age was [32.44±2.05].Those individuals who had habit of smoking, were at high risk (risk odds=15.1) of having periodontal disease with significant p value (0.000). Individuals who spent less time on brushing were 1.553 times at higher risk of having periodontal disease with significant p value (0.03). Patients with poor gingival status showed odds ratio of 7.24 also had furcation involvement with odd ratios of 1.63, co-presenting recession with odds ratio of 2.32. Regression model for probing depth and SARS-CoV-2 history with probing depths ranging 3-4 mm are at 3.11 times higher risk, 5mm and beyond are extremely prone to develop risk of periodontitis and probing depth greater than equal to 6mm and had history of Covid19 showed severe bleeding in less than 30 seconds and very poor periodontal status.CAL in Covid history positive patients showed that out of 3 categories, groups of mild and moderate CAL had 6.22 times higher risk to developing periodontal complications. Patients with Covid19 history and alveolar bone loss, mean value of 69.4 % (25 in number) showed severe attachment loss.

Conclusion: The increased prevalence and severity of COVID19 complications may unfold clinical signs and symptoms of periodontitis and lead to exodontia of tooth.

Keyword: Covid19, Oral health, periodontal disease, Pandemic, Periodontitis, SARS

Introduction:

Periodontitis is an inflammatory disease distressing the tissue that surrounds the teeth (1).When it progresses, its can damage PDL (periodontal ligament) and can worsen the condition and causes bone loss. It is thought to be one of the most serious hazards to one's dental health. In the world periodontal disease was the 11th most prevailing condition. The prevalence of periodontal disease was reported to range from 20% to 50% around the world and global burden of periodontal disease increased by 57.3% from 1990 to 2010 (2).
Corona virus disease (COVID19) a pandemic that provokes severe acute respiratory syndrome, It was first identified in the province of Wuhan, China, in December 2019 (3) World Health Organization declared Covid19 as global pandemic on 11 March 2020 (4).Covid19 is a non-segmented–single stranded RNA virus. It possesses proteins that contain membrane (M), nucleocaspid (N), envelop (E), and spike (S). It is divided into four types that contain gamma (γ), delta (δ), beta (β) and alpha (α) (5). According to the research, it has reached to 223 countries with more than 281 million confirmed cases, and more than 5.8 million deaths were reported globally, with many countries seeing outbreaks of second and third wave (6). Furthermore one million two hundred thirty-four thousand eight hundred twenty-eight (1,234,828) cases were confirmed and twenty-seven thousand four hundred eighty-two (27,482) *d*eaths were reported locally. In South East Asia prevalence of covid19 cases declined to 27 % whereas in western world death rate raised up to 7 % (7). The alpha, beta, gamma and delta variant were found in 170, 119, 71 and 85 countries respectively. Covid-19 date rate is influenced by age, underlying pre-existing conditions and severity of disease. Its rate rose up to 2.2% (8). Covid-19 symptoms include bad breath, swelling, pigmentation, fissured tongue, ulcer, erosion, vesicle, bulla, erythematic, necrosis, pustule, impulsive bleeding with altered taste is being prime oral symptom (9). Moreover the dissemination of Covid-19 around the globe has serious consequences, including increase in oral health disease such as periodontitis (10) Bi-directional causality of oro-systemic conditions is common understanding in masses by now. Likewise, studies have shown a strong association between systemic and periodontal diseases such as periodontitis. SARS COV-2 has impacted all parts of human life especially public health and fitness. Similarly it has brought about various challenges for health sector including dental professionals. It has broken the back bone of economy and provision of health services to masses (11). In addition dentists are at more risk especially as they are more expose to instruments and procedures that produce aerosols (12). The aim of this study is to identify the impact of SARS Covid-19 on periodontal health. This article details about bidirectional causality of SARS Covid19 with other confounding factors.

Material and Method

The study was approved by the Institutional Ethics Committee of the BUHS Bahria University Health Sciences Campus Karachi; with ERC number 124/2022.
It was a Case control study conducted at Bahria University and Dental College, Karachi in Periodontology department within 12 months' time period. The Sample size was 72 calculated by using Open Epi version 3, power of test will be 80%. Purposive sampling technique was used for the data collection. Study populations was divided into 2 groups, group-1 (36 cases), include those who had covid-19 history presenting with periodontitis .Whereas, and group, 2 (36 controls) was comprised of orally and systemically healthy individuals. Each subject will be

assessed through oral examination and questionnaire (20 minutes per subject) by principal investigator. Exclusion criteria for (CASES, CONTROLS) those who patients had active covid19 were excluded from both the groups. Whereas inclusion criteria included: Patients aged 12 - 70 years and had no history of antibiotic use since last six month, no scaling and root planning was performed within 6months, along with bleeding gums, erythema, swelling, bad breath, mobile teeth and habits like addiction of smoke and smokeless tobacco were included in the case group . Moreover those who came to OPD for dental checkup after the negative PCR report were included in the control group. However those patient with active covid19 history were excluded from the control group furthermore co-morbid condition such as diabetes, hypertension , immune-compromised condition, those taking corticosteroid and immune suppressant medications, smokers, alcoholics were not the part of the study from both case and control group. Individuals qualifying the inclusion criteria will be consented and recruited. Informed written consent will be obtained from each individual. Individual's qualifying the inclusion criteria will undergo detail periodontal examination using William's probe. And information about different variables will be obtained using questionnaire that will be filled under supervision of principal investigator. Patients with previous positive Covid-19 reports will be recruited as cases and completely healthy individuals will be observed as controls. Periodontal charting will be performed on the six surfaces per tooth of interest. Probing depth greater than equals to 3mm will be classified as periodontitis cross confirmed by signs of bone loss on peri-apical x-rays. Obtained responses in questionnaire will be transferred to software for statistical analysis.

Statistical analysis:

Statistical analysis was done using SPSS version 23.0. All quantitative and qualitative variables were presented as means, standard error and frequencies (percentages). Significance was tested using Chi square test and logistics regression model at P-value ≤ 0.05.

Results:

There were total 150 participants out of that 85 were agreed to participate in the study, but due to lack of time only 72 patients were able to complete the questionnaire. Covid positive individuals mean age was 34.92±1.99 and Covid negative individuals mean age was [32.44±2.05] as showed in. (Table 1)

Table-1: Age distribution of patient with Covid19 history.

	Age (years)	
	Mean± Standard error	**95% Confidence interval**
Covid + ve	34.92±1.99	30.87-38.97
Covid - ve	32.44±2.05	28.24-36.63

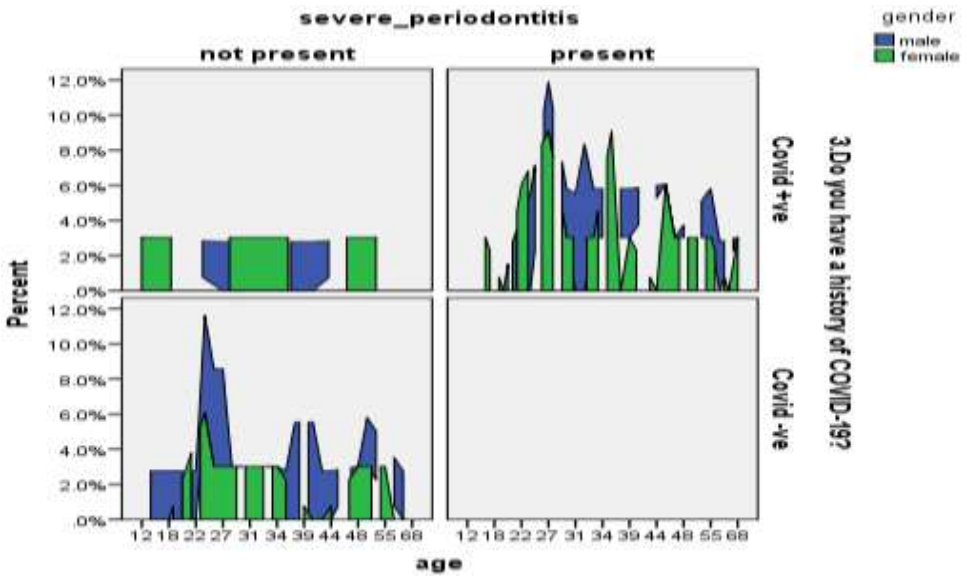

Figure 1: Gender distribution was presented with age and frequency of Covid history

Table 2: Logistics regression analysis was observed in subjects with Covid positive history.

		95% C.I. for Odds Ratio		
Variables	**Odds ratio**	**Lower**	**Upper**	**P-value**
Smoking	15.188	0.333	692.21	0.000
Bruxism	0	0	0.581	0.039
Biting	9.054	0.013	6475.6	0.044
Age of Brush	0.205	0.03	1.416	0.108
Type of Brush	0.134	0.018	1.028	0.053
Methods	2.264	0.584	8.773	0.023
Frequency of Brushing	0.158	0.015	1.615	0.12
Estimate Time Spent Brushing	1.553	0.673	3.581	0.033
Floss	2.734	2.113	35.391	0.048
Picks	3.191	0.243	41.847	0.037
Interproximal	0	0	.	0.999
Oral Health Index-Score	0.832	0.38	1.825	0.647
Interpretation	1.81	0.293	11.176	0.05
Gingival Status	7.24	0.077	0.077	0.004
Mucogingival Problems	0.043	0.001	3.245	0.154
Missing teeth	0.238	0.019	2.953	0.264
Furcation	1.639	6.567	40.889	0.015
Mobility	0.028	0	2.719	0.125
Recession	2.327	0.072	75.277	0.034
Pocketing	0.005	0	1.679	0.074

Those individuals who had habit of smoking, were at high risk odds=15.1 [95% CI 0.333-692.21] of having periodontal disease with significant p value (0.000) .Whereas, the individuals with history of bruxism were at lower risk odds ratio [0] and their p value (0.03) was significant. Individuals with nail biting history were at high risk odds ratio 9.0 [95% CI 0.013-6475.6] having diseases with significant p value (0.044).Those participants whose hygiene were moderate were at lesser risk as on the other hand those individuals following improper method of brushing were at 2.26 [95% CI 0.584- 8.773] times higher risk with significant p value (0.02) Individuals who spent less time on brushing were 1.553[95% CI 0.673-3.581] times at higher risk of having periodontal disease with significant p value (0.03). Patients with poor gingival status showed odds ratio of 7.24 [95% CI 0.077- 0.077] also had furcation involvement with odd ratios of 1.63[95%CI 6.567-40.889]. Co-presenting the recession with odds ratio of 2.32 [95% CI 0.072- 75.277] times higher risk of having periodontal disease as discussed in table 2.

The clinical parameters displayed proportional readings in deteriorative phase. Regression model for probing depth and SARS-CoV-2 history presented by subjects with probing depths ranging between 3-4 mm are at 3.11 times higher risk to develop complications as compare to those who have had history of Covid19 but no severe periodontitis observed among them. Beside, those who had probing depth ranging between 5mm and beyond are extremely prone to develop risk of periodontitis especially when they have positive Covid19 history. Those with the probing depth greater than equal to 6mm and had history of Covid19 showed severe bleeding in less than 30 seconds and very poor periodontal status, However severe periodontal loss was seen in 75%.As a matter of fact, probing depth and bone loss combines to present/state clinical attachment loss (CAL), the data was subdivided into categories of CAL that reflected the strong relationship between periodontal complications and presence of Covid19 history with significant p-values. Hence, increase in the severity of Covid19 episode will proportionally raise the detrimental effect on clinical attachments of the teeth. Severe bone loss was seen in 27 individuals and among Covid positive patients 32(88.9%) subjects displayed sign and symptoms of severe periodontitis co-presented with positive covid19 in past. Regression model between CAL versus Covid history showed that out of 3 categories, groups of mild CAL and moderate CAL has 6.22 times are at higher risk to develop periodontal complications as compare to normal category individuals, while severe group have already developed the periodontal complications. Severe CAL was presented by 32 out of 36 individuals after the covid19 exposure. Hence, it is clear those SARS-Cov-2 impacts not only the systemic organs but also influences the oral health status of individual in injurious manner. In addition 88.9% showed severe form of periodontitis in the presence of SARS-CoV-2 in past history.

Patients with Covid19 history and alveolar bone loss, mean value of 69.4 % (25 in number) showed severe attachment loss. Beside these observations, the regression model for the subjects with bone loss of $\geq$ 2mm on bitewing radiographs demonstrated that those who have covid19 history and fall in the category of moderate bone loss (middle third of root) were at 2.6 times higher risk to develop the periodontal problems as compare to those who are normal or mild. While severe group (apical third of root) has lesser risk, they have already started develop or about to develop periodontal complications among them. (Table 4)

Table-3:Co-relation between SARS-CoV-2 and Chronic periodontitis

Variable	Covid +ve History	Covid -ve	P value
CAL Normal Moderate Severe	2 (5.6%)	77 (100%)	.000
	7(19.4%)	0	
	27 (75%)	0	
PD Depth Normal Mild Severe	4 (11.1%)	7 (100%)	.000
	5 (13.9%)	0	
	27 (75%)	0	
Severe Periodontitis Not Present Present	4 (11.9%)	77 (100%)	.000
	32 (88.9%)	0	
Bone loss 1-3 Mild 3-4 Moderate ≥5 severe	0	35 (45.5%)	.000
	11 (30.6 %)	42 (54.5%)	
	25 (69.4%)	0	

Table-4: Regression Model for Clinical Attachment Loss, Probing Depth, Aggressive Form of Periodontitis And Bone Loss

		Odds Ratio	95% C.I. for Odds Ratio		P-value
			Lower	Upper	
CAL	normal	1			
	moderate	6.22	0.561	12.815	0.000
	severe	0.985	0.214	1.235	0.999
PD Depth	normal =3	1			
	mild >=4	3.112	0.216	6.325	0.042
	severe >=5	0.985	0.148	1.155	0.999
	Constant	0			
Severe Periodontitis	Absent	1			
	Present	3.11	0.599	5.962	0.05
Bone loss	1-3 Mild	1			
	3-4 Moderate	2.61	0.365	4.215	0.997
	>=5 severe	0.625	0.2111	1.202	0.998

Discussion:

The Covid-19 pandemic has impacted the global village in many different ways; by far two domains that had the most deleterious effect are economics and health sector. Results of this article showed much similarity with other studies conducted at same par around the globe. All clinical parameters will be discussed one by one in detail to explain the injurious effect of SARS-Cov-2 on each of the parameter.

The findings of our study reveal that after despite a major decrease in SARS-CoV-2 prevalence the quality of medical and dental health is still facing the challenges in human life. Multifactorial origin of periodontitis and bi-directional pattern of dental and systemic condition now in common understand of individuals belonging to field of health. Hence we cannot overlook the post Covid19 debilitation of periodontium and its consequent impact on general health, Therefore, it is required to focus on the management phase of complications that has occurred or yet to be seen due to decline in periodontal health (13,14,15). Oral dysbiosis presenting as a consequence to increase in periodontal indices, poor oral Hygiene status provides oral loading of pathogens that inflicts systemic complications via blood stream deputation of injurious organisms (16). Change in the normal oral flora after SARS CoV-2 interaction attributes to wide range of health issues (17- 28) that co presents periodontal complications (29–39), a list of studies that has proven the adverse impact of SARS-CoV-2 in chronic periodontitis and imbalance in systemic health (table-6).Considering periodontal status factors like probing depth, bleeding on probing, mobility, recession, furcation and bone loss increased significantly that is also in correspondence with previous literature (40). SARS-CoV-2 shares common risk factors with most chronic inflammatory diseases known to influence periodontitis severity (37), thus statistical treatment was facilitated by regression model to assess the direct impact, and found significant influence of severity of Covid19 episode on the all variables, that clinically compounds chronic periodontitis. Maximum majority during history recording informed that they quit or reduced to minimal of periodontal maintenance via brushing or other methods during Covid19 exposure as that resulted in more bleeding, pain and discomfort, consequently showed signs of more bone loss, mobility, CAL, Probing depth and mucogingival problems (table-3). Subjects who tried to manage their hygiene occasionally were also found with poor periodontal health but better in comparison to subjects who quit or left to negligible. More over subjects under the influence of Para functional habit despite improved hygiene maintenances or not irrespectively showed poor periodontal status which signifies that Para functional habits worsen the periodontal complication that were laid by Covid19 infection and hampered the immunity adversely. And as these habits are more prevalent among male gender attributing more disease presence among males as denoted by blue colour in table-2. It also implies that studies comprising of large different ethnic groups must be studies for periodontal health and covid19 exposure in the light of different types of smoke and smokeless tobacco to delineate the effect of particular confounder affecting the clinical presentation of periodontal disease. However in previous literature it was observed that smoking as Para functional habit alone and found to impose no significant outcome among the groups (14).Yet other suggested the contradicting effects as discussed in (39-42).The present study is pioneer in assessing the effect of SARS-CoV-2 individually in each subgroup as per severity with accuracy, due to steady progression of disease pattern. Besides this few limitations are also associated to the present study including observation of too many variables at the same time (which can be provided upon correspondence through author) in not much big sample size. Owing to the severe threat of transmission, active cases were not being made part of study due to which valuable data from the patients may have been lost, but advantageously periodontitis is slowly progressing condition so it has been recorded successfully

as mentioned earlier. (43-45). Further it was a uni centered study. This present study may serve as foundation for directing future researches with improvised methodology and larger sample unit to obtained unsurpassed understanding about bi-directional association between SARS-CoV-2 and periodontitis. In addition researches, including focus on interventional studies targeting on the influence of Covid-19 and Covid-19 treatment on periodontitis disease, will aid us in better understanding the causal link between the two of them. And multi-marker profiling should be carried out using randomized clinical and control trials to assess the mechanism underpinning the relation between Covid-19 and periodontitis.

Conclusion:

Hence it can be concluded that Severity of Covid19 determines the deterioration of tissue harvesting around tooth. The increased prevalence and severity of COVID19 complications may unfold clinical signs and symptoms of periodontitis like, formation of biofilms, dental plaque, calculus accumulation and gingival bleeding leading the cascade till exodontia of tooth. Further clinical trials must be executed to focus on minimizing the risk of periodontal complication resulting after Covid Exposure.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS:

Assistant Professor Dr. Tauqeer: Contributed in manuscript write up, Data collection and interpretation of the paper.

Prof. Dr. Farzeen Tanwir: Have made a substantial contribution to the conceptualization and design of the article, contributed in write up and peer review of entire manuscript of the article.

Dr. Bushra Ijazz: Contributed in manuscript write up, Data collection and interpretation of the paper.

Surg Lt Commander PN, **Dr Nabeel Hafeez:** Classified Oral & Maxillofacial Surgeon, PNS Shifa Hospital: Contributed to data collection and review of paper.

Senior Registrar Dr. Fatima Israr: Contributed in questionnaire making, proforma filling and data transferring.

Senior Registrar Dr. Saima Mazhar: Contribution in publication related correspondence of the article and data entry.

Assistant Professor Dr. Ahmed Bin Khalid: Contributed in data collection and data entry.

Senior Registrar Dr. Natasha Zaidi: Contributed in data collection and data entry.

Senior Registrar Faisal Fahim: Calculated sample size and performed statistical analysis of the article.

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References:

1.MkGasner NS, Schure RS. Periodontal Disease.In: StatPearls.hStatPearls Publishing, Treasure Island (FL); 2022. PMID: 32119477.

2. M.S. Tonetti S. Jepsen L. Jin J. Otomo-Corgel Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action J Clin Periodontol [Internet]. 44 5 2017 May 456 462 Available from http://www.ncbi.nlm.nih.gov/pubmed/28419559

3. 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.2020 Mar 2;5(4):536-44.

4.Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, evaluation, and treatment of coronavirus (COVID-19).Statpearls [internet].2022 Feb 5.

5. Bentum K, Shaddox S, Ware C, Reddy G, Abebe W, Folitse R, Martin P, Samuel T. Molecular phylogeny of coronaviruses and host receptors among domestic and close-contact animals reveals subgenome-level conservation, crossover, and divergence. BMC Veterinary Research. 2022 Dec; 18(1):1-0.

6.Gupta S, Mohindra R, Singla M, Khera S, Sahni V, Kanta P, Soni RK, Kumar A, Gauba K, Goyal K, Singh MP. The clinical association between Periodontitis and COVID-19. Clinical Oral Investigations. 2022 Feb; 26(2):1361-74.

7. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19).

8.https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---21-september-2021

9.Iranmanesh B, Khalili M, Amiri R, Zartab H, Aflatoonian M. Oral manifestations of COVID-19 disease: A review article. Dermatologic therapy. 2021 Jan; 34(1):e14578

10 Gupta S, Mohindra R, Singla M, Khera S, Sahni V, Kanta P, Soni RK, Kumar A, Gauba K, Goyal K, Singh MP. The clinical association between Periodontitis and COVID-19. Clinical Oral Investigations. 2022 Feb; 26(2):1361-74.

11.Ahmed MA, Jouhar R, Ahmed N, Adnan S, Aftab M, Zafar MS, Khurshid Z. Fear and Practice modifications among dentists to combat novel coronavirus disease (COVID-19) outbreak. International journal of environmental research and public health. 2020 Jan; 17(8):2821.

12.Rocha-Gomes G, Flecha OD, Miranda TS, Duarte PM, Shaddox LM, Galvão EL, Gonçalves PF. Impact of the coronavirus disease 2019 pandemic on periodontal practice: A questionnaire survey. Journal of Clinical Periodontology. 2021 Apr; 48(4):541-9.

13.Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. Nature reviews Disease primers. 2017 Jun 22;3(1):1-4.

14. 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). Journal of Periodontology. 2022 Apr;93(4):584-90.

15.Thakur B, Dubey P, Benitez J, et al. A systematic review and meta-analysis of geographic differences in comorbidities and associated severity and mortality among individuals with COVID-19. *Scientif Rep*. 2021; 11:8562.

16.Jeong JS, Heo SM. Oral health care in the long COVID era: Focusing on the relationship between COVID-19 and periodontal disease. 대한치과의사협회지 제. 2022;60(7):436.

17.Kapila YL. Oral health's inextricable connection to systemic health: Special populations bring to bear multimodal relationships and factors connecting periodontal disease to systemic diseases and conditions. Periodontology 2000. 2021 Oct;87(1):11-6.

18.Piekut T, Hurła M, Banaszek N, Szejn P, Dorszewska J, Kozubski W, Prendecki M. Infectious agents and Alzheimer's disease. Journal of Integrative Neuroscience. 2022 Mar 28;21(2):73.

19.Piekut T, Hurła M, Banaszek N, Szejn P, Dorszewska J, Kozubski W, Prendecki M. Infectious agents and Alzheimer's disease. Journal of Integrative Neuroscience. 2022 Mar 28;21(2):73.

20.Marouf N, Cai W, Said KN, Daas H, Diab H, Chinta VR, Hssain AA, Nicolau B, Sanz M, Tamimi F. Association between periodontitis and severity of COVID-19 infection: A case–control study. Journal of clinical periodontology. 2021 Apr 1;48(4):483-91.

21.Pfützner A, Lazzara M, Jantz J. Why do people with diabetes have a high risk for severe COVID-19 disease?—A dental hypothesis and possible prevention strategy. Journal of diabetes science and technology. 2020 Jul;14(4):769-71.

23. Pendyala GS, Kumar P, Joshi SR, Godara S, Shetty S. Periodontal Disease in Medically Compromised Patients and Its Relation with Covid-19. Journal of Evolution of Medical and Dental Sciences. 2021 May 17;10 (20):1558-61

24.Rana A, Tandon S, Kaur A, Faraz F, Agarwal K. Post Covid-19 and Dentistry Revealing the silent condition-Rhino Maxillary Mucormycosis. Biomedicine. 2021 Oct 29;41(3):690-1.

25. Said KN, Al-Momani AM, Almaseeh JA, Marouf N, Shatta A, Al-Abdulla J, Alaji S, Daas H, Tharupeedikayil SS, Chinta VR, Hssain AA. Association of periodontal therapy, with inflammatory biomarkers and complications in COVID 19 patients: a case control study. Clinical Oral Investigations. 2022 Jul 29:1-2.

26. Dembowska E, Jaroń A, Rasławska-Socha J, Gabrysz-Trybek E, Bladowska J, Gacek S, Trybek G. The Evaluation of the Periodontal Status of Hemodialysis Patients with End-Stage Renal Disease. Journal of Clinical Medicine. 2022 Feb 13;11(4):975.

27.Balaji TM, Varadarajan S, Rao UV, Raj AT, Patil S, Arakeri G, Brennan PA. Oral cancer and periodontal disease increase the risk of COVID 19? A mechanism mediated through furin and cathepsin overexpression. Medical hypotheses. 2020 Nov; 144:109936.

28. Sharma A, Chauhan S, Sharma R, Jindal V, Rajput P, Jindal V. How Chronic Periodontitis associated with Systemic Diseases increases the case fatality rate among COVID-19 Patients. Journal of Advanced Medical and Dental Sciences Research. 2020 Aug 1;8(8):71-7.

29. Lamba M. Relationship between Necrotizing Periodontitis and Novel Corona Virus: An Updated Review. Current Practice in Medical Science Vol. 5. 2022 Jul 14:84-7

30. Tamimi F, Altigani S, Sanz M. Periodontitis and coronavirus disease 2019. Periodontology 2000. 2022 Jun;89(1):207-14.

31.Jinling YU, Liuqing YA, Jingjing YA, Handan HU, Lu TA, Ying GA, Huili ZH, Jiwei RE, Zhihui LI. Research progress on oral characterization of Corona Virus Disease 2019. Journal of Prevention and Treatment for Stomatological Diseases. 2022 Jul 20;30(7):528.

32.Pagliuse B, Pedriali MB, Ito FA, Maia LP, Costa PP. Relação entre doença periodontal e COVID-19: revisão de literatura. Research, Society and Development. 2022 Aug 27;11 (11):e420111132483

33.Bhatnagar S, Goswami V, Bodhi S, Banchhor S. Viruses in Periodontology: A Short Review. International Journal. 2022 Mar;5 (2):629

34.Chandak V, Madhu PP, Chhabra KG, Reche A, Tijare R, Agrawal S. Impact of COVID-19 on Oral Health. Journal of Pharmaceutical Research International. 2021:308-13.

35.Ligade SS, Shah YS. Hypothesis: Relationship between Coronavirus Disease-19 and Periodontal status. Journal: Journal of Global Oral Health. 2021:48-55.

36.Campisi G, Bizzoca ME, Lo Muzio L. COVID-19 and periodontitis: reflecting on a possible association. Head & Face Medicine. 2021 Dec;17(1):1-6.

37.Gupta S, Mohindra R, Singla M, Khera S, Sahni V, Kanta P, Soni RK, Kumar A, Gauba K, Goyal K, Singh MP. The clinical association between Periodontitis and COVID-19. Clinical Oral Investigations. 2022 Feb;26(2):1361-74

38.Larvin H, Wilmott S, Wu J, Kang J. The impact of periodontal disease on hospital admission and mortality during COVID-19 pandemic. Frontiers in medicine. 2020 Nov 23;7:604980..

39.Jagannathan R, Balaji TM, Rajendran S, Prabhu VR, Varadarajan S, Ajitkumar S. Chronic Periodontal Disease and COVID–19 Complications: Mechanistic Links Through Increase of CD14+ CD16+ Monocytes Blood Count. Dental Hypotheses. 2021 Jan 1;12(1):39.

40.Fabri GM. Potential link between COVID-19 and periodontitis: cytokine storm, immunosuppression, and dysbiosis. Oral Health and Dental Management. 2020;20(1):1-5.

41. Haffajee AD, Socransky SS. Relationship of cigarette smoking to attachment level profiles. J Clin Periodontol. 2001;28:283-295.

42. Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: findings from NHANES III. national healthand nutrition examination survey. J Periodontol. 2000;71:743-751.

43- Mishra S, Gupta V, Rahman W, Gazala MP, Anil S. Association between Periodontitis and COVID-19 Based on Severity Scores of HRCT Chest Scans. Dentistry Journal. 2022 Jun 10;10(6):106.

44- Gardelis P, Zekeridou A, Suh N, Le Terrier C, Stavropoulos A, Giannopoulou C. A pilot clinical and radiographic study on the association between periodontitis and serious COVID-19 infection. Clinical and Experimental Dental Research. 2022 Aug 6.

45- Di Spirito F, Iandolo A, Amato A, Caggiano M, Raimondo A, Lembo S, Martina S. Prevalence, Features and Degree of Association of Oral Lesions in COVID-19: A Systematic Review of Systematic Reviews. International Journal of Environmental Research and Public Health. 2022 Jun 18;19(12):748