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Association Between Periodontitis And Covid-19 Infection, A Double-Edged Sword? - A Cross-Sectional Study

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ABSTRACT

INTRODUCTION:

Patients with severe COVID-19 usually present an exacerbated immune response, characterized by excessive levels of proinflammatory cytokines and widespread tissue damage; the so-called cytokine storm syndrome. Epidemiologic, experimental, and interventional studies have shown that periodontitis also impacts systemic health. COVID-19 complications are caused by a severe inflammatory reaction that shares common signals with periodontitis. Thus, this study was designed to investigate a possible association between COVID-19 infection, and the presence, and severity of periodontitis.

METHODOLOGY:

300 Patients visiting a Dental Hospital were enrolled during a period of one year. All patients above the age of 18 years were included. Patients were asked about their history of COVID Infection if they were hospitalized, their vaccination status, and their history of other co-morbidities. A complete intraoral examination was done to assess the patient's periodontal status. Data were collected and statistical analysis was performed.

RESULTS:

The study was conducted over the course of an entire year. A total of 167 males (55.48%) and 134 females (44.54%) were included in the study. Patients were classified based on their periodontal status as mild, moderate, and severe periodontitis. 69.10% of individuals were from the age of 17-44 years and 30.9% were 45 years and above. Out of the 302 patients included in the study, 71 (23.59%) were exposed to COVID-19 infection. 71.83% of COVID-19-infected patients had Moderate Periodontitis. 19% of total number of patients had co-morbidities. 12.7% and 2.8% of COVID-19-infected patients were Diabetic and Hypertensive respectively.

CONCLUSION:

This study concludes that there is a possible association between COVID-19 infection and Periodontitis. Future rese[1]arch, including interventional studies, focused on the influence of periodontitis on COVID-19 infection, would help better understand the connections between them.

Keywords *COVID-19 infection, Periodontitis, Co-morbid conditions.*

INTRODUCTION

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On December 31, 2019, Wuhan, China, declared the first case of coronavirus illness 2019 (COVID-19). On March 13, 2020, the World Health Organisation formally declared COVID-19 to be a pandemic.[1] The condition is brought on by 2019 nCoV, a new coronavirus that originates from human airway epithelial cells.[2] The angiotensin-converting enzyme II (ACE 2) is probably the 2019 nCoV virus's cell receptor, like the CoV virus that triggers severe acute respiratory syndrome. The tongue's epithelial cells have a high concentration of ACE 2 receptors, which also exist in other areas of the oral mucosa. The findings of the investigations performed clarified the primary cause of the oral cavity's potentially high COVID-19 viral susceptibility risk. As a result, the cells that express ACE 2 can act as target cells, are more likely to become infected with 2019 nCoV, and provide evidence for future preventive measures in daily life and dentistry practice.[2] Novel recommendations are put forth daily with methods for the management of potentially infected patients and limiting the spread of the disease, even though research is still being done worldwide to better understand the dynamics of transmission and the range of clinical illness and presentation.

According to the World Health Organisation, SARS-CoV-2 is a likely airborne virus that is spread through close contact with individuals who are asymptomatic, pre-symptomatic, or symptomatic as a consequence of exposure to infected droplets and aerosols [3]. Although oral activities like speaking, breathing, coughing, sneezing, and even singing can result in the transmission of Covid-19, the nasal-lung axis has attracted the majority of attention[4–9].

The virus infects human cells via the angiotensin-converting enzyme 2 (ACE2) receptor, according to recent research and scRNA-seq data analysis. The study found the organs that are at risk for and are more susceptible to SARS-CoV-2 infection (e.g., the lung; Zou et al. 2020). Thus, the cells with increased ACE2 receptor distribution and expression may act as host cells for the coronavirus and trigger an inflammatory response in tissues and organs that are associated with them, such as the salivary glands and the mucosa of the tongue (Wang et al. 2020; Xu, Li, et al. 2020; Xu, Zhong, et al. 2020). The SARS-CoV-2 virus's interaction with ACE2 receptors can also reduce taste buds' sensitivity, which could lead to or result in abnormal gustatory reactions (Mariz et al. 2020). The available data is yet to support the development of efficient and reliable pharmacologic therapy and management against COVID-19, and the potential therapies are associated with an array of negative side effects (Godinho et al. 2020; National Centre for Biotechnology Information 2020). Therefore, the purpose of this study was to look into any potential links between COVID-19 infection and the presence and extent of periodontitis.

MATERIALS AND METHODS:

Study Population

After Ethical Committee approval from BIHER (Bharath Institute of Higher Education and Research) University, 301 Patients of the South Indian Population visiting the Outpatient Department of Sree Balaji Dental College and Hospitals, Chennai were included in the study. Each patient was given a unique identification number for dental record maintenance. The study examined all patients who were over the age of eighteen years. Patients under the age of 18 were restricted from taking part in the study as they had a lower risk of developing COVID-19 problems and Periodontitis.

Study Design

The study was a cross-sectional study that was carried out after approval from Ethical Committee and informed consent obtained from the patient. The variables that were recorded are the History of COVID-19 infection, and whether they were hospitalised or not. In cases of Hospitalization, the duration or the number of days they were hospitalized and if they were on any ventilatory support. Patients were also asked about their vaccination status, that is the name of the vaccine and the number of doses.

A thorough medical history was obtained from the patients for the presence of any co-morbidities. The periodontal status of the patient was assessed by a complete intra-oral examination, intra-oral periapical radiographs or orthopantomograms were taken wherever necessary and the patients were classified as mild, moderate, and severe periodontitis.

Demographic information such as sex and age and other relevant risk factors associated with COVID-19 complications, such as smoking habits, asthma, other chronic respiratory diseases, chronic heart disease, diabetes, dermatitis, chronic diseases of the liver, autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus or psoriasis), organ transplant, peptic ulcers, immunosuppressive conditions, cancer, chronic kidney disease, hypertension, cerebrovascular accident, peptic ulcer, and deep vein thrombosis were obtained.

Sample size calculation and data analysis:

A prior sample size calculation for logistic regression was done to determine the sample size of the study. A significance level of α=0.05, a minimum sample size calculation of n = 300 was determined to achieve an 80% power. All models were adjusted for confounders such as age, sex, smoking, diabetes mellitus, and various other comorbidities. Age was used as a continuous variable; the remaining variables were categorical variables. Analysis of additional sensitivity was performed by data stratification according to age groups, diabetes, smoking, and other co-morbidities. Data were assessed and compared. Statistical analyses were performed using SPSS, version 20.0.

RESULTS:

A total of 167 males (55.48%) and 134 females (44.54%) were included in the study. Patients were classified based on their periodontal status as mild, moderate, and severe periodontitis. 208 patients (69.1%) of the individuals were between the age group of 18-44 years and 93 patients (30.9%) of the total number of patients were 45 years and above. 166 individuals (55.15%) were vaccinated and 135 (44.85%) individuals were non-vaccinated at the time of the study period. 126 (41.86%) of the total vaccinated individuals were vaccinated by the Covishield vaccine. 38 (12.62%) individuals had Covaxin and 2 (0.66%) individuals had Pfizer vaccine. 113 (37.54%) individuals were only one dose vaccinated whereas, 53 (17.61%) individuals were vaccinated with two doses.

	Covid Exposure Status(Yes/No)					
	Yes			No		
Periodontal Status	N	Row %	Col. %	N	Row %	Col. %
Mild	17	11.49	23.94	131	88.51	57.21
Moderate	51	37.50	71.83	85	62.50	37.12
Severe	3	18.75	4.23	13	81.25	5.68
Pearson Chi-Square Value: 26.685; P < .001						

Table 1: Shows the COVID-19 exposure status of the individuals included in the study.

Periodontal Status Vs. Covid Exposure Status

Periodontal Status		Covid Exposure Status(Yes/No)		Total
		Yes	No	
Mild	N	17	131	148
	Row %	11.49	88.51	100.00
	Col %	23.94	57.21	49.33
Moderate	N	51	85	136
	Row %	37.50	62.50	100.00
	Col %	71.83	37.12	45.33
Severe	N	3	13	16
	Row %	18.75	81.25	100.00
	Col %	4.23	5.68	5.33
Total	N	71	229	300
	Row %	23.67	76.33	100.00
	Col %	100.00	100.00	100.00
Pearson Chi-Square Value: 27.774; P < .001				

Table 2: Shows the Periodontal status of the COVID-19-exposed individuals.

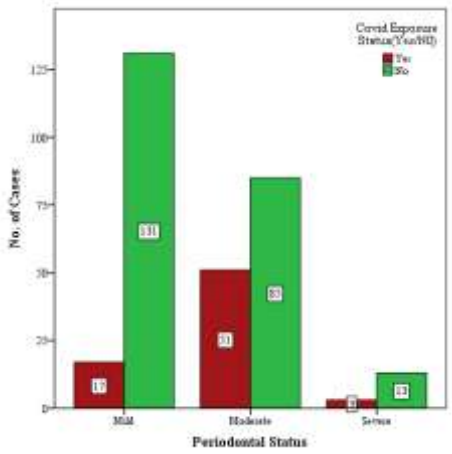

Fig 1: Shows the Periodontal status of the COVID-19-exposed individuals.

Out of the 302 patients included in the study, 71 (23.59%) were exposed to COVID-19 infection. 71.83% of COVID-19-infected patients had Moderate Periodontitis. 23.94% of the COVID-exposed individuals had Mild Periodontitis. 4.23% of COVID-infected individuals had Severe Periodontitis.

Periodontal Status Vs. Age

Periodontal Status		Age		Total
		17 - 44	≥ 45 Years	
Mild	N	133	15	148
	Row %	89.86	10.14	100.00
	Col %	64.25	16.13	49.33
Moderate	N	68	68	136
	Row %	50.00	50.00	100.00
	Col %	32.85	73.12	45.33
Severe	N	6	10	16
	Row %	37.50	62.50	100.00
	Col %	2.90	10.75	5.33
Total	N	207	93	300
	Row %	69.00	31.00	100.00
	Col %	100.00	100.00	100.00
Pearson Chi-Square Value: 60.497; P < .001				

Table 3: Shows Periodontal status of the patients Vs the age of the patients

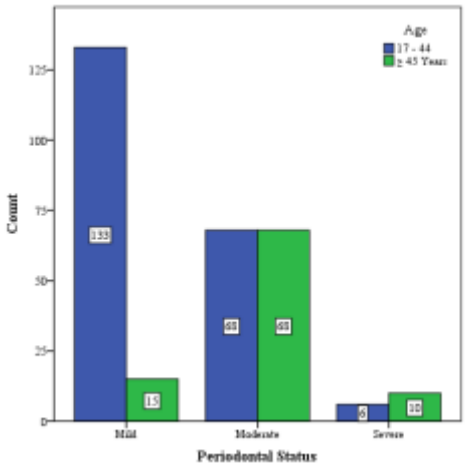

Fig 2: Shows Periodontal status of the patients Vs the age of the patients

In the age group 17-44 years, 64.25 % individuals had Mild Periodontitis, 32.85% individuals had Moderate Periodontitis and 2.90% had Severe Periodontitis. 16.13%, 73.12% and 10.75% had Mild, Moderate, and Severe Periodontitis respectively were above the age of 45 years.

Periodontal Status Vs. Gender

Periodontal Status		Gender		Total
		Male	Female	
Mild	N	78	70	148
	Row %	52.70	47.30	100.00
	Col %	46.71	52.63	49.33
Moderate	N	78	58	136
	Row %	57.35	42.65	100.00
	Col %	46.71	43.61	45.33
Severe	N	11	5	16
	Row %	68.75	31.25	100.00
	Col %	6.59	3.76	5.33
Total	N	167	133	300
	Row %	55.67	44.33	100.00
	Col %	100.00	100.00	100.00
Pearson Chi-Square Value: 1.793; P = .408				

Table 4: Shows Periodontal Status of the individuals vs Gender

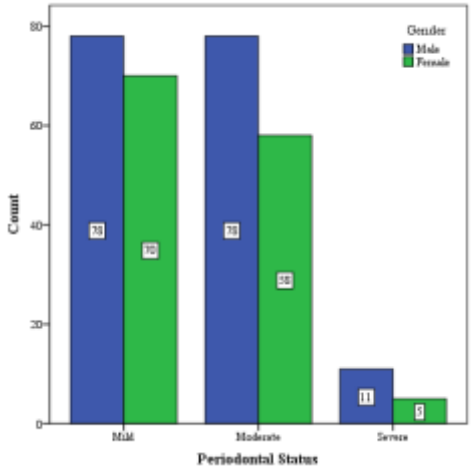

Fig 3: Shows Periodontal Status of the individuals vs Gender

Table 4 shows that there is no significant difference between the Periodontal status of the patient vs the Gender of the patient. However, Periodontitis was more prevalent in Males than in females that were included in the study.

Co-morbid conditions Vs. Periodontal Status (Combined)

Co-morbid conditions		Periodontal Status			Total
		Mild	Moderate	Severe	
NRH	Count	142	99	4	245
	Row %	57.96	40.41	1.63	100.00
	Col %	96.60	72.79	25.00	81.94
Diabetic	Count	1	19	7	27
	Row %	3.70	70.37	25.93	100.00
	Col %	.68	13.97	43.75	9.03
Diabetic& Hypertension	Count	1	5	2	8
	Row %	12.50	62.50	25.00	100.00
	Col %	.68	3.68	12.50	2.68
Hypertensive	Count	2	3	2	7
	Row %	28.57	42.86	28.57	100.00
	Col %	1.36	2.21	12.50	2.34
Thyroid	Count	0	3	0	3
	Row %	.00	100.00	.00	100.00
	Col %	.00	2.21	.00	1.00
Diabetic & Thyroid	Count	0	1	1	2
	Row %	.00	50.00	50.00	100.00
	Col %	.00	.74	6.25	.67
Others	Count	1	6	0	7
	Row %	14.29	85.71	.00	100.00
	Col %	.68	4.41	.00	2.34
Total	Count	147	136	16	299
	Row %	49.16	45.48	5.35	100.00
	Col %	100.00	100.00	100.00	100.00

Table 5: Shows the Periodontal status of the patients with Co-morbidities.

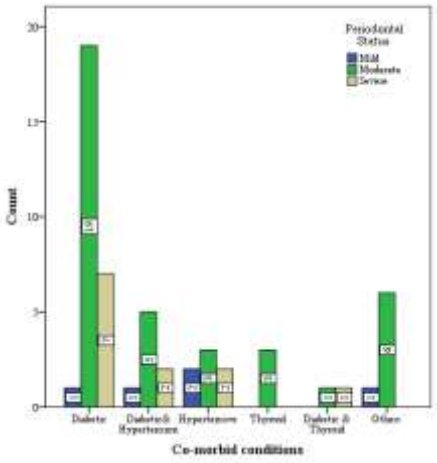

Fig 4: Shows the Periodontal status of the patients with Co-morbidities.

Co-morbid conditions of Covid Cases		
	Frequency	Percent
NRH	59	83.1
Diabetic	8	11.3
Diabetic& Hypertension	1	1.4
Hypertensive	1	1.4
Thyroid	2	2.8
Total	71	100.0

Table 6: Shows the Presence of co-morbidities in patients with a history of COVID infection

19% of total number of patients had co-morbidities. 12.7% and 2.8% of COVID-19-infected patients were Diabetic and Hypertensive respectively. Results also show that Patients with a history of COVID and who were hospitalized have Severe Periodontitis.

DISCUSSION:

This study identified that the risk of COVID-19 complications was significantly higher among patients with moderate-to-Severe periodontitis compared to those with mild or no periodontitis. Periodontitis shares common risk factors with most chronic inflammatory diseases known to influence COVID-19 severity [10-11]; Periodontitis has been shown to affect systemic health in multiple studies [12] and has been independently associated with increased risk of most chronic NCDs [13], in particular, cardiovascular diseases[14-16]; diabetes[17-19]; hypertension [20]; chronic renal disease [21], pneumonia [22] and cancer [23]. A recent systematic review of 57 studies with about 5.71 million participants reported the association of periodontitis with increased risk of mortality, specifically, in association with CVD, cancer, CHD, and cerebrovascular diseases [24]. These associations have been

explained, by some shared genetic and environmental risk factors, and through some common chronic inflammatory pathways [25].

Several hypotheses and mechanisms may explain the strong associations observed between periodontitis and COVID-19 infection and severity. By enhancing the expression of angiotensin-converting enzyme 2, a receptor for SARS-CoV-2, and inflammatory cytokines in the lower respiratory tract, Takahashi et al. hypothesized that aspiration of periodontopathic bacteria may exacerbate COVID-19 infection. [26]. Also, it was suggested that periodontopathic bacteria might enhance SARS-CoV- 2 virulence by cleaving its S glycoproteins [26,27] and that the oral cavity and especially periodontal pockets could act as a viral reservoir [28-32]. Gupta et al indicated that Neutrophil Extracellular Trap production is involved in the pathogenesis of both diseases [33], and Sahni et al suggested that the strong Th17 response in severe periodontitis could exacerbate the cytokine storm in COVID-19 [33,34]. During this pandemic, all of these hypothesized connections could possibly predict an increased prevalence of periodontal lesions, particularly necrotizing periodontal disease (NPD). [35].

Successful treatment of periodontitis has been shown to improve serum markers of systemic inflammation (CRP, IL-6) [36], as well as systemic metabolic control [37]. If a hypothesis can be established as a link between periodontitis and increased rates of adverse outcomes in COVID-19 patients, then establishing and maintaining periodontal/oral health may become an important part of the care of these patients.

Future studies that investigate the effects of Periodontitis and Periodontal therapies on COVID-19 infections, particularly interventional studies, will help us comprehend the causes of these infections. Furthermore, it is important to understand the mechanisms underpinning the relationship between periodontitis and COVID-19 infection and complications is a rising area of research.

CONCLUSION

This study concludes that there is a possible association between COVID-19 infection and Periodontitis. Future research, including interventional studies, focused on the influence of periodontitis on COVID-19 infection, would help better understand the connections between them.

COMPETING INTERESTS

The authors have declared that no competing interest exists.

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