Original Article

Assessment of correlation of COVID-19 infection and periodontitis- A comparative study

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Abstract

Background: Periodontal disease constitutes a group of diseases involving inflammatory aspects of the host caused by several microbial agents that affect periodontal tissues and could have systemic implications. **Objective:** The present study was conducted to assess the correlation of COVID-19 infection and severity of periodontitis in subjects who has mild form of the disease as compared to subjects having moderate form of the disease. **Materials and Methods:** The study included 116 subjects suffering from COVID-19 that were equally divided into two groups, each based on a convenient sampling methodology. Group I had a moderate form of COVID that required hospitalization and Group II had a mild form of COVID and were treated at home. The stage of periodontal disease was assessed in both groups. Also, laboratory parameters such as level of C-reactive protein (CRP), white blood cell (WBC), D-dimer, vitamin D, and lymphocytes were also assessed. Statistical analysis was done using Chi-square and multiple logistic regression analysis. **Results:** More than 75% of subjects in both groups were non-smokers. Subjects having more than one comorbid condition were more in number in Group I (51.7%) as compared to Group II (24%). Severe periodontitis (stages 2–4) was found in 81% of subjects in Group I and 46.2% of subjects in Group II [Figure 1]. The odds of getting severe periodontal disease were 6.32 times more in subjects belonging to Group I as compared to Group II. Subjects having more than one comorbid condition were 4.43 times at risk of severe periodontitis as compared to subjects with no co-morbidity **Conclusion:** Severe form of periodontal disease was associated with moderate-to-severe COVID-19 infection and levels of lymphocytes, WBCs, and CRP were elevated in subjects belonging to Group I.

Keywords: Comorbidity, COVID-19 infection, periodontitis, risk

Introduction

COVID-19 is a recent deadly viral disease that has claimed millions of lives globally since December 2019 with deadly strains being reported across various countries. SARS-CoV-2 is another name for this disease as it is responsible for the severe acute respiratory syndrome.[1] World Health Organization (WHO) declared this as pandemic and there have been 211,730,035 confirmed cases of COVID-19, including 4,430,697 deaths to date.[2] In India, 4,34,756 have been reported so far and approximately 30,000 cases are still being reported daily from various parts of the country.[2] The disease is characterized by flu-like symptoms such as fever,

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running nose, headache, sore throat, and sneezing.[3] Loss of taste and smell and diarrhea are evident in a few cases. Most of the patients recover at home, whereas a few require hospitalization. Oxygen support becomes mandatory in serious patients and survival becomes difficult in those who develop pneumonia with extensive lung involvement. The patient may also die from multi-organ involvement due to sepsis or septic shock.[4]

Patients possess exacerbated immune response with increase blood levels of pro-inflammatory cytokines in moderate-to-severe COVID-19 infection. They may also encounter extensive tissue damage, hence called cytokine storm syndrome.[5] There is an elevated level of C-reactive protein (CRP), D-dimer, interleukin-6, and ferritin. Patients with co-morbidities such as those with hypertension, diabetes, obesity, geriatric and cardio-vascular diseases (CVDs) are potential to develop the disease more severely.[6]

COVID-19 mainly spreads through the inhalation of respiratory droplets, thus coughing and sneezing is the leading cause of disease spread. The occurrence of lesions in the oral cavity is controversial.[7] The majority of the people with COVID-19 illness present with a mild or uncomplicated illness that can be managed at the primary care level and there will be high demand for primary care services during periods of increased transmission. Primary care physicians can render significant help by differentiating patients with respiratory symptoms from those with COVID-19 to come to an early diagnosis and reduce the demand for hospital services.[8]

As reported, patients suffering from COVID-19 may show signs of mild-to-moderate periodontitis and 10% of patients may suffer from severe periodontitis.[9] Destruction of attachment level and loss of teeth are common findings. Patients exhibit a high serum level of chemical mediators such as tumor necrosis factor (TNF)-α, interleukins-4, 6, 1β, and 10, CRP, and ferritin.[10] Therefore, the present study was conducted to assess the correlation of COVID-19 infection and severity of periodontitis in subjects who had a mild form of the disease as compared to subjects having a moderate form of the disease and requiring hospitalization.

Materials and Methods

Ethical clearance and consent

Ethical clearance to conduct the present study was obtained from concerned health authorities. Participation in the study was voluntary and only those subjects were enrolled in the study who gave written consent (informed consent). Pregnant ladies, patients less than 18 years old, and those unwilling or not in a position to give written informed consent were excluded from the study. Moreover, any type of information disclosing the identity of the subjects was kept confidential.

Study population and sample

The study was conducted in March 2021 in the COVID ward of a hospital in Punjab, India, and a residential area adjoining the hospital (in close proximity). The COVID status of the patients was confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) testing in the hospital. The present study employed a convenient sampling methodology as the study was conducted in a dedicated COVID ward of the hospital and residential area and required healthcare workers to be in a close proximity of the patient to conduct the oral examination. The present study comprised 58 COVID-19-positive patients (both male and female) (Group I) who were recovering from COVID-19 in the COVID ward of the hospital (a moderate form of COVID-19) but did not require intensive care unit (ICU) admission or assisted ventilation. Subjects in Group II comprised 58 patients who were recovering at home only (a mild form of COVID-19) and did not require hospitalization.

Examiner calibration and Clinical examination

Demographic information of patients such as name, age, and gender was recorded and kept confidential. The principal investigator was calibrated in the dental department of the hospital for conducting the periodontal health examination. Inter-examiner reliability was found to be 0.87 using Cohen kappa for categorical variables. A single examiner with a recording assistant conducted an oral examination of all subjects in the hospital as well as subjects who were recovering at home in the residential area adjoining the hospital. All COVID protocols were followed while conducting the examinations. After completion of examinations, RT-PCR testing of the examiner and the recording assistant was conducted to assess their COVID status. Oral examination comprised assessment of periodontitis, which was bone loss involving multiple teeth in the same arch. A portable digital Radio-Visio Graph (RVG) (Schick) was used to assess bone status. Bone loss in the interdental area was detected in posterior teeth using the cementoenamel junction (CEJ) line and length of the tooth root.

Stages 0–1 were indicative of healthy or initial periodontitis, which was detected as less than 2 mm bone loss recorded on bitewing radiographs and bone loss <15% (coronal third root length) on digital radiographs. Stages 2–4, periodontitis detected as >2 mm bone loss on bitewing radiographs and >15% bone loss (coronal third root length) on digital radiographs.[11] Assessment of smoking status, diabetes, comorbidities, body mass index (BMI) was done. The level of CRP, WBC, D-dimer, vitamin D, and lymphocytes was also assessed.

Statistical analysis

Descriptive and inferential statistical analyses were carried out in the present study Results of the study were clubbed and entered in an MS excel sheet. Data obtained from responses to the questionnaire were assessed using SPSS statistical package (SPSS, version 21.0, Chicago, IL, USA). Chi-square test was used to do comparison within groups. Multiple logistic regression analysis was also performed to obtain odds ratio. *P* value was regarded significant if it was found below 0.05.

Results

The present study enrolled 58 subjects in both groups (Group I and Group II). Demographic characteristics of the study subjects are depicted in [Table 1]. The majority of the subjects in both groups were males (65.5% in Group I and 55.1% in Group II). More subjects in Group I were in the age group of 60 years and above (39.6%) as compared to Group II in which the majority of the subjects belonged to the age group of 41 to 60 years (36.2%). More than 75% of subjects in both groups were non-smokers. Subjects having more than one comorbid condition were more in number in Group I (51.7%) as compared to Group II (24%). A vast majority of subjects in Group I had BMI above the normal range (81%). The findings were statistically significant ($P < 0.05$) among all the demographic parameters, except in the case of BMI.

Severe periodontitis (stages 2–4) was found in 81% of subjects in Group I and 46.2% of subjects in Group II [Figure 1]. The odds of getting severe periodontal disease were 6.32 times more in subjects belonging to Group I as compared to Group II. Also, subjects who were smokers were 3.32 times more at risk of getting severe periodontitis as compared to non-smokers. Moreover, subjects having more than one comorbid condition were 4.43 times at risk of severe periodontitis as compared to subjects with no co-morbidity [Table 2]. Assessment of laboratory parameters such as the levels of CRP, WBC, D-dimer, vitamin D, and lymphocytes according to the severity of periodontitis in both groups is shown in [Table 3].

Discussion

In this era, the emergence of COVID-19 has raised the alarm. A large amount of literature has already been published and numerous researches are still going on to study the exact nature of the virus as it has started mutating.[12,13] As this is a new virus to the already existing coronavirus family, lots of assumptions regarding disease progression and management have been made. Considering this, various studies have been conducted assessing

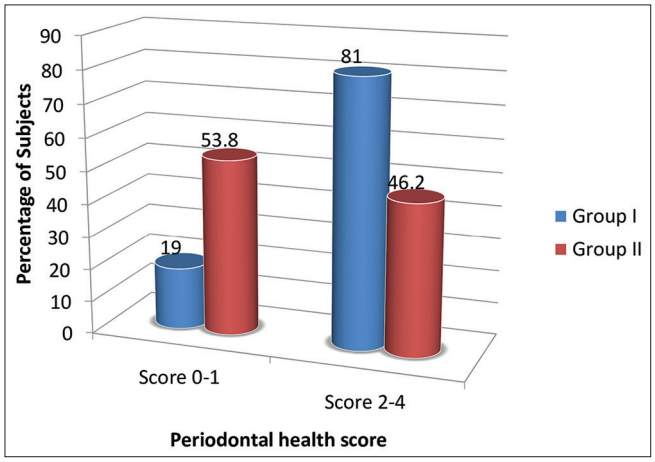

Figure 1: Periodontal disease status among subjects in both the groups

Table 1: Demographic characteristics of study population

Parameters	Group I	Group II	*P*
Gender			
Male	38 (65.5%)	32 (55.1%)	0.02*
Female	20 (34.4%)	26 (44.8%)	
Age (in y)			
18-40	16 (27.5%)	18 (31%)	0.01*
41-60	19 (32.7%)	21 (36.2%)	
60 and above	23 (39.6%)	19 (32.7%)	
Smoking			
Yes	12 (20.6%)	13 (23%)	0.01*
No	46 (79.3%)	45 (77%)	
Co-morbidity			
None	8 (13.7%)	26 (46.1%)	0.04*
1	20 (34.4%)	18 (30.7%)	
>1	30 (51.7%)	14 (24%)	
BMI			
Normal	11 (19%)	18 (31%)	0.72*
Overweight/Obese	47 (81%)	40 (69%)	

*P<0.05 significant, Chi-square test, BMI: body mass index

Table 2: Multiple logistic regression analysis on severity of periodontal disease (Scores 2-4)

Variable	OR (odds ratio)	95% CI	*P*
Groups			
Group I	6.32	2.80-14.62	0.024*
Group II	1	Ref	
Age-group			
18-40	1	Ref	0.045*
41-60	2.45	1.34-6.78	
60 and above	4.45	2.34-8.76	
Smoking			
Yes	3.32	1.67-6.34	0.014*
No	1	Ref	
Co-morbid condition			
None	1	Ref	0.028*
1	2.45	1.23-5.56	
>1	4.43	2.56-9.45	

OR: odds ratio; CI: confidence interval, Ref: reference. *Statistically significant

Table 3: Assessment of laboratory parameters in both groups

Periodontal condition	Variables	Group I	Group II	*P*
Stage 0-1	HbA1c (%)	6.8	5.1	0.05*
	Vit-D (ng/mL)	24.2	18.2	0.14
	D-Dimer (mg/L)	0.52	0.43	0.32
	Lymphocyte (10^3/μL)	1.86	1.71	0.04*
	WBC (10^3/μL)	5.9	5.1	0.07
	CRP (mg/L)	7.8	4.5	0.02*
Stage 2-4	HbA1c (%)	6.9	5.3	0.04*
	Vit-D (ng/mL)	24.6	18.0	0.16
	D-Dimer (mg/L)	0.58	0.41	0.34
	Lymphocyte (10^3/μL)	1.90	1.52	0.03*
	WBC (10^3/μL)	6.2	5.0	0.02*
	CRP (mg/L)	7.9	4.2	0.01*

*P<0.05 significant; HbA1c: glycosylated hemoglobin; Vit D: vitamin D; WBC: white blood cell; CRP: C-reactive protein

the role of medical status and systemic diseases in disease severity.[14] Periodontitis is a disease related to periodontium breakdown and subsequently loss of teeth. It is also evident in the literature that periodontitis has a deleterious effect on systemic health. It is also linked to diabetes, cardiovascular diseases (CVDs), and premature deaths.[15,16]

Most co-morbidities and risk factors reported in patients with severe COVID-19, also aggravate the development of periodontal disease. It is seen that smoking, faulty diet, diabetes, stress, genetics, and SE status are among risk factors for COVID-19 infection. Correction of periodontitis improves glycemic status in type 2 diabetes patients and metabolic syndrome.[17] The reports of the present study also found that subjects having more than one comorbid condition were 4.43 times at the risk of severe periodontitis as compared to subjects with no co-morbidity.

Studies have found that periodontopathic bacteria could play a direct role in the mechanism of entry of SARS-CoV-2 by cleaving the S-protein, and the cytokines produced during periodontitis could add to the cytokine storm found in the severe forms of COVID-19.[18] The findings of our study also point out that odds of getting severe periodontal disease were 6.32 times more in subjects belonging to Group I as compared to Group II. Marouf *et al.*[19] conducted a study on 568 patients and found that periodontitis had a significant association with COVID-19 complications such as death, ICU admission, and need for assisted ventilation. Results of this study expressed that WBC levels, D-dimer, and CRP content were significantly higher in subjects belonging to Group I as compared to Group II.

We observed in our study that patients suffering from a moderate form of COVID-19 had severe periodontal disease. Takahashi *et al.*[20] proposed that the aspiration of microorganism causing periodontitis may exacerbate COVID-19 infection by persuading the appearance of Angiotensin-Converting Enzyme (ACE) 2 and inflammatory cytokines in Lower Respiratory Tract (LRT). It is further assumed that bacteria may increase the infectivity of SARS-CoV-2 by breaking S glycoproteins. The presence of periodontal pockets may act as a reservoir for the virus.

It was observed in our study that subjects belonging to 60 and above years of age had higher odds of getting the severe periodontal disease as compared to younger ones, which is also an established fact.[21] This is because older people suffer from other risk factors such as poor oral hygiene habits, presence of chronic diseases, use of medications, smoking, or lack of timely dental treatment, which can alter gingival microbiota. Similarly, people of the 60 and higher age group are more prone to develop severe COVID-19 illness because of multimorbidity and lower immunity level, which allows rapid multiplication of the virus in the body.

The findings of the present study reveal that all the laboratory parameters such as levels of CRP, WBC, D-dimer, vitamin D, and lymphocytes are higher in subjects belonging to Group I as compared to Group II and Group I subjects who experienced a severe form of periodontal disease. It has been shown that the management of severe periodontitis reversely improves the levels of CRP and interleukins in the body. According to some study reports, there was an improvement in biomarkers such as IL-6, IL-1 β, CRP, and fibrinogen linked with atherosclerosis after periodontitis is treated.[22]

Primary care and oral health professionals can play an important role during a public health emergency such as COVID-19, primarily by maintaining essential health services and secondly by responding to the outbreak.

- Laboratory parameters such as levels of CRP, WBC, D-dimer, vitamin D, and lymphocytes can be easily checked and observed by a primary care physician and if they are not highly raised, primary care physician can advise patients for home care and thus not put extra pressure on already burdened health services.
- A response built around primary care has also been a more cost-effective measure. Primary care physicians can use telemedicine to deliver care during COVID-19 to people who do not have access to family clinics during a lockdown.
- Primary care physicians and oral health professionals residing in a particular area can engage in voluntary service for residents in community housing by supporting each other in diagnosing COVID-19 cases and providing home care to mild and uncomplicated cases.
- Supporting provision of vaccination services in their areas and removing any misconceptions from the minds of people regarding the vaccine.
- Ensuring availability of pulse-oximeters for screening and severity monitoring, operationalizing a patient's referral to a higher level facility when needed.
- Vulnerable groups such as infants, children, and people with co-morbidities can be given high priority and managed at the primary care level.

Conclusion

Our study found that chances of COVID-19 infection can increase with periodontitis as subjects in Group I had severe periodontitis. Moreover, the level of lymphocytes, WBCs, and CRP was also elevated in subjects suffering from moderate COVID-19 as compared to subjects with milder disease. Knowing periodontal disease is associated with moderate-to-severe COVID-19 could help identify risk groups and establish pertinent recommendations.

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Conflicts of interest

There are no conflicts of interest.

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