Original Article

Assessment of Periodontal Status in Patients with Chronic Obstructive Pulmonary Diseases: An Epidemiological Study

Anjaneya Mahapatra[1]*, K. Anil Kumar[1], N. Anwesh Reddy[1], Priyajeet Jena[2], Sheema Tasneem[1], G. Shivashankar[1]

[1]Department of Periodontology, Sree Sai Dental College and Research Institute, Srikakulam, Andhra Pradesh, India.
[2]Department of Critical Medicine and Pulmonology, MKCG College and Hospital, Berhampur, Odisha, India.

Abstract

Although poor dental health has been linked to the development of chronic obstructive pulmonary disease (COPD), few research have looked into the relationship between oral health and COPD exacerbations. We wanted to see if poor oral health is linked to COPD flare-ups and/or poor respiratory health. As we all know, COPD is a common preventable and treatable respiratory disease characterized by persistent airflow limitation that is usually progressive, as well as an increased chronic inflammatory response in the airways and lungs to noxious particles or gases. Adults with poor dental hygiene are more likely to develop periodontitis. Smoking is a common risk factor for both periodontitis and COPD. In the pathophysiology of respiratory infections, oral pathogens such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* play a role. As a result, the goal of this study is to determine the periodontal health of COPD patients.

Keywords: Chronic obstructive pulmonary disease, Epidemiology, Oral hygiene index, Periodontitis.

Introduction

Periodontitis is a chronic inflammatory and destructive disease which is characterized by loss of bone structure and the periodontal ligament which accompanies the loss of attachment of the periodontium from the tooth apparatus. Periodontitis has a couple of associated risk factors including deleterious habits such as smoking, alcohol consumption, prolonged usage of smokeless tobacco, and poor maintenance of oral hygiene along with the systemic disorders.[1-5] It was lately when the association of systemic diseases with periodontitis was realized and established with due evidence. Often the oral cavity has been depicted as the entrance of the entire body; hence, copious diseases have direct clinical presentations that can be detected orally. The bidirectional nature of the systemic diseases with the occurrence of clinical symptoms has been proven through literature reports since time immemorial. Periodontitis involves both a local and systemic host inflammatory response.

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction resulting from chronic bronchitis or emphysema. Bronchial mucous glands enlarge and an inflammatory process occurs in which neutrophils and mononuclear inflammatory cells accumulate within the lung tissue. Globally, the prevalence of the disease as per 2020 guidelines was 13.1% (95% CI =10.5–14.6) among individuals <40 years of age. The European states have reported the prevalence to be 12.4% while the Asian countries report the prevalence to be 13.4%. The disease has a mortality rate of 3 million deaths annually as reported through annual global reports.[6,7]

COPD shares a similar pathogenic mechanism with periodontal disease. In both diseases, a host inflammatory response is mounted in response to the chronic challenge by bacteria in periodontal disease by factors such as cigarette smoke in COPD. The resulting neutrophil influx leads to the release of oxidative and hydrolytic enzymes that cause tissue destruction directly. Recruitment of monocytes and macrophages leads to further release of pro-inflammatory mediators.[8,9]

Smoking affects the body responses by neutrophil or monocytic activities, altered vascular function, and production of antibodies, expression of adhesion molecule, and in the release

Access this article online

Website: www.jrad.co.in

DOI: https://doi.org/10.53064/jrad.2022.13.4.236

Address for correspondence: Dr. Anjaneya Mahapatra, Department of Periodontology, Sree Sai Dental College and Research Institute, Srikakulam, Andhra Pradesh, India.
E-mail: anjaneyamahapatra@gmail.com

Received: January 03, 2022; **Accepted:** March 22, 2022; **Published:** ***

How to cite this article: Mahapatra A, Kumar KA, Reddy NA, Jena P, Tasneem S, Shivashankar G. Assessment of Periodontal Status in Patients with Chronic Obstructive Pulmonary Diseases: An Epidemiological Study. J Res Adv Dent 2022;13(4):231-237.

of the inflammatory mediators such as strong cytokines and chemokines that contribute to the periodontal disease. During smoking certain pro-inflammatory mediators also increase and there is a strong relationship with interleukin (I)-12 levels and the severity of chronic periodontitis. The periodontal clinical markers including the mean pocket depth (PD) and gingival recession along with bone loss in severe forms of periodontitis are a common finding in smokers associated with COPD as compared to non-smokers.[10-12]

Age, stress, and ethnicity of the population at risk of COPD and periodontitis vice versa are some other prevalent risk factors. COPD patients' ability to clean their teeth is a crucial determinant in the development of mild-to-severe periodontal diseases. In comparison to chronic heart disease and other systemic illnesses, less is known regarding the clinical link between periodontal disease and COPD. This study contributes to the existing body of evidence that periodontitis has a negative impact on overall health. Bacteria present in the gingival sulcus or the resulting pockets may have easy access to blood vessels in people with periodontitis. Inhalation of the bacteria can also cause illness; however, aspiration of oropharyngeal secretions is the most common route of infection. As a result, it is possible that oral microbes infect the respiratory tract, resulting in COPD.[13-15]

The association of COPD and periodontal disease prevalence or vice-versa has been under research through a couple of observational, case–control, and cohort studies. The present study was conducted to assess the periodontal status in COPD patients. The aim of this cross-sectional study was to estimate the periodontal health status in COPD patients and to evaluate the association between COPD and periodontal disease.

Materials and Methods

The present descriptive cross-sectional study was conducted in different hospital of Srikakulam district of Andhra Pradesh. This study was conducted from February 2020 to July 2021 after obtaining ethical clearance from the ethical committee of the institution.

Source of data

Patients suffering from COPD in the outpatient department of pulmonology of RIMS hospital of Srikakulam, Andhra Pradesh. The sample size was calculated using G Power Software (Version 3.1) and found to be 500.

Method of collection of data

The study consisted of 500 patients suffering from COPD in the age range of 30–60 years. The inclusion criteria included in the study: Patients already diagnosed with the COPD, patients belonging to the age group of 30–60 years, and having at least 8–10 natural teeth. Patients who are edentulous or have underwent any type of periodontal therapy 6 months before the examination along with patients who have taken antibiotics in the past 6–8 weeks or having any other systemic and infectious diseases were excluded from the present study. Data collection was done by the principal investigator along with a trained recording assistant (Internee). Training and calibration of the investigator and the assistant was done by the guiding experts in the Department of Periodontology, Sree Sai Dental College and Research Institute, Srikakulam. This was done to ensure uniform interpretation, understanding, and application of the codes and criteria used to be observed and recorded.

Before conduction of the main study, a pilot study was conducted with $n = 20$ to check the feasibility of the study. Data were collected using a pre-fabricated proforma, with oral hygiene index simplified (OHIS) (Greene and vermillion, 1964) and CPI (Modified) Index and Loss of attachment Index (WHO). These forms have been designed to facilitate the examination of all age groups for the assessment of the prevalence of periodontal diseases. Standard codes were used for all the sections of the form. To ensure that all conditions were detected and diagnosed, the clinical examination followed the order of the assessment form.

Type III clinical examination was carried out as per ADA specification using plane mouth mirrors and community periodontal index (CPI) probes under adequate natural illumination. Subjects were made to sit on a chair or a raised platform with a comfortable armrest in an upright position. The examiner was seated next to the subject. All the examinations were carried out by a single examiner based on the WHO standards and criteria. The examiner was assisted by a trained recording assistant who was sitting close enough to the examiner so that instructions and codes could be easily heard and the examiner was able to see the data being entered correctly.

The PD, cement-enamel junction (CEJ) location, calculus, and debris scores, as well as a comprehensive inspection of the index tooth locations as per the index, were all conducted clinically. The findings were recorded using CPITN or the WHO probe. For each tooth, it was used at six different locations and the measurements were taken in millimeters. If the free gingival margin occurred apical to the CEJ, the gingival recession was recorded as a positive value. The distance between the CEJ and the pocket base is measured in centimeters (PD+ gingival recession = LOA). When any bleeding was observed, BI on probing was graded on a scale of 0–5. With 20 patients, the examiner's reliability of all periodontal metrics was tested. The PD and LOA agreement correlation coefficients were 0.90 and 0.94, respectively. GBI and PD had Kappa values of 0.85 and 0.87, respectively, for agreement.

The following required instruments and accessories were used in the study: Plane mouth mirrors, CPI probes, Tweezers, Sterilized Cotton rolls, Disposable mouth masks, Disposable gloves, Kidney trays, Disinfectant solution (Cidex solution), Povidine iodine solution, Cotton gauze, and Cotton holder.

An asepsis protocol was developed and strict procedures were followed for infection prevention. Sufficient numbers

of instruments were carried to the examination site to avoid interruptions during the study. The cold sterilization method was followed using Cidex® chemical solution. Using gloves, one part of Cidex® was diluted to nine parts of clean tap water to get a 10% solution, into which, pre-rinsed instruments were immersed for a minimum of 30 min before being reused if needed. Used instruments were placed in the disinfectant solution, then washed and drained well before resterilization. After each day of examination, the entire instruments were autoclaved.

The data obtained were compiled systematically, transformed from a pre-coded proforma, and entered into Microsoft Excel (Version 2016), and analyzed using Statistical Package for the Social Sciences (SPSS Version 25.0). Descriptive statistics were carried out for continuous measurements and presented as mean ± standard deviation (SD) and results on categorical measurements were presented in numbers (%). Inferential statistics were performed using Mann–Whitney *U*-test and ANOVA test.

Results

Comparative evaluation has been done among various demographic parameters along with individual category comparisons between the variables.

Figure 1 shows the demographic characteristics of the study population. It was seen that there were 54.2% male subjects and 45.8% female subjects. For the duration of the COPD group, there were 44.2% of the subjects who belonged to the 0–5-year group, 44% belonging to the 6–10 years group and, 11.8% in >10-year group. For the age groups, there were 7.4% subjects in the 30–40 years group, 43.2% of them in the 41–50 years group, and 49.4% in the 51–60 years group.

Table 1 represents the gender-wise comparison of the oral hygiene variables. For the male population, the mean score for the calculus index was 2.028 ± 0.34, and for the females, it was 2.145 ± 0.31. The difference between the groups was statistically non-significant ($P < 0.10$). For the debris index, the mean score was 2.678 ± 0.29, and for females, it was 2.694 ± 0.28. The difference between the groups was not statistically significant ($P = 0.537$). For the oral hygiene index (simplified), the mean score for the male population was 4.725 ± 0.58, and female population, it was 4.848 ± 0.52. The difference between the groups was statistically non-significant ($P = 0.14$).

Table 2 represents the age-wise comparison of the oral hygiene variables. For the age group of 30–40 years, the mean score for the calculus index was 2.067 ± 0.45, and for the 41–50 years age group, it was 2.101 ± 0.34, and for the 51–60 age years group, it was 2.06 ± 0.29. The difference between the groups was not statistically significant ($P = 0.465$). For the age group of 30–40 years the debris index, with a mean score for the calculus index was 2.647 ± 0.27, and for the 41–50 years age group, it was 2.697 ± 0.29, and for the 51–60 years age group,

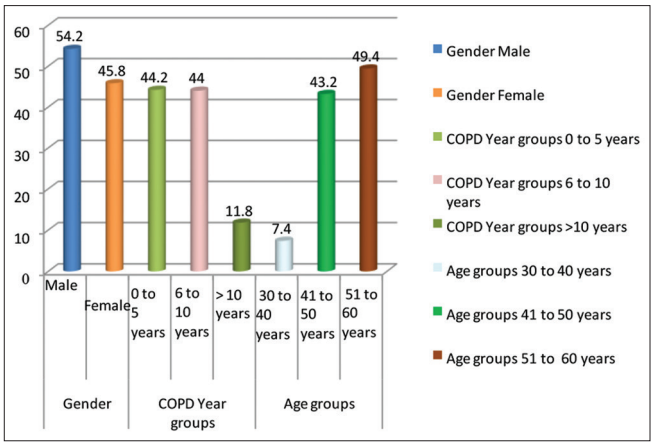

Figure 1: Graphical representation of the demographic factors of the study population

Table 1: Comparison of the Gender with the OHI (s) using Mann–Whitney U-test

Gender Groups	Calculus index		Debris index		Oral hygiene index simplified	
	Mean	SD	Mean	SD	Mean	SD
Male (*n*=271)	2.028	0.34	2.678	0.29	4.725	0.58
Female (*n*=229)	2.145	0.31	2.694	0.28	4.848	0.52
Z score	3.990		0.618		2.461	
P value	0.10		0.537		0.14	

OHIS: Oral hygiene index simplified

Table 2: Comparison of the age groups with the OHI (S) using one-way ANOVA test

Age groups	Calculus index		Debris index		OHIS	
	Mean	SD	Mean	SD	Mean	SD
30–40 years (*n*=37)	2.067	0.45	2.647	0.27	4.715	0.67
41–50 years (*n*=216)	2.101	0.34	2.697	0.29	4.798	0.57
51–60 years (*n*=247)	2.06	0.29	2.678	0.28	4.773	0.53
Total (*n*=500)	2.082	0.33	2.685	0.28	4.781	0.56
F score	1.767		1.617		1.384	
P value	0.465		0.540		0.681	

OHIS: Oral hygiene index simplified

it was 2.678 ± 0.28. The difference between the groups was not statistically significant ($P = 0.540$). For the oral hygiene index (simplified), for the age group of 30–40 years, the mean score for the calculus index was 4.715 ± 0.67, and for the 41–50 years age group, it was 4.798 ± 0.57, and for the 51–60 years age group, it was 4.773 ± 0.53. However, the difference between the groups was not statistically significant ($P = 0.681$).

Table 3 represents the duration of COPD as compared to the oral hygiene variables. For the COPD duration of 0–5 years, the mean score for the calculus index was 2.06 ± 0.36, and for the duration of 6–10 years, it was 2.11 ± 0.31, and for the >10 years,

it was 2.05 ± 0.29. The difference between the groups was statistically significant ($P = 0.02$). For the COPD duration of 0–5 years, the mean score for the debris index was 2.67 ± 0.28, for the 6–10 years, it was 2.70 ± 0.28, and for the >10 years duration, it was 2.66 ± 0.28. The difference between the groups was not statistically significant ($P = 0.431$). However, for the COPD duration of 0–5 years, the mean score for the OHIS was 4.74 ± 0.58, and for the 6–10 years, it was 4.83 ± 0.54, and for the >10 years, it was 4.71 ± 0.51. The difference between the groups was statistically significant ($P = 0.014$).

Table 4 represents the age-wise comparison of the periodontal parameters (CPI index Modified) for the age group of 30–40 years, the mean score for the teeth present with gingival bleeding was 1.47 ± 0.088, and for the 41–50 years age group, it was 1.48 ± 0.095, and for the 51–60 years age group, it was 1.47 ± 0.109. The difference between the groups was not statistically significant ($P = 0.663$). However, for the age group of 30–40 years, the mean score for the probing depth was 1.39 ± 0.232, and for the 41–50 years age group, it was 1.33 ± 0.138, and for the 51–60 years age group, it was 2.35 ± 0.123. The difference between the groups was statistically significant ($P = 0.05$).

Table 5 represents the duration of COPD as compared to the periodontal index. For the duration of 0–5 years group, the mean score for the gingival bleeding index was 1.47 ± 0.105, for the 6–10 years duration, it was 1.48 ± 0.099, and for the >10 years duration, it was 1.46 ± 0.097. The difference between the groups was statistically significant ($P = 0.034$). For the duration of 0–5 years, the mean score for the PD was 1.33 ± 0.151, for the duration of the 6–10 years group, it was 1.35 ± 0.138, and for the duration more than 10 years, it was 1.34 ± 0.102. The difference between the groups was not statistically significant ($P = 0.438$).

Table 6 represents the comparison of the loss of attachment index with the age groups and the groups showing the duration of COPD. It was seen that for the duration of the COPD group of 0–5 years, it was 1.75 ± 0.394, for 6–10 years, it was 1.74 ± 0.313, and for >10 years, it was 1.74 ± 0.241. The difference between the groups was not statistically significant ($P = 0.561$). However, for the age group of 30–40 years, it was 1.68 ± 0.785, 41–50 years, it was 2.50 ± 0.235, and 51–60 years, it was 2.74 ± 0.299. The difference between the groups was statistically significant ($P < 0.001$) .

Table 3: Comparison of duration of COPD with the OHI(S) using one-way ANOVA test

COPD duration	Calculus index		Debris index		OHIS	
	Mean	SD	Mean	SD	Mean	SD
0–5 years (*n*=221)	2.06	0.36	2.67	0.28	4.74	0.58
6–10 years (*n*=220)	2.11	0.31	2.70	0.28	4.83	0.54
>10 years (*n*=59)	2.05	0.29	2.66	0.28	4.71	0.51
Total (*n*=500)	2.08	0.33	2.68	0.28	4.78	0.56
F score	1.617		1.843		1.951	
P value	0.02*		0.431		0.014*	

*Statistically significant. COPD: Chronic obstructive pulmonary disease, OHIS: Oral hygiene index simplified

Table 4: Comparison of age groups with the gingival bleeding and pocket depth using one-way ANOVA test

Age groups	Teeth present with gingival bleeding (CPI modified index)		Pocket depth	
	Mean	SD	Mean	SD
30–40 years (*n*=37)	1.47	0.088	1.39	0.232
41–50 years (*n*=216)	1.48	0.095	1.33	0.138
51–60 years (*n*=247)	1.47	0.109	2.35	0.123
Total (*n*=500)	1.47	0.101	1.34	0.140
F score	0.411		2.728	
P value	0.663		0.05*	

*Statistically significant. CPI: Community periodontal index

Discussion

Periodontal diseases are globally prevalent and contribute significantly morbidity and tooth mortality. Furthermore, they

Table 5: Comparison of duration of COPD with the gingival bleeding and pocket depth using one way ANOVA test

COPD duration	Teeth present with gingival bleeding (CPI modified index)		Pocket depth	
	Mean	SD	Mean	SD
0–5 years (*n*=221)	1.47	0.105	1.33	0.151
6–10 years (*n*=220)	1.48	0.099	1.35	0.138
>10 years (*n*=59)	1.46	0.097	1.34	0.102
Total (*n*=500)	1.47	0.101	1.34	0.140
F score	1.094		0.828	
P value	0.034*		0.438	

*Statistically significant. COPD: Chronic obstructive pulmonary disease, CPI: Community periodontal index

Table 6: Comparison of age groups and duration of COPD with loss of attachment using one-way ANOVA test

	n	Mean	Standard deviation	*F* score	*P* value
LOA (duration of COPD)					
0–5 years	221	1.75	0.394	0.579	0.561
6–10 years	220	1.74	0.313		
>10 years	59	1.74	0.241		
Total	500	1.73	0.344		
LOA (age groups)					
30–40 years	37	1.68	0.785	13.166	<0.0001*
41–50 years	216	2.50	0.235		
51–60 years	247	2.74	0.299		
Total	500	1.73	0.344		

*Statistically significant. COPD: Chronic obstructive pulmonary disease

impose a significant infectious and inflammatory burden on the host that results in the state of systemic inflammation. COPD is a slowly developing, largely irreversible disease marked by airflow limitation. The predominant etiologic factor in this condition is cigarette smoking, which outweighs all other risk factors. As a result, the effects of cigarette smoke on the lungs are significantly linked to the pathogenesis of COPD. There is a broad link between the length of one's smoking history and the severity of airflow restriction, although there are a lot of individual variances.[16,17]

The disease was primarily considered as a disease of older smoking males, although COPD has become increasingly prevalent among women. Newer research suggested that the prevalence and mortality of COPD have increased more rapidly in women than in men. Although increasing tobacco consumption among women during the past several decades is linked to the rising prevalence of COPD in women, the relationship may be more complex, including additional factors such as differential susceptibility to tobacco, greater exposure to indoor air pollution, anatomic, and hormonal differences, as well as behavioral differences in response to available therapeutic modalities. Researches on COPD patients and their oral cavity status have shown a greater prevalence of periodontal infections among them. The present study reported unhealthy periodontal tissue among all the participants.[18-20]

Systemic inflammation is induced by oral infections and inflammatory cytokines produced by periodontal diseases, which may play a role in the development of COPD.[21] Periodontitis has been linked to several different disorders, including Type 2 diabetes, cardiovascular disease, and respiratory ailments, according to recent studies.[22,23] Three cross-sectional epidemiological studies found a link between poor oral health (including oral hygiene index, alveolar bone loss, and periodontal attachment loss)[24] and chronic pulmonary disease, though the precise mechanisms underlying such relationships remain unknown. A questionable correlation has also been discovered between periodontal disease and COPD.[25-28] A case–control research found a link between periodontal disease and airway obstruction, especially in former smokers; another study found that poorer periodontal disease increased the risk of COPD in the current smokers. According to a study by Didilescu *et al.* (2005), dental plaque in patients with chronic lung disorders frequently functions as a reservoir of bacteria that cause nosocomial pneumonia in vulnerable individuals. Because of the scarcity of data, nothing is known regarding the link between dental health and COPD.

Several recent microbiologic and epidemiologic investigations have revealed a link between poor periodontal health and respiratory disease, particularly in high-risk people. Several studies have demonstrated that COPD-causing bacteria invade the oral cavity of high-risk participants, such as those in intensive care units and nursing home residents. Preliminary experiments showed that changing oral hygiene reduced the rate of lower respiratory tract infection in institutionalized patients. These findings show that the mouth could be a major reservoir for infections of the lower respiratory tract. After adjusting for other confounding variables such as smoking, gender, age, and sex, Scannapieco *et al.*[31] and Scannapieco *et al.*[37] identified a link between poor dental health and COPD.[21-26]

The present study aimed to identify the severity of the periodontal conditions among COPD patients attending a tertiary care outpatient department of various hospitals in Srikakulam district of Andhra Pradesh, India. The gender distribution of the present study included 54.2% of COPD affected males and 45.8% of COPD affected females. The gender predilection of the disease included a greater prevalence of the disease among the female population but was not statistically significant. Silverman *et al.* indicated that women may be more susceptible to tobacco smoke than men and more likely to develop early-onset COPD. Age-wise comparisons showed the prevalence of COPD among middle to aged men as compared to younger age groups. The present study also reported a similar prevalence. The majority of the present study population belonged to the age group of >50 years, compared to 43.2% of them in 41–50 years age group and 7.4% among 30–40 years group. Similar reports have been documented by Miravitles *et al.*[33] and Tzanakis *et al.*[34]

In the present study, a decline in oral hygiene was seen as there was an increase in age, and one of the reasons for poor oral health status may be related to the lack of preventive oral health measures. These findings require indicating the need for more dental care programs and awareness regarding the impact of oral health on various systemic diseases. The comparison was made according to gender and it was seen that there was a higher prevalence of calculus among the female population with a score of 2.145 ± 0.31. The debris index scores were also more among the female population with 2.694 ± 0.28. The results were contrasting to the findings of Sreenivasan, and Rahman *et al.* where they have stated that oral hygiene index scores were higher among males as compared to females.[30]

The present study shows a decline in oral hygiene when there is an increase in the duration of COPD which is in accordance with Vikas deo *et al.*, 2019. The present study also reported a comparative evaluation among the age groups in terms of teeth with gingival bleeding and it was shown that the gingival bleeding or the oral hygiene index scores were higher among the age group of more than 41 years. Similar findings with increased prevalence of oral health conditions among aged individuals have been reported by Bair *et al.* and Anand *et al.*[36]

Because of the link between COPD and periodontitis, it is been highlighted how important it is for individuals with COPD to maintain optimal dental health. Oral and periodontal germs are also thought to play a role in bacterial pneumonia.[32] Peter *et al.* have inferred from his case–control study that individuals with COPD had significantly higher CAL, PD, and OHI compared with the control group after adjusting for covariates. Similar results were observed in the present study showed which an

increase in gingival bleeding scores with an increase in the duration of the disease and age of the subject. The mean PD was comparatively lesser as reported by other authors which may be due to the larger sample size.[33,34]

Clinical attachment loss is used to measure periodontal disease in most of the studies. Correlation of the duration of the disease with loss of attachment showed that subjects having COPD for 0–5 years had poor periodontal status compared with higher duration of COPD disease having a mean score of 1.75 ± 0.394 but was not statistically significant and, however, the study showed an increase in the loss of attachment as the age progressed. Loss of attachment scores was reported to be lesser among the participants having COPD for 6–10 years with the mean score of 1.74 ± 0.313 as compared to those of other duration of COPD disease. Review reports are comparing the long-term effects of COPD with the periodontal tissues, but to the stretch of our knowledge, we could not find any case–control studies comparing the duration of COPD with the periodontal parameters.[35]

The study provides evidence for a greater severity and prevalence of the periodontal disease among COPD patients. As with all retrospective studies, the present study being cross-sectionally designed does not establish a cause and effect relationship which prevented the association of temporal or causal relationship. The present study compared the duration of COPD with various periodontal parameters as there were minimal studies in the literature.[36] There is a need for long-term prospective studies to assess the casualty of the association between COPD and periodontitis. The sample size in the present study may not be large enough to establish the relationship. Further studies are required to evaluate the effect of periodontal treatment on the disease outcome for patients with COPD, and also to understand the impact of various treatment modalities for COPD on the periodontal health.

Conclusion

Findings in the present study showed a poor periodontal health status in COPD patients and the study provides no evidence of increased periodontal destruction with an increase in duration COPD.

References

1. Khijmatgar S, Belur G, Venkataram R, Karobari MI, Marya A, Shetty V, *et al.* Oral candidal load and oral health status in chronic obstructive pulmonary disease (COPD) patients: A case-cohort study. Biomed Res Int 2021;2021:5548746.
2. Kedlaya MN, Ramesh A, Hosmane GB, Bhandary R, Sajna HR, Thomas B. Comparative evaluation of serum cotinine levels in chronic periodontitis and chronic obstructive pulmonary disease. J Indian Soc Periodontol 2021;25:405-10.
3. Apessos I, Voulgaris A, Agrafiotis M, Andreadis D, Steiropoulos P. Effect of periodontal therapy on COPD outcomes: A systematic review. BMC Pulm Med 2021;21:92.
4. Fowler EB, Breault LG, Cuenin MF. Periodontal disease and its association with systemic disease. Mil Med 2001;166:85-9.
5. Teng YT, Taylor GW, Scannapieco F, Kinane DF, Curtis M, Beck JD, *et al.* Periodontal health and systemic disorders. J Can Dent Assoc 2002;68:188-92.
6. Yang X, Zhang T, Zhang Y, Chen H, Sang S. Global burden of COPD attributable to ambient PM2.5 in 204 countries and territories, 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019. Sci Total Environ 2021;796:148819.
7. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, *et al.* Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. J Glob Health 2015;5:020415.
8. Winning L, Linden G. Periodontitis and systemic disease. BDJ Team 2015;2:15163.
9. Kelly N, Winning L, Irwin C, Lundy FT, Linden D, McGarvey L, *et al.* Periodontal status and chronic obstructive pulmonary disease (COPD) exacerbations: A systematic review. BMC Oral Health 2021;21:425.
10. Qureshi H, Sharafkhaneh A, Hanania NA. Chronic obstructive pulmonary disease exacerbations: Latest evidence and clinical implications. Ther Adv Chronic Dis 2014;5:212-27.
11. Duan P, Wang Y, Lin R, Zeng Y, Chen C, Yang L, *et al*. Impact of early life exposures on COPD in adulthood: A systematic review and meta-analysis. Respirology 2021;26:1131-51.
12. Lee SC, Son KJ, Han CH, Park SC, Jung JY. Impact of COPD on COVID-19 prognosis: A nationwide population-based study in South Korea. Sci Rep 2021;11:3735.
13. Lacedonia D, Scioscia G, Santomasi C, Fuso P, Carpagnano GE, Portacci A, *et al.* Impact of smoking, COPD and comorbidities on the mortality of COVID-19 patients. Sci Rep 2021;11:19251.
14. Bomble N, Shetiya SH, Agarwal DR. Association of periodontal status with lung function in patients with and without chronic obstructive pulmonary disease visiting a medical hospital in Pune: A comparative study. J Indian Soc Periodontol 2020;24:67-71.
15. Di Stefano A, Caramori G, Oates T, Capelli A, Lusuardi M, Gnemmi I, *et al.* Increased expression of nuclear factor-κB in bronchial biopsies from smokers and patients with COPD. Eur Respir J 2002;20:556-63.
16. Di Stefano A, Capelli A, Lusuardi M, Balbo P, Vecchio C, Maestrelli P, *et al.* Severity of airflow limitation is associated with severity of airway inflammation in smokers. Am J Respir Crit Care Med 1998;158:1277-85.
17. Kim WD, Kim WS, Koh Y, Lee SD, Lim CM, Kim DS, *et al.* Abnormal peripheral blood T-lymphocyte subsets in a subgroup of patients with COPD. Chest 2002;122:437-44.
18. Majori M, Corradi M, Caminati A, Cacciani G, Bertacco S, Pesci A. Predominant TH1 cytokine pattern in peripheral blood from subjects with chronic obstructive pulmonary disease. J Allergy Clin Immunol 1999;103:458-62.
19. Retamales I, Elliott WM, Meshi B, Coxson HO, Pare PD, Sciurba FC, *et al*. Amplification of inflammation in emphysema and its association with latent adenoviral infection. Am J Respir Crit Care Med 2001;164:469-73.
20. Agustí A, MacNee W, Donaldson K, Cosio M. Hypothesis: Does COPD have an autoimmune component? Thora×2003;58:832-4.
21. Majo J, Ghezzo H, Cosio MG. Lymphocyte population and apoptosis in the lungs of smokers and their relation to emphysema. Eur Respir J 2001;17:946-53.
22. Keatings VM, Collins PD, Scott DM, Barnes PJ. Differences in interleukin-8 and tumor necrosis factor-α in induced sputum from patients with chronic obstructive pulmonary disease or asthma. Am J Respir Crit Care Med 1996;153:530-4.
23. Selby C, MacNee W. Factors affecting neutrophil transit during acute pulmonary inflammation: Minireview. Exp Lung Res 1993;19:407-28.
24. Sparrow D, Glynn RJ, Cohen M, Weiss ST. The relationship of the peripheral leukocyte count and cigarette smoking to pulmonary function among adult men. Chest 1984;86:383-6.
25. Stănescu D, Sanna A, Veriter C, Kostianev S, Calcagni PG, Fabbri LM, *et al.* Airways obstruction, chronic expectoration, and rapid decline of FEV1 in smokers are associated with increased levels of sputum neutrophils. Thora×1996;51:267-71.
26. Rahman I, van Schadewijk AA, Crowther AJ, Hiemstra PS, Stolk J, MacNee W, *et al.* 4-Hydroxy-2-nonenal, a specific lipid peroxidation product, is elevated in lungs of patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2002;166:490-5.
27. Wesselius LJ, Nelson ME, Skikne BS. Increased release of ferritin and

iron by iron-loaded alveolar macrophages in cigarette smokers. Am J Respir Crit Care Med 1994;150:690-5.
28. Cantin AM, Fells GA, Hubbard RC, Crystal RG. Antioxidant macromolecules in the epithelial lining fluid of the normal human lower respiratory tract. J Clin Invest 1990;86:962-71.
29. Linden M, Håkansson L, Ohlsson K, Sjödin K, Tegner H, Tunek A, *et al.* Glutathione in bronchoalveolar lavage fluid from smokers is related to humoral markers of inflammatory cell activity. Inflammation 1989;13:651-8.
30. Rahman I, Li XY, Donaldson K, Harrison DJ, MacNee W. Glutathione homeostasis in alveolar epithelial cells *in vitro* and lung *in vivo* under oxidative stress. Am J Physiol 1995;269:L285-92.
31. Pacht ER, Kaseki H, Mohammed JR, Cornwell DG, Davis WB. Deficiency of vitamin E in the alveolar fluid of cigarette smokers. Influence on alveolar macrophage cytotoxicity. J Clin Invest 1986;77:789-96.
32. Lopez-de-Andrés A, Vazquez-Vazquez L, Martinez-Huedo MA, Hernández-Barrera V, Jimenez-Trujillo I, Tapias-Ledesma MA, *et al.* Is COPD associated with periodontal disease? A population-based study in Spain. Int J Chron Obstruct Pulmon Dis 2018;13:3435-45.
33. Miravitlles M, Soriano JB, García-Río F, Muñoz L, Duran-Tauleria E, Sanchez G, *et al.* Prevalence of COPD in Spain: Impact of undiagnosed COPD on quality of life and daily life activities. Thora 2009;64:863-8.
34. Tzanakis N, Anagnostopoulou U, Filaditaki V, Christaki P, Siafakas N, COPD group of the Hellenic Thoracic Society. Prevalence of COPD in Greece. Chest 2004;125:892-900.
35. Rahman I, MacNee W. Regulation of redox glutathione levels and gene transcription in lung inflammation: Therapeutic approaches. Free Radic Biol Med 2000;28:1405-20.
36. 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 2022;93:584-90.
37. Scannapieco FA, Bush RB, Paju S. Associations between periodontal disease and risk for nosocomial bacterial pneumonia and chronic obstructive pulmonary disease. A systematic review. Ann Periodontol 2003;8:54-69.