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Original Article

Periodontal indices in patients with chronic obstructive pulmonary disease and their correlation with disease severity: A cross-sectional study

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a chronic respiratory condition primarily influenced by oral microbiota, which is the source of the microbiome. This study evaluated selected periodontal indices in COPD patients and their relationship with COPD severity among patients referred to Khorshid Hospital and Day Clinic in Isfahan in 2023.

Methods: This cross-sectional study involved 221 subjects diagnosed with COPD based on spirometry testing. According to spirometry values, the subjects were classified into mild, moderate, severe, and very severe COPD categories. Periodontal indices including pocket depth (PD), bleeding on probing (BOP), plaque index (PI) and clinical attachment loss (CAL), were assessed. In addition, relevant demographic and medical information, along with smoking status and severity of periodontal disease, were evaluated. The data were analyzed using one-way ANOVA, chi-square test, t-test, and rank regression with SPSS software.

Results: All evaluated patients had periodontitis. Overall, higher COPD grades were associated with increased periodontal disease indices (PD, BOP, PI, and CAL) ($p<0.001$). Greater periodontitis severity correlated with increased COPD severity, with moderate and severe periodontitis raising the risk of severe and very severe COPD by 8.1 and nearly 62 times, respectively. In severe and very severe COPD cases, periodontal disease severity showed the highest level of association with COPD severity compared to age and pack-years of smoking.

Conclusion: COPD severity significantly correlated with PD, BOP, PI, and CAL. However, further clinical studies are needed to establish a definitive association between these conditions due to the shared pathophysiology of COPD and periodontal disease.

Keywords: Chronic obstructive pulmonary disease (COPD), Periodontal diseases, Periodontal indices.

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Dental and oral diseases are among the most significant community health issues, with high prevalence and incidence rates. They can cause pain, discomfort, and dysfunction, negatively impacting people's lives (1, 2). Periodontal diseases encompass a group of inflammatory pathologies mainly divided into gingivitis and periodontitis. Changes in the color and consistency of gingiva, along with bleeding and edema, are common symptoms of both gingivitis and periodontitis (3). These conditions are prevalent in both developed and developing countries, especially among adults (4). Periodontal diseases are complex conditions influenced by multiple factors, including poor oral hygiene, smoking, diabetes, medication, age, and heredity (5). Periodontitis is characterized by microbially-associated, host-mediated inflammation in periodontal tissues, leading to periodontal attachment loss. It develops when gingivitis is left untreated in susceptible individuals (6).

Emerging interest and evidence support the link between periodontitis and various systemic conditions. The epithelium covering the periodontal pocket can be ulcerated due to inflammation caused by host-bacterial interactions. The wound in the periodontal pocket can serve as a pathway for bacteria or their products to enter the bloodstream, leading to bacteremia. Over time, this phenomenon can negatively influence general health, worsen cardiovascular diseases and diabetes, and increase the rate of preterm birth (7, 8). It is also worth mentioning that the oral microbiota is known as the primary source of the lung microbiome (9). Microbes indigenous to the oral micro-ecosystem will likely be inhaled into the lower respiratory tract. They can potentially contaminate the lungs and trachea with pathogens or alter the respiratory mucosal microenvironment, leading to the colonization of respiratory pathogens. In addition, the various environments within the oral micro-ecosystem can provide surreptitious sites for common respiratory pathogens to inhabit (10). Many studies have observed a relationship between oral health, oral diseases, and the risk of respiratory diseases such as pneumonia, chronic obstructive pulmonary disease (COPD), and lung cancer (11-14).

COPD is a chronic condition characterized by limitations in lung airflow, which includes chronic bronchitis and emphysema (15). This systemic disease can lead to pulmonary complications (shortness of breath, chest infections, persistent wheezing, cough, sputum production from the chest, and dyspnea) (16), as well as extrapulmonary complications (17). The leading cause of COPD is smoking (18), but occupational and environmental pollutants, as well as genetic predisposition, have also been implicated in its development (19). The gradual and chronic nature of COPD results in a decline in the health status of affected individuals over time, often leading to disruptions in their social lives, physical functioning, and daily activities (20, 21).

Statistics in Iran show that about 8.3% of people suffer from this disease (22). In 2019, COPD was the third leading cause of death globally, contributing to 3.23 million deaths, with most deaths (80%) occurring in low- and middle-income countries (23). In this disease, it seems that not only the lungs and respiratory system are affected, but there can also be cardiopulmonary complications, weight loss, muscle weakness, and cognitive dysfunctions such as depression and anxiety (24-27). Additionally, those diagnosed with this condition have reported experiencing higher fatigue levels than individuals with other respiratory diseases (28). Recently, Kelly et al., in a systematic review, found a possible association between poor periodontal health, the frequency of exacerbations, hospitalization, and quality of life in COPD patients (29). In another systematic review, Yang et al. showed that periodontal disease is not associated with the risk of COPD or COPD-related events (30). Considering the high incidence of periodontal diseases in the community, the possible association between periodontal disease and COPD, and the inconsistent findings from prior research, the present study aimed to assess clinical periodontal indices in individuals diagnosed with COPD.

Methods

Study population: We conducted a descriptive-analytical cross-sectional study, with the statistical population comprising patients referred to Khorshid Hospital and Day Clinic in Isfahan from April 2023 to August 2023. The inclusion criteria for participation in the study were individuals diagnosed with COPD based on a spirometry test and aged 30 years or older. The exclusion criteria included individuals under 30, those with fewer than ten teeth, a history of COPD exacerbation, modification in drug therapy due to respiratory symptoms, absence of a previous spirometry test within the last 48 months, and failure to complete the consent form.

Pulmonary function test (Spirometry test): The study included 221 diagnosed with COPD from Khorshid Hospital and Day Clinic. To determine the sample size, considering a type I error rate of 0.05 and a type II error rate of 0.20, as well as an average prevalence of moderate to severe periodontitis of 78.4% in patients with COPD and 63.7% in the non-disease group (31), the sample size for each group was calculated to be 52 individuals using the following formula:

$$n = \frac{\left[Z_{1-\alpha/2}\sqrt{2\,\overline{P}(1-\overline{P})} + Z_{1-\beta}\sqrt{(p_1q_1 + p_2q_2} \right]^2}{(p_2 - p_1)^2}$$

Using the spirometry test, these patients were categorized into four subgroups based on the severity of their respiratory condition: mild, moderate, severe, and very severe (29) (table 1). Additionally, the severity of COPD and pulmonary function were assessed under the supervision of a pulmonologist (R.S.).

Data collection: Before commencing the research, the patients were provided with an explanation of the study's objectives and methodology. Upon obtaining informed consent, the participants were enrolled in the study. Their demographic information, including age, gender, education, corticosteroid medication usage, marital status,

hospitalization history, pack-years of smoking, and current smoking status, categorized as non-smokers (those who reported smoking <100 cigarettes in their lives), former smokers (those who had previously smoked >100 cigarettes in their lifetime but were not currently smoking) (32) and current smokers, severity of COPD, as well as periodontal indices, including pocket depth (PD), bleeding on probing (BOP), plaque index (PI), and clinical attachment loss (CAL), were documented. The presence of periodontitis was examined and recorded in the data collection form.

Table 1. Classification of COPD based on spirometry (34).

Stage	Severity	Spirometry value (% of predicted)
I	Mild	$FEV_1 \geq 80\%$
II	Moderate	FEV_1 50% to <80%
III	Severe	FEV_1 30% to <50%
IV	Very severe	$FEV_1 < 30\%$

COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second

Measurement methods: To assess PI, the Williams periodontal probe was utilized to evaluate teeth (excluding the third molar) along the gingival margin at four sites: buccal, lingual, mesial, and distal. A score of 1 was assigned in cases without plaque on the gingival margin. Scores 2, 3, and 4 corresponded to a thin layer, moderate layer, and excessive plaque accumulation on the gingival margin, respectively. Consequently, each tooth received four scores; the average score was recorded for the entire oral cavity (33). PD was measured with a periodontal probe, which assessed the distance between the free gingival margin and PD in millimeters (34). For BOP measurement, after gently probing the four points around each tooth, if there was bleeding in any area within 10 seconds, the number 1 was given; if there was no bleeding, the number 0 was assigned. The final result was a percentage representing the percentage of areas with bleeding (BOP^+) (35).

CAL was measured using a periodontal probe. It determined the distance between the cementoenamel junction and PD. A researcher performed this measurement for all teeth, except the third molar, at four levels: mesial, distal, buccal, and lingual. The average number recorded for each tooth was obtained for each index, and considering the total number of teeth, the severity of periodontitis could be determined. People with interdental attachment loss of 1 and 2 millimeters were classified in the mild group (stage I), those with 3 and 4 millimeters were classified in the moderate group (Stage II), and those with 5 millimeters or more were classified in the severe group (stages III and IV) (36, 37). These measurements were performed by a single examiner (S.H.Sh) under the supervision of a periodontist (N.N) using a Williams periodontal probe (Town, Pakistan).

Statistics analysis: The data analysis encompassed both descriptive and analytical statistical approaches. Descriptive analysis involved mean, standard deviation, and frequency distribution measures. The analysis was conducted using one-way analysis of variance (one-way ANOVA), chi-square test, t-test, and rank regression (four grades of COPD) with SPSS software Version 26 (SPSS Inc., Chicago, IL, USA), with α=0.05 considered the significance level.

Results

This study examined 221 patients suffering from COPD who were referred to Khorshid Hospital and Day Clinic in Isfahan in 2023. All participants exhibited periodontitis, with an average age of 63.1±11.1 years. A gender distribution analysis shows that 147 of the participants were men and 74 were women. There was no significant difference in the means of the periodontal indices (PD, BOP, PI, and CAL) between male and female subjects ($P > 0.05$). Analysis of the relationship between gender and COPD grades revealed that a majority of patients of both genders had mild COPD grades, with 40.5% being women and 34% men. Consequently, no significant association was observed between COPD grades and gender ($P = 0.67$). There was no significant relationship between marital status and periodontal disease indices ($p > 0.05$), nor was there a significant difference in COPD grades between single and married individuals ($P = 0.07$).

In terms of education, 57 individuals (25.8%) demonstrated a lack of literacy, while 94 (42.5%) had a degree lower than a diploma, and the remaining 70 (31.7%) held a diploma or higher degree. Analysis of the smoking habits of the participants revealed that 62 patients (28.1%) were non-smokers, 39 patients (17.6%) were former smokers, and 120 patients (54.3%) were current smokers. Demographic information about the patients is shown in table 2. Individuals with a higher level of education exhibited lower average probing depth ($p < 0.001$), PI ($p < 0.001$), and attachment loss ($P = 0.002$). The data showed that as the education level decreased, there was a corresponding increase in the severity of COPD ($p < 0.001$). Moreover, individuals with a diploma or higher education predominantly exhibited mild COPD, while those with lower education levels were more frequently represented in

the severe COPD category. A comparison of periodontal indices in hospitalized patients and outpatients indicated that, except for the BOP index, which exhibited no significant difference (P = 0.16), other indices demonstrated significantly higher averages in the hospitalized patient group (p < 0.001). Notably, Mann-Whitney test showed that the prevalence of severe and very severe COPD cases among hospitalized patients surpassed that of outpatient cases (p < 0.001).

Correlation between periodontal indices and COPD grades: There was a significant statistical difference between the average of all periodontal indices and COPD grades. In general, as COPD grades increased, the average of periodontal disease indices also increased (p< 0.001) (figure 1). Tukey's test showed that in severe and very severe cases of COPD, the mean values for PD, BOP, PI, and CAL were significantly higher than in mild and moderate grades (p < 0.05).

Table 2. The distribution of patients with chronic obstructive pulmonary disease (COPD) based on age, gender, marital status, treatment status, hospitalization status, periodontal disease severity, smoking and education status.

Variables		Number	Percentage
Age	60 years and under	96	43.4
	Over 60 years old	125	56.6
Gender	Male	147	66.5
	Female	74	33.5
Marital status	Single	63	28.5
	Married	158	71.5
Under drug therapy with corticosteroids	Yes	147	66.5
	No	74	33.5
Hospitalized status	Hospitalized	129	58.4
	Outpatient	92	41.6
Severity of periodontal disease (periodontitis)	Mild	124	56.1
	Moderate and severe	97	43.9
Current smoking status	Non-smoker	62	28.1
	Former smoker	39	17.6
	Current smoker	120	54.3
Education status	Illiterate	57	25.8
	Under diploma	94	42.5
	Diploma and higher	70	31.7

Correlation of periodontal disease severity and COPD grades: Table 3 presents the relationship between the severity of periodontal disease and COPD grades. The results showed a significant relationship between these two variables (Mann-Whitney test). Comparing the average periodontal disease indices between the two groups treated with corticosteroids and the group that did not receive corticosteroids, the results showed that, except for the BOP index, which was not significant (P=0.54), other indices had a significantly higher mean in the corticosteroid-treated group (P < 0.05). Individuals who used corticosteroids demonstrated a higher prevalence of severe and very severe COPD compared to those not receiving corticosteroid treatment (P=0.01). Since the number of cigarettes consumed by study patients did not follow a normal distribution, the median and IQR indices were used to describe and measure their relationship with COPD grades and education. An examination of the relationship between COPD severity and pack-years showed no significant relationship between these two variables. Furthermore, based on Mann-Whitney analysis there was no difference in the amount of smoking across different COPD grades (P=0.59).

Investigating the correlation between periodontal indices and age, pack year, and severity of COPD: It was observed that pack-years had no significant correlation with any of the periodontal indices ($p<0.05$). Based on Spearman's correlation test, COPD grades showed a significant positive correlation with four periodontal indices ($p<0.001$). Age also demonstrated a significant positive correlation with the probing depth index (P=0.002) and PI (P=0.01) (table 4). Finally, a regression model was used to predict COPD grades based on the variables of age over 60 years, high severity of periodontitis, and smoking according to pack-years (table 5).

Table 3. Investigating the relationship between COPD grade and the severity of periodontitis in patients with COPD

COPD grades / Periodontitis Severity	Mild Number (Percentage)	Moderate Number (Percentage)	Severe Number (Percentage)	Very severe Number (Percentage)	P-value
Mild	58 (46.8)	55 (44.4)	10 (8.1)	1 (0.8)	<0.001
Moderate, Severe	22 (22.7)	18 (18.6)	32 (33.0)	25 (25.8)	

Mann-Whitney test. , COPD: Chronic Obstructive Pulmonary Disease

Table 4. Correlation between periodontal indices with age, pack year and COPD grades

	PD	BOP	PI	CAL
Age	**0.205 (0.19-0.43)	0.084 (0.05-0.35)	0.163* (0.08-0.34)	0.065 (-0.003-0.26)
Pack year	0.080 (-0.07-0.19)	-0.010 (-0.016-0.10)	0.002 (-0.11-0.16)	0.009 (-0.12-0.14)
COPD grade	0.563** (0.46-0.64)	0.512** (0.40-0.60)	0.613** (0.52-0.69)	0.501** (0.39-0.59)

*Statistically significant at a level below 0.05.** Statistically significant at a level below 0.001. Spearman's correlation test. PD: Pocket depth, BOP: Bleeding on probing, PI: Plaque index, CAL: Clinical attachment loss

Table 5. Logistic regression results and calculation of odds ratio for different grades of COPD disease

COPD grade	Predictive variable	Odds ratio	Confidence intervals	P-value
Mild	Age over 60 years	0.737	0.430 – 1.432	0.703
	Moderate and severe periodontitis	0.787	0.387 – 1.712	0.808
	Pack year	0.990	0.973 – 0.992	0.720
Moderate	Age over 60 years	0.845	0.1 – 447.598	0.604
	Moderate and severe periodontitis	0.878	0.1 – 425.817	0.818
	Pack year	0.997	0.1 – 982.012	0.726
Severe	Age over 60 years	1.645	0.3 – 710.866	0.243
	Moderate and severe periodontitis	8.125	3.19 – 414.337	<0.001
	Pack year	1.001	0.1 – 985.017	0.935
Very Severe	Age over 60 years	1.284	0.3 – 458.603	0.635
	Moderate and severe periodontitis	61.969	7.486 – 888.844	<0.001

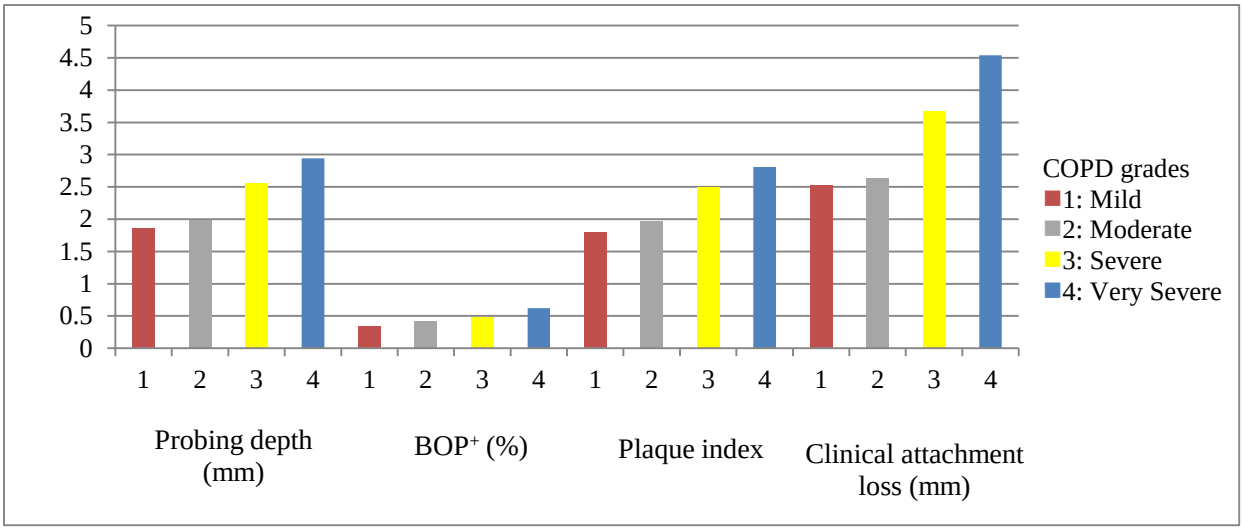

Figure 1. Investigating the relationship between periodontal indices and COPD grades
BOP: Bleeding on probing

Discussion

This study was designed to assess indices of periodontal disease in individuals with COPD and to examine their association with COPD severity, acknowledging the clinical significance of both conditions. It should be noted that all the subjects studied had periodontitis and none of them had gingivitis alone. The results demonstrated that mean probing depth, bleeding on probing, plaque index and clinical attachment loss differed significantly across COPD severity groups. Specifically, these periodontal parameters were elevated in patients with severe and very severe COPD relative to those with milder forms of the disease. Consequently, the data suggest a direct and significant correlation between COPD severity and the progression of periodontitis, a link previously explored in the scientific literature.

In 2018, Parashar et al. investigated the association between periodontal health and respiratory diseases in a cohort of 198 participants. The researchers found significantly higher values for all periodontal parameters in COPD patients compared to the control group. They observed a positive, significant, robust relationship between periodontal disease and COPD (38). Sapey et al. studied the possible associations between periodontitis and COPD with and without alpha-1 antitrypsin deficiency (AATD). They observed shared pathophysiology between periodontitis and COPD, especially when associated with AATD (39). In contrast, in 2020, Jung et al. conducted a study to examine the association between oral health status and COPD in adults over 40 years. Although they established a link between the number of missing teeth and COPD, their findings did not reveal a significant correlation between COPD and periodontal diseases. (14). However, this controversy still exists in observational studies and also systematic reviews. Considering the importance of periodontal disease, COPD, and their association, this investigation aimed to evaluate some periodontal disease indices in individuals with COPD and their correlation with disease severity in patients seeking medical care.

In this research, most individuals were over 60 years old, male, married, receiving corticosteroid therapy, hospitalized, and had mild periodontitis. It is worth mentioning that all individuals studied had periodontitis, and none had gingivitis alone. Additionally, in terms of education and smoking status, the majority of participants had a low education level and were current smokers. Regarding gender, despite the higher number of male COPD patients and the older age of female subjects, no significant differences were observed in periodontal indices and COPD severity between men and women. Furthermore, age over 60 was not associated with COPD.

Regarding marital status, the only notable difference was in PI, which was higher among married individuals; however, there were no significant differences in other periodontal indices and COPD severity. In the study, the participants were classified into three smoking categories: current, former, and non-smokers. Although smoking is considered a risk factor for the occurrence of COPD (40), there were no significant differences in periodontal indices between the two groups. Hamalinen et al. investigated the relationship between COPD and periodontal conditions and concluded that complete dental prostheses can reduce FEV

in COPD patients (41). Javaheri et al. in a case-control study found that periodontal indices including PD, BOP and CAL were positively associated with COPD severity (42). In the study by Abrishami et al., 90 participants were categorized into three groups: current smokers, ex-smokers, and non-smokers. The findings indicated that non-smokers displayed reduced periodontal indices in comparison to ex-smokers. Moreover, the periodontal parameters among former smokers were lower than those observed in current smokers (43). Nevertheless, the outcomes of the current study did not reveal a significant difference. It is noteworthy that the present investigation focused on individuals with COPD, whereas Abrishami et al.'s research involved non-COPD subjects. A few points regarding the patient's PI should also be highlighted. This index is highly variable and depends on factors such as the examination time, whether the patient has eaten before the examination, and whether they have brushed their teeth beforehand. Changes in these factors can lead to different results in various studies. Individuals with academic education had significantly lower probing depth, PI, and attachment loss than those who were illiterate. Furthermore, in addition to the periodontal indices, the severity of COPD increased as the educational level decreased. The present research observed that patients receiving corticosteroids displayed increased severity of COPD and elevated periodontal index values compared to those not receiving corticosteroids. In addition, this issue was investigated in patients who were treated as outpatients and those who were hospitalized, with periodontal indices and COPD severity being higher in hospitalized patients.

Significant differences were observed in the periodontal indices in COPD patients, except for the BOP index. These findings suggest a potential influence of hospitalization and corticosteroid use on the periodontal indices of COPD patients. The results of the current study were consistent with those reported by Shen et al. (44). They asserted that patients undergoing corticosteroid treatment are at a heightened risk of developing periodontal diseases. The escalation of periodontal parameters in hospitalized individuals compared to outpatients may be attributed to the challenges of maintaining adequate oral hygiene in a hospital setting. Generally, individuals with more severe COPD are more likely to receive corticosteroid therapy. Hence, it can be hypothesized that as COPD worsens, a patient's adherence to oral hygiene and its significance diminishes. In light of the absence of a substantial correlation with the BOP index, the anti-inflammatory properties of corticosteroids can be utilized to mitigate inflammatory symptoms; a clear example is BOP. Overall, the findings (figure 1) show that periodontal indices were associated with the severity of COPD, demonstrating a direct and significant connection between them. Several studies in this area have provided evidence supporting a relationship between periodontal disease and COPD or other respiratory diseases.

Sharma et al. reported that individuals with respiratory diseases exhibited markedly poorer periodontal health, characterized by a higher prevalence of gingivitis, deeper periodontal pockets, and increased CAL compared to the control group (45). On the other hand, in the study by Peter et al. (46), a definitive relationship between periodontal disease and COPD was not established. However, significant evidence indicated that poor periodontal health was associated with obstructive lung disease. Parashar et al. also reported that all periodontal parameters in COPD patients were significantly higher than in the control group. The study also found a positive, significant, and strong correlation between periodontal disease and COPD (38). Apessos et al. also concluded that periodontal treatment in patients with COPD was effective in improving lung conditions. In addition, periodontal treatment in COPD patients was associated with lower hospitalization rates and lower mortality from this disease (47).

Contrary to the results of the present study and the studies mentioned before, Jung et al. did not find any correlation between COPD and periodontal diseases, although the rate of missing teeth was confirmed to be associated with COPD (14). The results demonstrated in figure 1 led us to investigate the relationship between the severity of periodontitis and the severity of COPD. As shown, the severity of periodontal disease was associated with the severity of COPD. Individuals with mild periodontitis mainly experienced mild or moderate COPD, with about 9% having severe or very severe disease. On the other hand, in the group with moderate to severe periodontal disease, 58.8% had a severe or very severe form of COPD.

Based on the results presented in table 4, which aimed to investigate the prediction of COPD severity using the variables of age over 60, severity of periodontal disease, and pack-years, it can be concluded that cigarette smoking, in terms of pack-years and age over 60 did not have predictive power for any levels of COPD severity. On the other hand, moderate to severe levels of periodontal disease increased the likelihood of developing severe COPD by approximately 8.1 times and very severe COPD by approximately 62 times. Ultimately, it can be stated that although COPD and periodontal disease share the common risk factor of smoking, the results of the current study indicate that the predictive capacity for the severity of periodontitis outweighed the number of pack-years smoked

by the patient. As previously mentioned, it is believed that IL-6 functions as a pivotal orchestrator of systemic effects, inducing hepatic production of acute-phase proteins such as C-reactive protein (CRP). The ulcerated periodontal epithelium provides a direct portal for these cytokines and bacterial products to enter the systemic circulation. This phenomenon creates a state of low-grade systemic inflammation, characterized by elevated levels of circulating IL-6, TNF-α, and CRP. This heightened inflammatory burden exacerbates the core pathology of COPD, where these same cytokines perpetuate a cycle of pulmonary inflammation, neutrophil recruitment, and tissue destruction—notably, TNF-α is a key driver of neutrophilic airway inflammation and emphysematous changes. Thus, this 'inflammatory spillover' from the periodontal niche likely contributes to the systemic inflammatory phenotype observed in COPD patients, suggesting a vicious cycle whereby each disease potentiates the other through a common cytokinetic network. (48-50). In addition to bacterial infection and the associated inflammation, the aspiration of periodontal pathogens into the airways may also significantly increase the likelihood of COPD development after periodontitis (51).

This cross-sectional study had some limitations. First, the small sample size was due to strict inclusion and exclusion criteria. Therefore, our findings may not be directly generalizable to other populations. As the confidence interval in the regression analysis was large, studies with larger sample sizes are needed. Second, a single study could not fully evaluate other potential confounding factors, such as genetic predisposition, socioeconomic status, asthma, plaque control status, disease duration, and occupational exposure. Third, other periodontal indices, such as gingival index and recession, were not assessed due to the dental equipment required for periodontal examination in the hospital environment. The strength of this study is that it evaluated different stages of periodontitis and some demographic data concerning the severity of COPD. The correlation between periodontal disease and COPD does not necessarily imply a causal relationship. Therefore, long-term follow-up studies are needed to establish causality. We plan to conduct large-scale studies in the future and include all important factors in the analysis. With the increase in COPD grades, the average PD, BOP, PI, and CAL were also higher. Within the limitations of this study and based on the obtained results, it can be stated that in severe and very severe cases of COPD, among age, pack-years of smoking, and severity of periodontal disease, the latter had the highest level of association. More longitudinal studies with larger sample sizes are needed.

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Authors' contribution: N.N. developed the theoretical framework of this manuscript, performed and supervised the project, and contributed to the final version of the manuscript. S.M.Sh. measured the clinical parameters. F.K. wrote and prepared the final manuscript and corresponded with the journal. M.J.T. performed the statistical analysis. R.S. collected the samples. All authors read and approved the final version before submission.

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