

## Bidirectional relationship between chronic obstructive pulmonary disease and oral disease

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### Abstract

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease that has various comorbid conditions and systemic complications. One of the complications is dental and oral disease, which can occur through systemic inflammatory mechanisms and the long-term side effects of inhaled drugs. Dental and oral diseases can also cause COPD progression, increase the risk of exacerbations, and affect the patient's quality of life. Some mechanisms that may play a role include aspiration of oral pathogens, aspiration of inflammatory proteins, and systemic inflammation. Dysbiosis of the lung microbiome can result from dental and oral conditions, increasing the risk of COPD and pulmonary infections. The association between COPD and oral disease includes the presence of systemic inflammatory conditions, the risk factor of smoking, and the indirect effects of inhaled medication use. Comprehensive management of COPD patients regarding dental and oral health is needed, which includes prevention of dental and oral disease, routine assessment of dental and oral health, provision of specific dental therapy, and personalized treatment in selecting COPD therapy.

**Keywords:** COPD; Oral health; Periodontal disease; Smoking

### 1. Introduction

Patients with chronic respiratory disease, primarily COPD, may have higher risk of dental and oral health problems, which can be caused by various factors, such as systemic inflammation, limitations to regular oral health care, and long-term side effects from the use of inhaled medications.(1) In most COPD cases, attention to dental and oral health is still minimal and superficial. In the previous study, the results stated that dental and oral diseases can increase the risk of progression of COPD. Likewise, COPD can increase the risk of dental and oral diseases. Smoking can be a joint risk factor for the development of COPD and oral disease.(2)

Tooth caries, tooth erosion, periodontal disease, and oral infections, including candidiasis, may be linked with COPD. There is evidence from earlier studies which show a relationship between periodontal disease and COPD. Additionally, biomarkers associated to these two conditions can be identified in serum and saliva, and there are bacteria that are distinct to the interaction between periodontitis and COPD. Studies conducted in recent years indicate that periodontal disease may raise the incidence of COPD exacerbations and become a risk factor for COPD, particularly in smokers. (3)

The pathogenesis of dental and oral disease in COPD patients involves a complex and multifactorial process. Periodontal disease may be associated with the risk of COPD and COPD exacerbations. The mechanism of the relationship between oral dental disease and COPD still cannot be explained certainty. Several speculative hypotheses regarding the relationship between these two diseases exist. Smoking is a confounding factor in these two relationships, so randomized clinical trial research with a large population is needed.(2,3)

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Dental and oral problems in COPD patients can cause more severe complications of dental and oral disease, a higher risk of lung infections and COPD exacerbations, and have an impact on the quality of life of COPD patients. One mechanism that causes COPD exacerbation in periodontitis is the transfer of bacteria from oral plaque to the respiratory system. (3) Poor dental health can damage the symbiosis between the host's immune reaction and the microbiome in the oral cavity, which risks dental and oral disease and chronic inflammation. (4) Clinical trial research shows that therapy for periodontal disease can prevent COPD exacerbations. (3) Therefore, a comprehensive assessment is needed to understand more clearly the relationship between COPD and dental and oral health disorders. This review will discuss the mechanisms underlying the relationship between COPD and oral diseases and efforts to prevent and manage them.

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## 2. Epidemiology

Periodontal disease is more common in COPD cases compared to non-COPD cases, and tooth loss is more common in COPD patients. (5) Research by Gaeckle et al. shows that COPD patients have fewer teeth than non-COPD and have a lower quality of life-related to oral health. (6) COPD patients often have poor oral hygiene, characterized by few teeth, dental plaque, and low quality of life. COPD patients showed a higher DMFT (decayed, missing, and filled teeth) index compared to non-COPD. (7)

Factors that can play a role in oral disease in COPD patients are educational status, socioeconomic status, physical activity, frequency of dental visits, oral hygiene regimen, and diet patterns, but prospective research is still needed. Research on hospitalized COPD patients shows that COPD patients have a lower frequency of toothbrushing, poor periodontal health, and higher gingival inflammation than non-COPD patients. (8) Other studies have shown that oral health status is not associated with COPD exacerbations but is associated with patient-reported respiratory symptoms, so further prospective research is needed. (9)

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## 3. Pathogenesis

### 3.1. Pathogenesis of oral disease in COPD

Periodontal disease is the most common oral disease which has relation with COPD. The pathogenesis of periodontal disease and COPD may be interrelated through chronic inflammatory processes and shared risk factors, including age and smoking. (10) Some of the mechanisms thought to play a role are pathogens and inflammatory cytokines involved in periodontal disease and COPD. Oral microbes can enter the respiratory system, which can cause infection or exacerbation of COPD. COPD exacerbations can also occur due to the entry of salivary enzymes in periodontal disease into the respiratory system. Cytokines involved in periodontal disease can cause impaired pulmonary immunity through damage to the alveolar epithelium, making lung vulnerable to infections. Research by Cunningham shows that the combination of smoking status and tooth loss has a higher tendency for COPD patients. The relationship between smoking, COPD, and oral health has a complex mechanism. (2)

Treatment that COPD patients undergo includes inhaled bronchodilators and inhaled corticosteroids, which can affect oral health. Side effects of inhalation corticosteroids (ICS) can cause oral and periodontal immunity disorders. The inhaled bronchodilators, such as short-acting beta-2 agonists (SABA) and short-acting muscarinic agonists (SAMA), can cause hyposalivation and xerostomia. The results of research by Jung (2020) show that patients with poor periodontal health status are more likely to have COPD, and COPD patients experience more tooth loss than patients without COPD.(11)

COPD patients can experience the condition of acute exacerbations which cause a progressive decline in lung function. One factor that plays a role in acute exacerbations of COPD is bacterial infection. Most COPD patients have a decrease in natural immune function in the airways, including decreased mechanical sensitivity in the larynx and trachea and decreased airway clearance, thereby increasing the risk of aspiration of oral secretions and bacteria. Research related to the lung microbiome shows that in COPD, there is an increase in microbial diversity. (12) The mechanism of pathogenesis and progression of COPD related to teeth and mouth can be caused by aspiration of oral bacteria, aspiration of inflammatory protein, and systemic inflammation. (10,13)

### 3.1.1. *Aspiration of oral pathogenic bacteria*

Influencing factors include the frequency and volume of aspirated material, comorbidities, the patient's immune status, the effectiveness of the airway clearance mechanism, bacterial virulence, and the degree of dysbiosis of the lung microbiome. In patients with COPD, a decrease in forced expiratory volume (FEV)<sub>1</sub> is related to the number of bacteria in the airway. (14)

### 3.1.2. *Aspiration of inflammatory proteins*

In periodontitis patients, there is an increase in enzymes and cytokines related to inflammation. This increased inflammatory protein is also often found in COPD patients. These cytokines include MMP-9 and IL-6. (13)

### 3.1.3. *Systemic inflammation*

Patients with periodontitis and COPD have increased inflammatory markers. This relationship still not fully understood, whether they are related or different inflammatory events. There is still a need to investigate whether inflammation in dental and oral diseases can contribute to COPD and the effectiveness of dental care interventions in reducing inflammation in COPD. (10,13)

## 3.2. Relationship between COPD and oral disease

Relationship between COPD and oral disease can occur by three mechanisms such as direct relationship, indirect relationship, and shared risk factor.

### 3.2.1. *Direct relationship*

Chronic inflammation can be directly related to oral health problems. The inflammatory response caused by oral bacteria triggers local and systemic inflammation, increasing the risk of chronic inflammatory diseases, including COPD.(12) Patients with COPD experience impaired natural immunity in filtering pathogens due to aspiration. Aspiration of oral material, including pathogenic bacteria, enzymes, and inflammatory cytokines, can trigger inflammatory processes and lung infections and cause COPD exacerbation.(10)

### 3.2.2. *Indirect relationship*

COPD treatment and drug side effects can be indirectly related to oral health problems. Saliva plays an essential role in oral health, especially on periodontal; if there is any disturbance in saliva secretion, such as when using inhaled SABA and inhaled corticosteroids, it can increase the risk of periodontal disease. (14)

### 3.2.3. *Shared risk factor*

COPD and oral disease also have the same risk factors, namely smoking and chronic inflammation. Smoking is a major risk factor for COPD and dental diseases, especially periodontitis. (13) Smoking can have an impact on oral, lung, and gut microbiome dysbiosis, which can cause chronic inflammatory diseases such as periodontitis and COPD. (15)

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## 4. Impact of COPD on Oral Health Problems

COPD patients use inhaled medications that include inhaled bronchodilators and inhaled corticosteroids. This inhaled medication can impact dental and oral health depending on the dose, frequency, and duration of use. (16) Conditions that are often encountered due to long-term side effects of inhaled drugs are xerostomia, dental caries, oral candidiasis, gingivitis, impaired sense of taste, and periodontitis. The underlying pathophysiology is the presence of inhaled drug residues in the oral cavity and oropharynx. (14)

Using inhaled beta-2 agonist drugs can reduce saliva production and secretion, thereby increasing the risk of dental caries and causing relaxation of the smooth muscles of the lower esophageal sphincter. The impact of inhaled corticosteroids on dental and oral diseases occurs due to glucocorticoid deposition in the oropharyngeal area, reducing oral immunity and worsening periodontal health. (11)

### 4.1. Periodontitis

Periodontitis is a disease of the tooth-supporting tissue caused by periodontal bacteria, which can cause chronic inflammation and damage to the surrounding tissue and cause tooth loss. COPD patients experience severe periodontal disease, which is characterized by deeper periodontal pockets, high levels of clinical attachment loss, poor oral hygiene,

severe inflammation, bleeding in the gingival tissue, and tooth loss. Poor oral health can increase the risk of exacerbations, hospitalization, and reduced quality of life in patients with COPD. Through good management of periodontal disease, the frequency of COPD exacerbations can be reduced. (12) Based on research by Lin et al., it was found that periodontitis, which exacerbates COPD, is associated with the transfer of bacteria in dental plaque to the respiratory system. The bacteria that play an essential role in this case is *Fusobacterium nucleatum*. A study by Hayata et al. (2019) shows that inflammation in bronchial and pharyngeal cells can be induced by Heat-inactivated *Fusobacterium nucleatum*. (3)

#### **4.2. Gingivitis**

Gingivitis is often found in patients using inhaled corticosteroids and is worsened by the habit of mouth breathing. (14)

#### **4.3. Dental caries**

Dental caries can be caused by imbalance condition of saliva secretion, dental plaque, microflora, and food substrate over a long period of time. Saliva is a reservoir of phosphate and calcium ions, which are essential in tooth remineralization. When saliva flow decreases, the ability of saliva as a buffering agent also decreases so that aciduric bacteria which fermenting carbohydrates, create an acidic environment in the oral cavity leading to tooth demineralization. (14)

#### **4.4. Oral mucosal changes**

Inhalation corticosteroids can cause oral candidiasis with smooth white pseudomembranous plaque lesions, which, when scraped, will leave lesions with surface erythema, erosion, or ulcers. (14,16)

#### **4.5. Xerostomia**

This dry mouth condition can be caused by decreased saliva production. This condition often happened in patients using inhaled corticosteroids, beta-2 agonists, and anticholinergics. Clinical presentations include difficulty in speaking or swallowing, impaired sense of taste, oral pain, and poor retention of artificial dentures. (14)

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### **5. Impact of oral health problem in COPD**

One of the impacts of dental and oral health problems in COPD patients is increased risk of lung infections and COPD exacerbations. The increased incidence of COPD exacerbations is related to oral health problems. Research shows that periodontal disease is associated with a decrease in FEV1, which can occur due to an increase in the frequency of COPD exacerbations. Cytokines in periodontal disease can cause changes in the alveolar epithelium and natural immunity against respiratory pathogens, resulting in a high risk of infections such as bacterial pneumonia and lung mycosis. (11)

Patients with COPD can be suffered from nutritional problems. Many people suffering from COPD experience tooth loss, which can cause problems in the eating/chewing process. This can cause a decrease in the intake and variety of nutrients that can be given to patients. In patients with COPD, there is a relationship between inflammation, nutritional condition, and periodontal health. Hypoalbuminemia can result from decreased protein intake in COPD patients who have diminished chewing ability from tooth loss. In addition to protein consumption, calorie intake and inflammation in individuals with long-term medical conditions can also contribute to this illness. Because inflammation and diet have an impact on the rate of albumin synthesis, low serum albumin levels are also closely associated with poor periodontal health in COPD patients. (17)

Dental and oral problems, including tooth loss and periodontal problems, can cause a low quality of life, thereby increasing the risk of depression. Based on research from Zhou et al, a low level of periodontal health, which is reflected in many tooth loss and high plaque index, is significantly associated with a decrease in the quality of life of patients with COPD. (18) Periodontal health education in patients with COPD is essential to improve their quality of life and prevent worsening of COPD.

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### **6. Management**

Comprehensive management of oral disease in COPD include prevention, early diagnosis, and specific treatment.

## 6.1. Prevention

Efforts are needed to prevent oral diseases in COPD patients, especially for those who regularly use inhalers to treat COPD. Health workers, especially pediatricians, pulmonologists, and dentists, must be more aware of COPD patients' dental and oral health conditions. (5) Proper knowledge and understanding of the relationship between COPD and oral disease is also required. Education that can be given to COPD patients includes education on the dangers of smoking and their relationship with oral health, promotion of dental health, routine dental and oral care for COPD patients, education on the correct selection and use of inhalers, sugar-restricted diet patterns, and regular oral pH measurements.(2)

For patients who use inhalers, education can be provided in the form of side effects of inhalation therapy on the oral cavity, education about checking dental health every six months, education about how to maintain oral health at home with proper tooth-brushing techniques and the use of dental floss once daily or more. Additionally, instructions should include rinse mouth with water or neutral-pH mouthwash containing 0.05% sodium fluoride after using inhaler, especially before bed. Using an antimicrobial mouthwash, such as mouth rinses with 0.2% chlorhexidine, is also advised. Dietary changes that are advised include consuming more foods high in fiber, cutting back on refined carbs, and consuming less snacks or beverages that contain sugar in between main meals. Nuts, cheese, fruit, and vegetables are examples of foods with low cariogenic potential. Artificial sweeteners can be made with sugar replacements such sorbitol, aspartame, saccharin, and xylitol. In addition, patients are counseled to drink extra water. Applying fluoride gels, varnishes, and pit and fissure sealants can help prevent dental cavities.(14)

## 6.2. Early diagnosis

In managing oral diseases in COPD, efforts are needed for early diagnosis of oral disorders, specific dental therapy, and comprehensive management of COPD. Early diagnosis through routine oral dental examinations is required in all COPD patients. A clinical pathway is needed in COPD primary care that is integrated with dental and oral health, which includes efforts to prevent oral disease in COPD, early diagnosis, and comprehensive management. (19)

## 6.3. Specific treatment

### 6.3.1. Dental treatment

According to research, people with COPD who receive adequate periodontal care have a lower risk of hospitalization, fewer exacerbations, and a higher quality of life. (12) Periodontal treatment, including advanced dental cleaning, is associated with reduced exacerbations and a slower decline in lung function. Based on these findings, it is highly recommended that COPD patients undergo regular dental check-ups and care. (20) In managing dental care for patients with COPD, dentists must pay attention to the patient's health status. Patients with COPD who use portable oxygen are unable to sit in a dental chair horizontally. To prevent instruments and aerosols containing bacteria that can infect the upper and lower respiratory tract from being inhaled, a rubber dam is required. Patients with anxiety may receive tiny dosages of oral premedication including diazepam. In certain patients with asthma, certain drugs should be avoided after taking aspirin or NSAIDs. Asthma episodes can also be triggered by sulfites, which are preservatives and antioxidants used in anesthetic cartridges containing vasoconstrictors like levonordefrin or epinephrine. Propoxyphene and acetaminophen are suggested analgesics. Drugs that are related to codeine or that include this ingredient may cause bronchospasm. The adverse effects of narcotics, sedatives, and tranquilizers include respiratory depression, which is why they should be avoided. (21)

### 6.3.2. COPD treatment

A personalized therapy approach can be used in the management of COPD. Through personalized medicine, all individual patient factors, including the use of biomarkers, treatable traits, and comorbid factors, are being considered in selecting a therapeutic regimen. This is important to achieve therapeutic targets for COPD and prevent complications and side effects that can occur, especially in dental and oral health conditions. (22)

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## 7. Conclusion

COPD and oral dental disease have a mutually influencing relationship. Dental and oral disorders can increase the risk of COPD and the risk of exacerbations. COPD itself can cause dental and oral disorders or diseases through exposure to cigarettes, inflammation, side effects of COPD drugs, and physical disorders of COPD. One of the mechanisms underlying the development and progression of COPD is through oral bacterial aspiration. Comprehensive educational strategies and improving dental and oral health in COPD can prevent the occurrence and detection of dental and oral diseases. This intervention can play a role in preventing and reducing the frequency of complications and exacerbations of COPD.

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## Compliance with ethical standards

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### *Disclosure of Conflict of interest*

The author declares no conflicts of interest.

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