

# Oral health and periodontitis: why should we care?

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## ABSTRACT

Periodontitis is an inflammatory disease characterized by symptoms such as bleeding gums and bad breath. Severe periodontal disease is associated with systemic diseases. Diabetes is a group of diseases characterized by high blood glucose levels and can cause oral manifestations such as dry mouth, burning and susceptibility to candidal infections. There is a reciprocal relationship between diabetes and periodontitis. Various diseases such as hypertension, kidney disease, multiple sclerosis, liver disease and inflammatory bowel disease are also associated with oral health. Periodontal treatment can play an important role in the management of these diseases.

**Keywords:** Periodontitis, oral disease, other disease

## INTRODUCTION

The mouth is an integral part of our body and one of the parts that contains many microorganisms. Periodontitis is an inflammatory disease characterized by clinical loss of attachment, gingival bleeding, bad breath, tooth mobility and swelling of the gums. Attachment loss can be defined as the loss of periodontal ligament cells and supporting alveolar bone. Severe periodontal disease affects approximately 11.2% of the world. Scientists recognize that there is a relationship between oral diseases and systemic diseases. Systemic diseases can be defined as diseases that affect a person's life and require medical treatment. In this chapter, the relationship between oral diseases and diseases such as heart diseases, respiratory diseases, cerebrovascular diseases, metabolic diseases, hypertension, kidney diseases, rheumatoid arthritis will be discussed.

## DIABETES MELLITUS

This is a group of diseases characterized by high blood glucose levels caused by a lack of insulin production, ineffective insulin or both. There are two main types of diabetes. Type 1 diabetes or insulin-dependent diabetes mellitus is an autoimmune disease that causes the destruction of insulin-producing  $\beta$  cells in the pancreas. Type 1 diabetes occurs primarily in children and young adults and accounts for about 5% of diabetes cases. Type 2 diabetes, or non-insulin-dependent diabetes mellitus, is characterized by resistance to insulin and insufficient insulin production. Type 2 diabetes is the most common form of diabetes in adults, accounting for 90% to 95% of cases.<sup>1</sup> Patients with diabetes may present with dry mouth and

burning in the mouth as oral symptoms. There may also be increased susceptibility to oral candidal infections.

Disorders of collagen metabolism, neutrophil dysfunction and vascular changes in diabetes increase susceptibility to periodontal disease. Poor glycemic control in diabetes is associated with worsening of existing periodontal disease. On the other hand, periodontitis is associated with increased risk of diabetes complications such as dysglycemia and increased insulin resistance in patients with diabetes. Interleukin (IL)-1 $\beta$ , tumor necrosis factor (TNF)- $\alpha$ , IL-6, receptor activator of nuclear factor-kappa B/osteoprotegerin ratio, oxidative stress and Toll-like receptor 2/4 have been implicated in the mechanisms associated between oral diseases and diabetes.<sup>2</sup> Advanced glycation end products (AGEs) are a heterogeneous, complex group of compounds formed by the non-enzymatic reaction of glucose with amino acids in proteins and other macromolecules. They can also be exogenously ingested through food. As a result of the accumulation of AGEs in diabetes, there is an increase in the parameters mentioned above due to their interaction with RAGE. Another mechanism is that periodontal bacteremia/endotoxemia resulting from daily activities such as eating and tooth brushing causes low-grade systemic inflammation through CRP and neutrophil oxidative stress responses. Increased inflammation is associated with increased glucose. In patients with diabetes, periodontal treatment can reduce HbA1C by 0.36% after three months. Hyperglycemia increases the risk and severity of periodontitis and adversely affects the outcomes of periodontal treatment. The magnitude of short-

term HbA1C reductions achieved following periodontal interventions is similar to that usually achieved by adding a second drug to a pharmacologic regimen. Emerging evidence also suggests that people with severe periodontitis have an increased risk of developing type 2 diabetes.

All patients with diabetes should receive oral health education as part of their general education program. It should be recognized that diabetes increases the risk of periodontal disease and if left untreated, periodontitis can have a negative impact on metabolic control and increase the risk of complications of diabetes. Successful periodontal treatment has a positive impact on metabolic control and complications of diabetes. Physicians should ask patients with diabetes about a previous history of periodontal disease. If a positive diagnosis of periodontitis is made, they should refer the patient to a periodontologist to ensure that periodontal care and maintenance is provided. Questioning the presence of periodontal disease should be an integral part of the diabetes care visit. Patients with diabetes should be asked about positive signs and symptoms of periodontitis, including bleeding gums during brushing or eating, loose teeth, gapping or angulation of teeth, foul odor in the mouth, presence of abscesses in the gums, swelling, redness of the gums. Periodontal assessment should be recommended for all newly diagnosed diabetics as part of ongoing diabetes management.

## CARDIOVASCULAR DISEASES (CVD)

CVD are among the leading diseases that place a significant burden on global health services. Ischemic heart disease, rheumatic heart disease, cardiomyopathy and atrial fibrillation cause more than 95% of CVD-related deaths. The term CVD is used as a general term for atherosclerotic diseases, particularly coronary heart disease, cerebrovascular disease and peripheral vascular disease. Diseases such as rheumatoid arthritis, psoriasis, systemic lupus erythematosus and periodontitis are associated with an increased risk of developing CVD. Although there is evidence that more than 50 gene polymorphisms are involved in the modulation of atherogenesis, the main traditional risk factors are smoking, dyslipidemia, impaired glucose metabolism, hypertension and lifestyle factors.<sup>3</sup>

An association between periodontitis and CVD has been shown in studies in several different populations. In populations with multiple morbidities, such as comorbid diabetes and chronic kidney disease, periodontitis is significantly responsible for cardiovascular mortality. It appears that periodontitis may be a modifiable non-traditional risk factor for CVD. The mechanisms associated between periodontitis and CVD are thought to be mediated by elevations in bacteremia, CRP and oxidative stress. The periodontopathogenic bacteria present in periodontitis and the systemic inflammation caused by periodontitis pose strong risks for atherosclerotic CVD. In addition, it can directly or indirectly induce systemic inflammation that influences the development of atherothrombogenesis.<sup>6</sup> Bacteria in the oral microbiota can translocate into the circulation. *Porphyromonas gingivalis* (*P. gingivalis*) and *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*), which are potent periodontopathogens, have been shown in atheroma plaques.<sup>7</sup> Dyslipidemia may increase the risk of CVD by increasing oxidative stress. In a study, it was found that decreased CRP decreased inflammation in brachial

artery endothelium. *P. gingivalis* has been shown to accelerate atherosclerosis in murine models, induce fatty streaks in the aorta of rabbits and induce aortic and coronary lesions after normocholesterolemia. A polymicrobial infection such as periodontitis has been shown to induce an enhanced oxidative stress reaction, Toll-like receptor and inflammatory signaling produced in aortic endothelial cells. *P. gingivalis* facilitates the entry and attachment of Hag a-expressing bacteria into coronary artery endothelial cells. Periodontal treatment is known to cause a decrease in IL-1 $\beta$ , IL-8, IL-6 and fibrinogen levels.<sup>4</sup>

It should be recognized that periodontitis may have a negative impact on CVD and may also increase CVD complications. Conversely, effective periodontal treatment has positive effects on cardiovascular health. Physicians should ask about a prior history of periodontal disease in CVD. If a positive periodontitis diagnosis is made, they should refer the patient to a periodontology specialist to ensure that periodontal care and maintenance is provided. In CVD, questions should be asked about signs and symptoms of periodontitis, including bleeding gums during brushing or eating, loose teeth, gapping or gapping/rotting of teeth, bad breath and/or gingival abscesses or suppuration.

## HYPERTENSION

An arterial blood pressure higher than 140/90 mmHg on repeated measurements is known as hypertension. Hypertension is a systemic disease characterized by persistently high blood pressure and is an important health problem because it causes serious adverse conditions and is widely prevalent in the society.

Periodontitis and hypertension share risk factors such as old age, male gender, smoking, overweight/obesity, diabetes, low socioeconomic status and poor education. One of the mechanisms associated between hypertension and periodontitis is endothelial dysfunction. It is known that endothelial dysfunction can improve with periodontal treatment and a decrease of 1.3 mm Hg in blood pressure value has been reported in studies. Another mechanism is that periodontitis acts as a source of inflammation and oxidative stress and in the long term causes functional and anatomical vascular changes such as arterial stiffness and increased vascular resistance. It has shown that T cells play a central role in the development of hypertension. Specifically, following hypertensive stimuli, activated T cells accumulate in perivascular tissue. T cells are also known to be involved in periodontitis.<sup>4</sup>

The estimated surface of the periodontium is equal to the palm of one hand. The impact of this significant amount of local inflammation during generalized periodontitis can have a significant impact on systemic inflammation. The burden of periodontitis causes hypertension to worsen. Achieving periodontal health may provide effects equivalent to lifestyle modification in the control of hypertension. The effects of antihypertensive drugs that cause gingival enlargement should also be carefully evaluated and should not be confused with periodontitis. Calcium channel blockers among antihypertensive drugs may cause this effect. In such cases, gingival treatment should first be performed by a periodontologist and if there is no improvement, this drug group should be changed.

## KIDNEY DISEASES

Chronic kidney disease (CKD) is defined by abnormalities in kidney structure or function and is characterized by persistent nephron loss and ultimately a decrease in glomerular filtration rate. CKD can be classified into glomerular, vascular, renal tubulointerstitial, cystic and other congenital diseases. Due to its generally poor prognosis, the CKD mortality rate has increased by 31.7% in the last 10 years, making it one of the leading causes of death worldwide.<sup>5</sup>

In periodontitis, red complex bacteria consisting of *Tannerella forsythia* (*T. forsythia*), *Treponema denticola* (*T. denticola*) and *P. gingivalis* are the main causes of periodontitis. Oral bacteria can spread through the bloodstream and ingestion and use the circulatory system to induce inflammatory responses in distant tissues. One of the mechanisms associated between periodontitis and CKD is that oral bacteria reach kidney tissue via the bloodstream. One study showed an increased frequency of *P. gingivalis*, *T. forsythia* and *T. denticola* in CKD patients. The antibody titer of *A. actinomycetemcomitans*, which is also responsible for oral diseases, was found to be high in CKD. Indirect effects of inflammatory mediators in periodontitis are another mechanisms associated between CKD and periodontitis. Inducible nitric oxide produced in periodontitis may affect the kidney.<sup>5</sup>

Evidence supports the role of periodontal inflammation and elevated serum inflammatory mediators in the development of renal atherosclerosis, renal impairment and end-stage renal disease. Patients should be assessed by asking them about symptoms of periodontitis, including bleeding gums during brushing or eating, loose teeth, gapping or gapping/rotting of teeth, bad breath and/or gingival abscesses or suppuration.

## MULTIPLE SCLEROSIS (MS)

MS is an acquired, chronic, immune-mediated, inflammatory condition of the central nervous system that can affect the brain, brainstem and spinal cord.<sup>8</sup> It occurs when autoantibodies attack the myelin sheath proteins that surround neurons. The resulting inflammation affects neuronal function and leads to scarring and plaque formation. Lack of oral care and difficulties in accessing a dentist have the potential to increase the risk of developing periodontal disease and tooth decay in patients with MS. The mechanism linking MS and periodontal disease is that periodontal disease affects MS patients because it is an inflammatory disease. Patients should be evaluated for symptoms such as gingival bleeding, bad breath, elongated appearance of teeth, and loose teeth that may be suspicious for periodontitis.<sup>9</sup>

## LIVER DISEASES

Chronic liver disease (CHD) is a general term used to refer to a range of pathologies characterized by a progressive deterioration in liver function over a period of more than six months. Viral infections, toxin exposure, alcohol abuse, autoimmune diseases, genetic and metabolic disorders can lead to destruction of the liver parenchyma and increased AST and ALT release. The associated mechanisms between periodontitis and CHD are reactive oxygen products and oral dysbiosis. The oral cavity has the second largest microbiota

after the gut and interacts with diverse microbial populations in different parts of the body. Oral dysbiosis can lead to intestinal dysbiosis. The resulting gut dysbiosis affects liver function. Several studies using rabbits have shown that the introduction of major periodontal bacteria, especially *P. gingivalis*, by oral gavage directly caused liver damage. Periodontal disease has been shown to increase MCP-1, TNF- $\alpha$  and IL-17 levels.<sup>10</sup> Periodontitis increased Galectin-3, the most important molecule that induces liver fibrosis as CHD progresses to cirrhosis. It is known that Smad2, Smad3 and ERK1/2 phosphorylations and TGF- $\beta$ 1 production are stimulated in hepatocyte cells infected with *P. gingivalis*.

## INFLAMMATORY BOWEL DISEASE (IBD)

IBD is characterized by chronic recurrent intestinal inflammation and consists mainly of ulcerative colitis and Crohn's disease.<sup>10</sup> IBD morbidity has increased dramatically since the twentieth century. Studies suggest that environmental factors, genetic predisposition, gut microbiota and immune responses play a role in the development of IBD. Among these factors, gut microorganisms play a key role in the development and progression of IBD. The associated mechanism between periodontitis and IBD is oral dysbiosis. An unbalanced microecology affects the gut.<sup>11</sup> The second mechanism is that periodontitis produces inflammation that exacerbates IBD. Periodontitis has been suggested as a potential predisposing factor in IBD. *T. denticola* and other bacteria have been shown to be present as an opportunistic pathogen in the subgingival plaque in IBD.<sup>12</sup>

## RAMATOID ARTHRITIS (RA)

RA is a systemic inflammatory autoimmune disease characterized by chronic inflammation and joint tissue destruction, potentially leading to functional limitation. Similar to periodontitis, anaerobic bacterial dysbiosis is seen in RA.<sup>13</sup> The association between RA and periodontal disease has been associated with higher periodontal disease compared to healthy controls, independent of the duration of RA disease or factors such as smoking. Periodontal disease is now recognized as a risk factor for RA and appears to play a central role in disease onset. The gram-anaerobic bacterium *P. gingivalis* is associated with RA and periodontal disease through its ability to induce citrullination of proteins via the endogenous peptidylarginine deiminase enzyme.<sup>14</sup> RA activity is significantly greater in patients with periodontitis and decreases with nonsurgical periodontal treatment.

## LUNG DISEASES

The lung microbiome is important not only in the classic infection-related diseases, pneumonia, bronchiectasis and cystic fibrosis, but also in chronic non-infectious lung diseases such as chronic obstructive pulmonary disease (COPD), asthma and pulmonary lung disease. Studies have shown an association between periodontitis and asthma, COPD and pneumonia as a result of oral dysbiosis affecting the lung microbiome.<sup>15</sup> Periodontitis and respiratory diseases are public health problems and oral health is important in the management of respiratory diseases.

## CANCER

Clinical studies have confirmed the impact of periodontal disease on the systemic immune response, showing that serum markers of inflammation, particularly CRP levels, increase with advanced periodontal disease. The link between systemic inflammation and cancer is well recognized. Interest in the role of inflammation in cancer has led to studies showing positive associations between periodontal disease and lung cancer risk. Associations have been found between oral cancers, gastrointestinal cancers, lung cancer, pancreatic cancer and periodontal disease.<sup>16</sup>

## ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is a cerebral dysfunction associated with loss of cognitive function. It can be caused by many causes such as alcoholism and other toxic substances, vascular disease, malignancy, trauma, and metabolic disorders. The most important clinical findings of AD are memory loss, difficulty in performing daily tasks, impairments in language functions and visual perception. Hallucinations and depression are common at the onset of the disease. Periodontitis is common in the elderly and may become more prevalent in FH due to a reduced ability to pay attention to oral hygiene as the disease progresses. High antibodies against periodontal bacteria, increased systemic proinflammatory state may occur. Increased proinflammatory cytokines have been associated with an increased rate of cognitive decline in AD. Periodontitis may exert an increase in cognitive decline that may be mediated in AD through its effects on systemic inflammation.<sup>17</sup>

## THYROID DISEASE

The thyroid organ regulates many functions of the body thanks to the hormones it produces. Too little or too much secretion of these hormones can lead to different diseases in the body. The thyroid is a typical organ in which organ-specific autoimmune disease and chronic inflammation often occur. Thyroid hormones play an important role in oxidative stress and inflammation in humans. In studies, periodontitis is associated with thyroid diseases through oxidative stress and inflammation.<sup>18</sup>

## CONCLUSION

The World Health Organization has stated that oral diseases are serious health problems, and that oral health awareness worldwide should be considered as an important condition for overall health and quality of life. There is evidence that periodontitis is associated with approximately 60 non-oral diseases, including but not limited to cardiovascular disease, hypertension, obesity, atherosclerosis, diabetes and stroke. Physicians should consider the impact of periodontal disease when evaluating patients with systemic diseases and provide disease management.

## ETHICAL DECLARATIONS

### Referee Evaluation Process

Externally peer-reviewed.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

## Financial Disclosure

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## Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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