Review Article

# Metabolic syndrome and periodontal disease: An overview for physicians

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## Abstract

The metabolic syndrome (MetS) (also known as insulin resistance syndrome, syndrome X) is a cluster of factors associated with increased risk of developing coronary heart disease or type 2 diabetes mellitus. Several studies in the past have reviewed an association between MetS and periodontitis. Periodontal disease is considered an infectious and chronic inflammatory disease, and it has been considered to be a potential risk in cardiovascular and respiratory diseases and diabetes, and has implications in adverse pregnancy outcomes, osteoporosis, and so on. These systemic disorders have been documented as capable of affecting the periodontium or treatment of periodontal disease. Oral inflammatory lesions have different basic mechanisms concerning the possible association with systemic diseases. They concern local spread, metastatic spread, or immunologic cross-reactivity. In many studies, sometimes contrasting, periodontal pathogens have been evaluated in atheromatous plaques isolated from patients with chronic periodontitis. Oral inflammatory lesions have been shown unequivocally to contribute to elevated systemic inflammatory responses. In some studies, intensive periodontal therapy showed a significant reduction in c-reactive protein levels, interleukin-6, and low-density lipoprotein cholesterol after 2 months. The aim of this article is to reflect the association between MetS and periodontitis and to suggest an understanding to promote interprofessional practice; with proper oral care and plaque control, we can reduce the severity of MetS.

**Keywords:** Metabolic syndrome, obesity, periodontal diseases, type 2 DM

## Introduction

The components of metabolic syndrome (MetS) include dysglycemia, visceral obesity, atherogenic dyslipidemia (elevated triglycerides and low levels of high-density lipoprotein), and hypertension. This association is believed to be the result of systemic oxidative stress and an exuberant inflammatory response.[1] The endocrine and the immune system demonstrate a mutual relationship under pathophysiologic conditions. Diabetes has been linked to nephropathy, retinopathy, neuropathy, cardiovascular disease (CVD), and periodontitis. Periodontal diseases, considered as inflammatory diseases, have proved to have a spectrum of systemic implications.[2] Periodontitis may also be associated with systemic conditions such as metabolic disorders (diabetes mellitus, female hormonal alterations, obesity), drug-induced disorders, hematologic disorders/leukemia, and immune system disorders.[3] Our aim was to review and critically evaluate comprehensive literature and provide knowledge to medical practitioners on these associations so as to pave way for

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closer interactions between medical and dental practitioners in implementing better health care. Electronic databases such as PubMed, Google Scholar, and Cochrane databases were used as the source of the data for relevant studies published from 2010 upto 2019 with the following keywords, "Periodontal disease," "systemic conditions," "periodontal disease and Endocine," "Periodontal disease and Metabolic Syndrome," "Periodontal disease and Obesity," and "Periodontal disease and Hypertension."

This article reviewed the mechanisms of the relationship between MetS and periodontal disease and to determine whether oral health care in individuals exhibiting MetS has the potential to reduce the incidence of various systemic diseases. type 2 diabetes mellitus (T2DM) is a growing health concern, with incidence increasing in parallel with obesity.[4,5] There has been a fundamental change in the prevailing periodontal disease model of the 1960s, which suggested that the susceptibility to periodontitis increases with age, and that all individuals are susceptible to severe periodontal disease. More recent research has changed the belief in universal susceptibility to the current view that only 5%–20% of any population suffer from severe generalized periodontitis, and that only moderate disease affects a majority of adults.[6] One major risk factor is smoking, as there is now a clear association between smoking and periodontal disease independent of oral hygiene, age, or any other risk factor.[7] Periodontitis is a known risk factor for the deterioration of glycemic control over time.[8] In a 2-year longitudinal trial, patients with diabetes and severe periodontitis had a six-fold increased risk of deteriorating glycemic control compared with patients with diabetes and no periodontitis.[9] Periodontitis may also be associated with an increased risk of other diabetic complications. For example, 82% of diabetic patients with severe periodontitis experienced the onset of one or more major cardiovascular, cerebrovascular, or peripheral vascular events compared with 21% of the diabetic subjects without periodontal disease.[10,11] The death rate from ischemic heart disease and diabetic nephropathy was 2.3 and 8.5 times, respectively, higher in severe periodontitis than in healthy or mild periodontal disease subjects. These results suggest that the presence of the chronic inflammatory status associated with periodontal disease in patients with diabetes may be associated with systemic deterioration.

## Periodontitis as an inflammatory disease

Periodontitis being a chronic oral infection is associated with numerous bacterial species organized in biofilms posing a perpetual threat to the defense mechanisms triggering inflammatory and immune responses with release of inflammatory mediators as an elevated C-reactive protein, prostaglandin E2 (PGE2) with an increase in cytokines with proinflammatory action such as interleukin (IL-1β), and tumor necrosis factor-alpha (TNF-α). These responses are not only limited to periodontitis but also can be observed in systemic conditions such as diabetes, obesity, and arthritis.[12] MetS is believed to originate from a proinflammatory state, which can occur as a result of the effects of insulin resistance.[13] Insulin resistance is a condition in which insulin is produced by the pancreas, but is not efficiently bound by muscle, fat, and liver cells, as a result of dysfunctional signaling. The outcome is reduced glucose uptake from the bloodstream. Insulin resistance may promote inflammation through a number of mechanisms, including increased free fatty acid concentration and interference with the anti-inflammatory effects of insulin. The endocrine and the immune system demonstrate a mutual relationship under pathophysiologic conditions.[14] Although there is proven bidirectional influence of systemic diseases on periodontium, there are fewer studies on the effect of periodontal therapy on the hormone levels.[15] To rationally treat and prevent periodontal disease, we need to know the etiologic agents for specific patients and the mechanism of bacterial pathogenesis in periodontitis. In systemic diseases in which the periodontal tissues are affected as well, early detection and carefully managed therapeutics with the physician and periodontist working together may prove beneficial to the patient's general health and quality of life. The relationship between diabetes and periodontal disease has been related to systemic immunoinflammatory responses and subsequent wound healing.[8] Upregulation of inflammatory cytokines has been reported in individuals with diabetes and chronic periodontitis.[16] In a two-way relationship, therapeutic measures to control hyperglycemia and/or chronic periodontitis may improve the systemic health of individuals afflicted with these disease processes.

## HbA1c assessment

Intervention trials have assessed the potential effects of periodontal therapy on glycemic control in diabetics.[17] A meta-analysis showed an overall decrease in glycohemoglobin (HbA1c) of 0.36 [95% confidence interval (CI) 0.19, 0.54] in diabetic subjects treated with periodontal therapy when compared with nontreated control.[18] Another meta-analysis showed HbA1c reduction of 0.65% (95% CI 0.43, 0.88) after scaling and root planing (SRP).[19] Whereas a multicenter trial by Engebretson *et al.* (2013)[18] contradicted such effect, showing a nonstatistically significant increase on HbA1c after SRP therapy. Therefore, conflicting evidence on the effect of SRP on glycemic control remains. Data obtained from several studies strongly suggest diabetes as a risk factor for gingivitis and chronic periodontitis.[20] Evidence also suggests that periodontal changes are the first clinical manifestation of diabetes. Looking from the other perspective, an increase in the severity of chronic periodontitis was closely related to the development of glucose intolerance. It has been reported that subjects with severe chronic periodontitis and T2DM are six times more likely to have poorer glycemic control. Longitudinal studies have reported that infections of periodontal origin have an adverse effect on glycemic control. A chronic state of hyperglycemia negatively affects neutrophil function causing a dysfunctional inflammatory response and hampering tissue repair. The concentration of advanced glycation end-products (AGE) which can directly affect normal protein function or indirectly act by reacting with RAGE (receptors for AGE) on the cell membrane of a variety of cells is elevated in people with T2DM. These glycated products alter the functional properties of several important matrix molecules such as type 1 collagen and laminin. The change in HbA1c levels at 4 months was the primary outcome.

## MetS and periodontal disease assessment

Abdominal obesity, hypertension, and hyperglycemia are the most frequently occurring components of MetS. MetS seems to be a graded condition, with the likelihood of sequelae, such as CVD and T2DM, increasing as the number of components of MetS increases.[21] The occurrence of certain cancers has also been associated with MetS, but longitudinal studies linking the two are lacking. Some racial/ethnic groups with a large proportion of immigrants have a high prevalence of cardiovascular risk factors including hypertension, hypercholesterolemia, and diabetes. In this case, we assume that most of the ailments come from dental or periodontal foci, as in the bacterial endocarditis; but instead of considering them as possible pathogenetic mechanism of an immune nature, we consider them as originated by the body's response to the presence of bacterial antigens through the formation of specific antibodies. Periodontal status was evaluated for the extent (frequency of affected sites) and severity of clinical parameters under the classification given by the American Academy of Periodontology.[22] This study evaluated the following periodontal parameters – probing depth (PD): measured from the free gingival margin to the bottom of the sulcus; clinical attachment level (CAL): measured from the cementoenamel junction to the bottom of the sulcus; recession (REC): measured as the distance from the free gingival margin to the exposed cement–enamel junction; bleeding on probing (BOP): measured as the percentage of sites with presence of blood upon probing.

## Limitations of this review

Most of the studies taken as a part of the review were included based on the strength of the evidence. Considering these as novel associations, the maximum strengths of the evidence available in the literature were the cohort and case–control study designs. There were neither systematic reviews nor meta-analysis to associate periodontal disease with any of these novel associations, considered as a drawback when a causal association has to be established. Considering the paucity of studies, self-reported alveolar bone loss and radiographic evidence of bone loss alone too have been considered indeed a limitation.

## Implications for medical practitioners

Most of the medical practitioners are unaware of the consequences of periodontal disease on other systemic conditions. However, considering the pathogenic potential of periodontal disease on diabetes, CVDs, and obesity highlighted by this article, medical practitioners can provide proper education and guidance in collaboration with the dentists to contribute for oral health and eventually for the overall health of the patients.

# Conclusion

Mouth is the gateway to the body, and it is filled with bacteria. It is believed that there are more bacteria in the mouth than people on earth. "Oral health" is connected to "overall health" and it has suggested that people exhibiting several components of MetS should be encouraged to undergo oral examination. Periodontal therapy plays a major role in improving periodontal conditions by reducing inflammatory markers and thereby influencing the systemic conditions. Thus, periodontal treatment could become part of therapy for MetS. Oral health providers who identify patients at risk for MetS could refer them to a medical provider, and physicians could refer patients to dentists to ensure that patients with MetS receive a dental evaluation and any necessary treatment.

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## Conflicts of interest

There are no conflicts of interest.

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