Review of obesity and periodontitis: an epidemiological view

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Key points

- Explains the current knowledge regarding the links between obesity and periodontitis.
- Examines the literature that evaluates the association between these two diseases.
- Describes the effects of obesity on the outcome of non-surgical periodontal therapy.

Abstract

Obesity and periodontitis are among the most common non-communicable diseases, and epidemiological studies report the influence of obesity in the onset and progression of periodontitis. Data indicate that increased body mass index, waist circumference, percentage of subcutaneous body fat, and serum lipid levels are associated with increased risk to develop periodontitis. The underlying biological mechanisms of this association involve adipose tissue-derived cytokines, such as tumour necrosis factor-α and interleukin-6, which affect whole-body metabolism and contribute to the development of a low-grade systemic inflammation. Multiple studies report a positive association between these two diseases across diverse populations. Obesity does not appear to impair the success of periodontal therapy. However, currently available evidence is variable and therefore inconclusive. Despite the limited evidence about recommendations on treatment planning, oral healthcare professionals need to be aware of the complexity of obesity to counsel their patients about the importance of maintaining healthy body weight and performing good oral hygiene procedures.

Introduction

Obesity and periodontitis are among the most common chronic disorders affecting the world population.[1] Obesity is a complex, multifactorial chronic disease that is strongly associated with multiple comorbidities.[2] Epidemiological studies suggest that obesity is also associated with periodontitis.[3,4] Multiple authors report that increased body mass index (BMI), waist circumference (WC), percentage of subcutaneous body fat, and serum lipid levels are associated with increased risk of developing periodontitis compared with normal-weight individuals.[5,6,7]

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While there is preliminary evidence for these relationships, a causal relationship remains elusive. The mechanisms that link obesity and periodontitis are not completely understood. However, obesity has several harmful biological effects that might be related to the pathogenesis of periodontitis.[8] Tumour necrosis factor-α (TNF-α), and interleukin-6 (IL-6) form part of the pathophysiology of both diseases.[8] The literature about the effect of obesity on the outcome of non-surgical periodontal therapy remains controversial.[9]

The association of obesity and periodontitis constitutes an important topic due to the inflammatory component they share and their high prevalence in the adult population.[3] This narrative review aims to describe the reported association between these two conditions. Relevant literature was extracted from PubMed in the Medline electronic database, using the following keywords in different combinations: periodontal diseases OR periodontitis OR alveolar bone loss AND obesity OR body mass index OR waist circumference. The filters used in this search were studies conducted in humans and publications in English.

Obesity

Obesity is defined as abnormal or excessive fat accumulation that may impair health.[10] The World Health Organisation (WHO) defines overweight as a BMI ≥25 kg/m^2 and obesity as a BMI ≥30 kg/m^2 (Table 1).[10] BMI is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2).[10] This traditional BMI classification underestimates risk in Asian and South Asian people.[11] A separate guideline for this population classifies overweight as a BMI between 23 and 24.9 kg/m^2 and obesity as a BMI ≥25 kg/m^2.[11]

BMI is the most frequently used indicator by WHO because it is inexpensive and easy to use in clinical and epidemiological studies.[12] However, this measure has some limitations. BMI does not assess body fat distribution, because it is a measure of excess weight rather than excess body fat. Factors such as age, sex, ethnicity, and muscle mass can influence the relationship between BMI and body fat.[13] Alternative measures that reflect abdominal obesity such as WC have been suggested.[13] WC is strongly correlated with cardiovascular

Table 1 The international classification of adult underweight, overweight and obesity, according to BMI and risk of comorbidities. Adapted from Obesity: preventing and managing the global epidemic. World Health Organization, Defining the problem, p. 9, Copyright (2000)

Classification	BMI	Disease risk (relative to normal weight and waist circumference)	
		Men <102 cm Women <88 cm	Men ≥102 cm Women ≥88 cm
Underweight	<18.5	–	–
Normal range	18.5–24.9	–	–
Overweight	25–29.9	Increased	High
Obesity:	≥30	–	–
Obesity class I	30–34.9	High	Very high
Obesity class II	35–39.9	Very high	Very high
Obesity class III	≥40	Extremely high	Extremely high

disease (CVD) because abdominal adipose tissue secretes a greater number of cytokines and hormones in comparison to the subcutaneous adipose tissue.[13] The WHO suggests when WC is ≥102 cm (40 inches) in men and ≥88 cm (35 inches) in women, it is considered a risk factor for CVD. The biologic rationale for relating measures of central adiposity to CVD risk is that abdominal adipose tissue is related to decreased glucose tolerance, reduced insulin sensitivity, and adverse lipid profiles.[13,14]

Obesity is responsible for 3.4 million deaths, 3.9% of years of life lost and 3.8% of disability-adjusted life years globally.[15] Multiple factors, including genetics, socioeconomic status, environment and individual decisions play a significant role in the pathogenesis of obesity.[2] Obesity is either an independent factor or aggravating factor for a variety of non-communicable diseases, including cardiovascular diseases, osteoarthritis, type 2 diabetes and cancer.[2,16]

Worldwide, obesity has nearly tripled since 1975, contrary to other major global risks such as tobacco use and childhood malnutrition, which are declining.[12,15] Increase in prevalence occurs in developed and developing countries, and will continue to grow in the future.[17] In 2016, 1.9 billion adults aged 18 years and older were overweight. Out of these, over 650 million adults were obese. Approximately 13% of the world's adult population (11% of men and 15% of women) were obese.[12] These trends project 65 million additional obese adults in the United States and 11 million additional obese adults in the United Kingdom by 2030.[17] The large increments in obesity over the past years have focused on a number of potential contributors, including increases in caloric intake, declining levels of physical activity, changes in the composition of diet, and changes in the gut microbiome.[15]

Periodontitis

Periodontitis is a chronic inflammatory disease of bacterial origin that affects the supporting and surrounding structures of the teeth.[18] Historically, all individuals were considered equally susceptible to develop periodontitis. Poor oral hygiene, biofilm accumulation and possibly occlusal trauma were sufficient to initiate disease.[19]

Predisposition to periodontal disease is highly variable and depends on the host's response to periodontal pathogens.[20] The current aetiological concept implies a bacterial infection as the primary cause. *Porphyromona gingivalis*, *Prevotella intermedia*, *Tannerella forsythia*, *Campylobacter rectus*, *Eubacterium nodatum*, *Treponema denticola*, *Fusobacterium nucleatum*, and *Eikenella corrodens* have been closely associated to periodontitis.[21]

After the publication of several studies by Van Dyke, Offenbacher and Heaton, the existence of certain risk factors (genetic and acquired) that can modulate the susceptibility or resistance of the host to periodontitis, is accepted. Hence, this disease has a multifactorial aetiology.[19,22,23] There is great interest in developing indicators that allow for identification of susceptible individuals and to identify modifiable risk factors that can prevent or alter the course of periodontitis.[19] With the recent discovery of possible associations between periodontal disease and systemic health, the research on susceptibility to periodontitis has taken a broader and more significant meaning.[19]

The prevalence of periodontitis varies in different regions of the world, according to the case definition used and the studied population.[20] In the United States, the National Health and Nutrition Examination Survey (NHANES 2009–2014), reported in a sample of 10,683 participants aged 30 years or older that 42.2% of adults presented periodontitis with a distribution of 7.8% for severe periodontitis and 34.4% for non-severe periodontitis (mild or moderate).[24] The mean age of the population examined was 50.8 years. Periodontitis was greatest among men (50.2%), Mexican Americans (59.7%), adults below 100% of the federal poverty levels (60.4%), current smokers (62.4%), and those who self-reported diabetes (59.9%).[24] In general, the occurrence of periodontitis decreases with improved quality of life. It tends to be more common in economically disadvantaged populations.[25] Individuals from Yemen, Israel, North of Africa, South Asia and the Mediterranean present a greater prevalence of periodontitis compared to Europeans.[25]

Biological plausibility

The underlying biological mechanisms of the association between obesity and periodontitis involve adipose tissue-derived cytokines and hormones (also known as adipokines).[26] Obesity is associated with a chronic low-grade inflammatory state due to increased expression of pro-inflammatory adipokines and diminished expression of anti-inflammatory adipokines.[27] Pro-inflammatory adipokines include TNF-α, IL-6, leptin, resistin, among others. In addition to the numerous adipokines with pro-inflammatory effect, adipose tissue secretes a smaller number of anti-inflammatory factors including adiponectin.[27]

Many researchers agree that the most important mediators related to obesity and periodontitis are TNF-α, IL-6, which are involved in the pathophysiology of both diseases.[8] It appears that pro-inflammatory biomarkers show a pleiotropic effect and can target specific cells by controlling activation of cells, cell proliferation and function in the periodontium. As a result, raised pro-inflammatory biomarkers levels such as TNF-α and IL-6 cause periodontal tissue destruction.[26] Leptin is a pleiotropic cytokine secreted by adipocytes, linked

Table 2 Systematic reviews and meta-analysis that have evaluated the association between obesity and periodontitis

Reference (authors, year)	Age range (years)	Studies included	OR or RR 95% (IC)	Main results
Chaffee and Weston, 2010.[3] Systematic review and meta-analysis	>18	28	OR 1.35 (1.23–1.47)	Positive association between obesity and periodontitis. Inability to distinguish the temporal ordering of events
Suvan *et al.*, 2011.[4] Systematic review and meta-analysis	>18	19	OR 1.81 (1.42–2.30)	Association between BMI overweight and obesity and periodontitis. The magnitude is unclear. Insufficient evidence to provide guidelines to clinicians on the clinical management of periodontitis in overweight and obese subjects
Moura-Grec *et al.*, 2014.[54] Systematic review and meta-analysis	>15	31	OR 1.30 (1.25–1.35)	Obesity was associated with periodontitis. The risk factors that aggravate these diseases should be better clarified to elucidate the direction of this association
Nascimento *et al.*, 2015.[55] Systematic review and meta-analysis	>18	5	RR 1.33 (1.21–1.47)	Positive association between weight gain and new cases of periodontitis; due that only prospective longitudinal studies were included. Results are originated from limited evidence and its results should be interpreted with precaution
Martinez-Herrera *et al.*, 2017.[56] Systematic review	>18	28	–	Nineteen observational studies and nine clinical trials. Obesity was associated with periodontitis in 17 observational studies. Insulin resistance could be implicated in the association between both diseases
Khan *et al.*, 2018.[57] Systematic review	13–17 to 18–34	25	–	Of 25 studies included, 17 showed an association between obesity and periodontitis in adolescents and young adults (OR ranged from 1.1–4.5)

to several systemic diseases. Besides the control of appetite, leptin stimulates energy expenditure and modulates lipid and bone metabolism, haematopoiesis, coagulation, the function of pancreatic beta cells, and insulin sensitivity.[14,28] Furthermore, leptin regulates the immune system and inflammatory response, with mainly pro-inflammatory behaviours.[14] An experimental study demonstrated that leptin negatively interferes with the regenerative capacity of periodontal ligament cells, suggesting that leptin may be one of many pathologic links between obesity and compromised periodontal healing.[28] Adiponectin is a circulating hormone that is involved in glucose and lipids metabolism; its levels are lower in subjects with obesity, insulin resistance, or type 2 diabetes. This substance improves insulin sensitivity and may have anti-atherogenic and anti-inflammatory properties.[27] In contrast, resistin exhibits a potent pro-inflammatory effect and is involved in several inflammatory diseases.[29] In humans, this cytokine forms part of inflammatory processes.[27] Zimmermann *et al.*[30] measured serum and gingival crevicular fluid levels of adipokines in obese and normal-weight subjects, with and without chronic periodontitis. They found that in serum, resistin levels were higher whereas adiponectin levels were lower in groups with periodontitis.[30] The role of resistin in inflammatory periodontal disease has yet to be clarified. Further research will shed light into the precise biological mechanism responsible for the association between these two diseases.

Studies

The initial report of this association in humans was established in 1998 by Saito *et al.*[5] who studied 241 Japanese subjects aged 20 to 59. Periodontal status was measured by the community periodontal index of treatment needs (CPITN). After adjusting for confounding variables such as age, sex, oral hygiene status and smoking history, the estimated odds ratio (OR) for periodontitis was 3.4 (95% CI, 1.2–9.6) in overweight and 8.6 (95% CI, 1.4–51.4) in obese subjects. Further studies from Japan,[31,32,33] the United States[8,34] and South Korea[35] also found that obesity was associated with an increased risk of periodontitis.

Al-Zahrani *et al.*, in a sample size of 13,655 participants from the NHANES III, reported a significant association between overall and abdominal obesity, with the prevalence of periodontitis in young participants (ages 18–34) with an adjusted OR of 2.27 (95% CI, 1.4–3.4).[7] In Brazil, Dalla Vecchia *et al.*[36] evaluated the relationship between overweight, obesity and periodontitis. Overweight and obesity were assessed by BMI using the WHO criteria and periodontitis was defined as ≥30% of teeth with clinical attachment loss ≥5 mm. The authors found that obesity was only associated with periodontitis in non-smoker women (OR 3.4, 95% CI, 1.4–8.2). The association between periodontitis and obesity, but not overweight, is confirmed by Khader *et al.*[6] who, in a sample of 340 Jordanian adult subjects, reported that the association was not different between normal and overweight participants. Obese subjects had three times the probability of having periodontitis compared to subjects with normal weight (OR 2.9, 95% CI, 1.3–6.1). A more recent study by Eke *et al.*[24] analysed 10,683 participants aged 30 years or older from the NHANES 2009–2014. They found that periodontitis was more prevalent among people with co-occurring chronic conditions. Periodontitis significantly co-occurred with diabetes and increasing number of missing teeth but not with obesity.[24]

Although most evidence has come from cross-sectional studies, stronger evidence has come from longitudinal studies. Linden *et al.*[37] evaluated the association between obesity and periodontitis in a group of 60–70-year-old Western European men. They assessed the periodontitis at two levels, as suggested by Tonetti and Claffey.[38] Obesity increased prevalence of periodontitis (OR 1.77, 95% CI, 1.2–2.6) when they used a low-threshold definition (at least two teeth with ≥6 mm loss of attachment and at least one site with a pocket of ≥5 mm). However, with a high-threshold definition (≥15% of sites with attachment loss ≥6 mm and at least one site with pocket of ≥6 mm) obesity was not significantly associated with periodontitis.[37] A prospective study in Finland by Saxlin *et al.*,[39] of 214 non-diabetic subjects who had never smoked, concluded that body weight was weakly but not statistically significantly associated with the development of periodontal infection (RR 1.3, 95% CI, 0.7–2.1). However, the authors stated that the results of their study should be interpreted cautiously due to its small size.[39] Gorman *et al.*[40] in a longitudinal study with criteria for periodontitis which met the

threshold (two or more teeth with alveolar bone loss ≥40%, probing pocket depth ≥5 mm, or clinical attachment loss ≥5 mm) found that overall obesity and central adiposity are associated with an increased hazard of periodontal disease progression events in men (41–72% higher).[40]

Significant variability exists in the definitions used to identify periodontitis, with few studies that meet stringent criteria for periodontitis. For example, one study utilised loss of clinical attachment as the only diagnostic criterion for periodontitis,[36] which is inappropriate because this disease cannot be reflected by measurements of a single variable.[41] Loss of clinical attachment is considered a physiological condition that takes place during the ageing process. Even though it is one of the clinical signs of periodontitis, it may occur in the absence of this disease.[42] In other studies, the criterion used to define periodontitis included shallow pockets and was >3.5 mm,[5,31] which could be considered low-level periodontal damage. The use of low thresholds results in a higher number of subjects with periodontitis. The lack of consensus across accepted case definitions for periodontitis also complicates the comparison of prevalence estimates across surveys.[43] The strength of the association between obesity and periodontitis may be overestimated due to the definitions used in the evaluated studies. Currently, it is recommended to use the case definitions originally developed by the Centre for Disease Control, and the American Academy of Periodontology (CDC/AAP) to provide standardised clinical case definitions for population-based studies of periodontitis.[41,44] The case definition for periodontitis requires ≥two interproximal sites with attachment loss ≥3 mm, and ≥two interproximal sites with probing depth ≥4 mm not on same tooth, or one site with probing depth ≥5 mm).[41] Use of these standards could facilitate comparison of periodontal prevalence estimates worldwide.[43]

Most of the studies that showed a positive association between obesity and periodontitis are cross-sectional,[5,6,7,31,32,36] in which the prevalence of periodontitis and obesity were ascertained at a single point in time and therefore a temporal sequence or cause and effect cannot be determined.[45] Cross-sectional studies describe the frequency and distribution of events of health and disease. Although they are also used to explore and generate research hypotheses, they only provide information from one observation performed at a single point in time. Therefore, to reach a causal relationship, it is necessary to develop studies specifically designed for this purpose.[45]

Furthermore, the risk factors that aggravate these conditions must be clarified to determine the direction of the association. An example is diabetes mellitus is a metabolic disorder characterised by the presence of hyperglycaemia due to defective insulin secretion, defective insulin action or both.[46] It is well established that obesity is an independent risk factor for type 2 diabetes.[47,48] Recent studies have identified links between obesity and diabetes involving pro-inflammatory cytokines, deranged fatty acid metabolism, insulin resistance, and cellular processes such as mitochondrial dysfunction and endoplasmic reticulum stress.[48,49,50] Numerous epidemiological studies also document the association between type 2 diabetes and periodontitis.[51,52] In fact, Löe described periodontal disease as the sixth complication of diabetes.[53] This statement implies that diabetes can be a confounding variable of the association between obesity and periodontitis, and thus should be controlled when performing cross-sectional studies.

Several systematic reviews and meta-analysis evaluated the relationship between obesity and periodontitis in the last decade (Table 2).[3,4,54,56,57] Chaffee and Weston[3] found a positive association between these two diseases in 41 of the 70 studies included in their review. A meta-analysis of 28 studies reported an OR of 1.35 (95% CI, 1.23–1.47) for the association between obesity and periodontitis. Suvan *et al.*[4] reported a stronger association between both conditions with an OR of 1.81 (95% CI, 1.42–2.30) from a meta-analysis of 19 studies. Nascimento *et al.*,[55] in a meta-analysis from prospective longitudinal studies, concluded that subjects who became obese had an increased relative risk of 1.33 (95% CI, 1.21–1.47) of developing periodontitis compared with counterparts who stayed within normal weight. The results do provide a clear positive association between weight gain and new cases of periodontitis. However, the authors stated that this conclusion should be interpreted carefully due to limited evidence. A more recent meta-analysis included 25 studies from 12 countries, from which 17 showed an association between obesity and periodontitis (OR ranged from 1.1–4.5).[57] These systematic reviews concluded that it is possible to find a high prevalence of periodontitis in obese subjects.

The influence of obesity on periodontal treatment

The relationship between body weight and periodontitis appears clearer when the influence of obesity in periodontal disease treatment is studied. Interventional studies provide the strongest evidence of a causal relationship and can provide further evidence for the benefit of eliminating the risk factor.[19] Lakkis *et al.*[58] evaluated whether weight loss by bariatric surgery in initially obese subjects can improve the response to non-surgical periodontal therapy. They found a statistically significant improvement in the response of these subjects to periodontal treatment compared to obese subjects (the control group). Probing depth had a mean reduction of 0.45 mm vs 0.28 mm, the reduction in clinical attachment loss was 0.44 mm vs 0.3 mm, the percentage of sites with bleeding on probing 16% vs 15% and the gingival index was 1.03 vs 0.52 in the bariatric surgery group vs the control group, respectively. Although these measurements have a statistically significant impact ($p < 0.05$), the clinical relevance may be debatable. These results contrast with those reported by Zuza *et al.*[59] who showed that non-surgical periodontal treatment allows the reduction of all clinical parameters of inflammation in obese and normal-weight subjects, supporting that obesity does not negatively affect the success of periodontal therapy. Altay *et al.*[60] reported similar findings.

Gerber *et al.*,[9] in a systematic review, reported that obesity has a clear negative effect on the outcome of non-surgical periodontal therapy in five of eight studies. The remaining three studies did not report treatment differences between obese and normal-weight participants. However, the authors stated that the included studies did not correspond to the highest level of quality. Nascimento *et al.*[61] and Papageorgiou *et al.*[62] found no differences in clinical periodontal parameters between obese and non-obese subjects in the included studies in their meta-analysis. In summary, obesity does not appear to play a negative role in the treatment outcome of non-surgical periodontal therapy. However, the available evidence is variable.

Conclusion and future perspective

The present review suggests a positive association between these two conditions with a general direction that could be from obesity to periodontitis. The relationship between these

two disorders could travel through multiple pathways. However, these results should be interpreted cautiously due to the heterogeneity of criteria to assess periodontitis and the paucity of longitudinal studies, which hamper our ability to determine the relative contribution of periodontitis to obesity. Further research should take into consideration an adequate definition of cases of periodontitis based on the criteria previously established by the CDC/AAP. Presently, there is limited evidence to recommend changes in treatment planning.

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