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REVIEW ARTICLE

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The association of periodontal diseases with metabolic syndrome and obesity

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1 | INTRODUCTION

Periodontitis is a chronic noncommunicable disease that shares social determinants and risk factors with the major noncommunicable diseases that cause around two-thirds of deaths such as heart disease, diabetes, cancer, and chronic respiratory disease.[1] Obesity, poor nutrition, and physical inactivity have been associated with an increased risk of periodontitis.[2,3] Trends in risk factors are likely to impact the burden of periodontitis and the obesity/diabetic epidemic will further drive incident periodontitis.[1] Recently, the importance of obesity has also been recognized by the new classification of periodontal diseases and conditions. Here, obesity is recognized as one of the systemic conditions/metabolic disorders that affect the periodontal attachment apparatus by influencing periodontal inflammation.[4,5] Metabolic syndrome is a group of conditions defined by the presence of obesity, dyslipidemia, hypertension, and dysglycemia leading to an increased risk of diabetes and cardiovascular disease. A bidirectional relationship between periodontal disease and metabolic syndrome/obesity has been suggested. It is the purpose of this review to give an update on the evidence from epidemiologic, mechanistic, and intervention studies regarding the link between periodontitis, obesity, and metabolic syndrome.

2 | OBESITY

Obesity is defined as abnormal or excessive fat accumulation that presents a risk to health.[6] It is also considered to be a complex multifactorial chronic disease.[7] Initially, alteration of the body's fat stores occurs because of an imbalance of energy intake and expenditure, also referred to as overnutrition. This in turn may initiate interactions of environmental, genetic, and neuroendocrine factors involved in the complex feedback systems in response to food intake or activity of the fat cells.[8,9] More than ever before, it is understood that systemic inflammation occurs as a consequence of obesity.[10]

With adipose tissue at the forefront of understanding obesity and its associated health consequences, measurements of overweight or obesity aim to quantify the amount or proportion of fat tissue in an individual's body. Originally used in epidemiologic studies, body mass index, calculated as body weight in relation to height, is used in measuring/categorizing obesity, and is defined as a body mass index of ≥ 30 kg/m^2, with overweight categorized as a body mass index of 25-29.99 kg/m^2. It is recognized that body mass index is valuable in assessing possible risk but may be less meaningful at an individual level because of differences in fat distribution. Recognition of the role of visceral fat in increased health risk has resulted in measurements of waist circumference or waist-hip ratio. The threshold

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of waist circumference defined as related to increased health risk is 94 cm for men and 80 cm for women.[11] As mentioned, obesity is a complex multifactorial chronic inflammatory disease, therefore such measures suggest a level of risk of comorbidities rather than a diagnosis of metabolic state.

The World Health Organization predicted obesity as an emerging epidemic in the late 1990s. Amidst the current worldwide epidemic, 1.9 billion people are now overweight, of whom 650 million are obese. This equates to 39% of adults aged ≥ 18 years[12] (Figure 1). In 2016, worldwide, 41 million children aged < 5 years, and 340 million aged 5-19 years, were reported as overweight or obese. This represents an increase from 4% in 1975 to 18% in 2016.[12] Perhaps more devastating are the common health consequences of obesity, which have also increased over recent decades. These include cardiovascular diseases, metabolic diseases such as diabetes, musculoskeletal disorders, and some cancers.[13]

Investigation of metabolic disorders has identified a distinct relationship between excess nutrition and innate immune system activation in organs that play a role in energy homeostasis, with the result referred to as obesity-induced inflammation. Characteristic of obesity-induced inflammation is its involvement of numerous organs, including the pancreas, liver, skeletal muscle, heart, and brain, in addition to adipose cells.[14] Research from the last 2 decades has confirmed that adipose tissue is actively involved in regulation of inflammation and immunity associated with the dysregulated or altered release of a variety of pro-inflammatory and anti-inflammatory factors (eg leptin, adiponectin, cytokines, and chemokines).[13] Variations exist in the type and location of fat tissue and their role in inflammation with visceral fat (associated with central adiposity) demonstrating greater activity than peripheral fat cells in the production of endocrine secretions responsible for the effect of fat mass on immune function.[15,16]

The crucial role of adipose tissue in obesity-related systemic inflammation is attributed to this active production of hormones and cytokines acting as the link with many comorbidities of obesity.[17] Obese fat tissue (enlarged adipocytes compared with lean fat tissue), characterized by macrophage accumulation because of migration of inflammatory monocytes that infiltrate from the circulation into the adipose tissue, results in tumor necrosis factor-alpha and interleukin-6 secretion by both adipocytes and macrophages. These cytokines, also classified as adipo(cyto)kines, have been shown to regulate systemic inflammation, affecting insulin sensitivity and glucose metabolism (associated with chemokine signaling). Interleukin-6 is associated with decreased insulin signaling and induction of fatty acid oxidation as well as secretion of C-reactive protein by the liver. Interleukin-6 expression and lipolysis (in the fat cells) are increased by tumor necrosis factor-alpha and are known to play a role in insulin resistance.[18,19] Evidence has demonstrated that some of the anti- or pro-inflammatory effects of adipokines are active in innate immune response, and others stimulate an adaptive immune response.[19]

3 | METABOLIC SYNDROME

The metabolic syndrome consists of a spectrum of conditions—a group of metabolic abnormalities—associated with an increased risk of developing type 2 diabetes mellitus and cardiovascular disease.[20] The metabolic syndrome has been recognized as a predominant factor for the development of atherosclerotic cardiovascular disease.[21] All of the risk factors for cardiovascular disease that are comprised in the metabolic syndrome, namely hypertension, dyslipidemia, and type 2 diabetes mellitus along with its main clinical outcome atherosclerotic cardiovascular disease, contribute to a large extent to global morbidity and mortality.[22,23]

Several health organizations have proposed diagnostic criteria for the metabolic syndrome that vary slightly but all focus on the following conditions: obesity (particularly central adiposity), dyslipidemia (low high-density lipoprotein cholesterol levels, or elevated

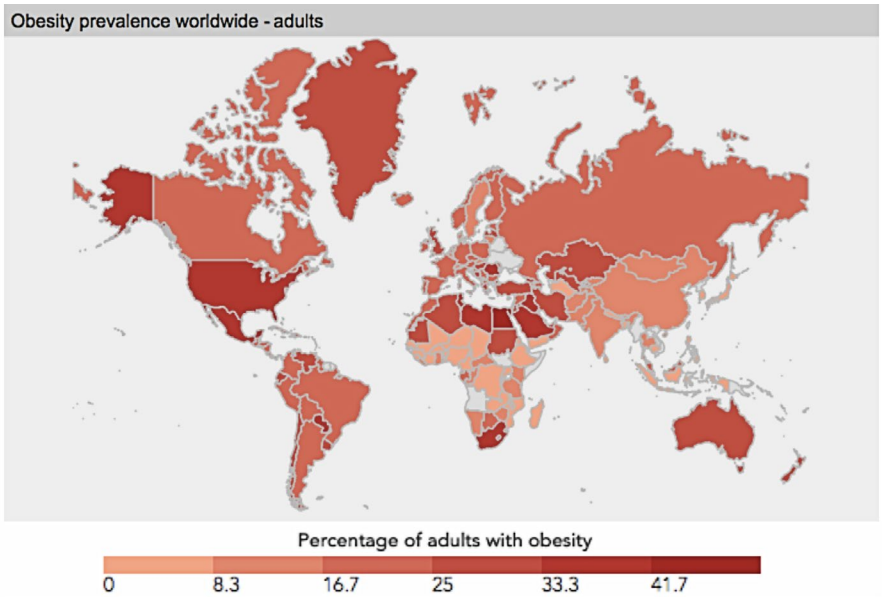

FIGURE 1 Prevalence of obesity in 2017. World Obesity Federation (with permission)[232]

triglyceride levels), hypertension, and dysglycemia.[24] The most commonly referenced diagnostic criteria for the metabolic syndrome were developed by The National Cholesterol Education Program's Adult Treatment Panel III.[25] They were revised by the American Heart Association and National Heart, Lung, and Blood Institute.[26] Both diagnostic criteria define the metabolic syndrome as the presence of three or more conditions from a list of five. Separate diagnostic criteria for the metabolic syndrome were established by the International Diabetes Federation[27] with central obesity as a requirement, and the World Health Organization[28] with dysglycemia as a requirement. For harmonization the metabolic syndrome has been defined as the presence of three out of the above interrelated conditions.[29]

The most frequent components of the metabolic syndrome are abdominal obesity, hypertension, and hyperglycemia.[30] As the number of components of the metabolic syndrome increases, the probability of sequelae, such as cardiovascular disease and type 2 diabetes mellitus, appears to increase.[31] The presence of three metabolic syndrome components has been reported to increase the risk for cardiovascular disease by 2.7 times, and by 5.9 times if four or more components exist. The presence of three metabolic syndrome components increases the risk for type 2 diabetes by nearly 10-fold, and the presence of four or more components by nearly 35 times.[32]

The prevalence of metabolic syndrome has increased over the last decade, with an estimated prevalence of 34.7% in the USA in 2011-2012. In adults aged ≥ 60 years the reported prevalence was 46.7% compared with 18.3% in the 20-39 years age group.[33] Indeed, the risk of developing this condition increases with age. From 2003 to 2012, the overall prevalence of the metabolic syndrome in the USA was 33% (95% CI, 32.5-33.5), with significantly higher prevalence in women compared with men (35.6% vs 30.3%). When stratified by race/ethnicity, the highest prevalence of the metabolic syndrome was seen in Hispanics (35.4%; 95% CI, 34.2-36.6), followed by non-Hispanic whites (33.4%; 95% CI, 32.6-34.2) and blacks (32.7%; 95% CI, 31.5-33.9). Overall, prevalence of the metabolic syndrome increased from 32.9% (95% CI, 31.6-34.2) in 2003-2004 to 34.7% (95% CI, 33.5-36.0) in 2011-2012. Among patients aged ≥ 60 years, more than 50% of women and Hispanics had the metabolic syndrome. A recent meta-analysis of cross-sectional studies on the prevalence of metabolic syndrome in Middle East countries revealed that prevalence rates fluctuated by country and time of study. They were 2.2%-44% in Turkey, 16%-41% in Saudi Arabia, 14%-63% in Pakistan, 26%-33% in Qatar, 9%-36% in Kuwait, 22%-50% in the United Arab Emirates, 6%-42% in Iran, and up to 23% in Yemen. The pooled estimate amounted to 25%.[34]

It is interesting to note that although there is evidence that body mass index predicts metabolic syndrome, metabolic abnormalities may also be present in individuals who are not overweight or obese. A total of 1367 Asian adults were assessed for the prevalence of metabolic syndrome across different body mass index categories using the thresholds proposed by the World Health Organization for Asian populations. The overall prevalence of metabolic syndrome was 51% with the condition diagnosed in 29.6% of the body mass index normal (body mass index 18.5-22.9 kg/m^2), 38.9% of the overweight (body mass index 23-24.9 kg/m^2), 56.9% of pre-obese (body mass index 25-29.9 kg/m^2), and 62.4% of obese (body mass index 25-29.9 kg/m^2). The prevalence of central adiposity was highest in those individuals with metabolic syndrome. This distribution across body mass index groups suggests a dose response relationship but also demonstrates that high body mass index or excess weight is associated but not required for the presence of metabolic dysregulation.[35]

Metabolic syndrome is believed to originate from a pro-inflammatory state, which can occur as a result of the effects of insulin resistance. Insulin resistance is associated with an increasing body mass index and increasing waist circumference, reflecting increased deposition of visceral adipose tissue.[36] Insulin resistance may also be induced by oxidative stress, which is significantly higher in individuals with the metabolic syndrome compared with controls.[37]

Plausible relationships exist between metabolic syndrome, obesity, and periodontal disease.[24,38,39] The so-called adipose/metabolic inflammation is the body adapting to overnutrition. In a generic sense, the metabolic syndrome most often reflects the response of the body to factors produced by adipose tissue. Periodontitis, also chronic inflammatory in nature, shares common inflammatory pathways with the metabolic syndrome and obesity. The section which follows highlights the current evidence from epidemiologic studies reporting on the association between periodontal disease, metabolic syndrome, and obesity.

4 | EPIDEMIOLOGIC EVIDENCE OF THE ASSOCIATION BETWEEN PERIODONTAL DISEASE AND METABOLIC SYNDROME, AND OBESITY

4.1 | Periodontal disease and metabolic syndrome

Electronic searches of Ovid PubMed, and EMBASE resulted in identification of three systematic reviews[40-42] and numerous narrative reviews reporting on the association between periodontitis and metabolic syndrome published over the preceding 5 years. The three systematic reviews included 45 original articles in total, 42 of which were cross-sectional, and three which were longitudinal.

The review by Nibali et al[40] included 20 articles, 16 of which were included in the most recent review published by Daudt et al[41] summarizing 33 articles, with many additional articles that were published since 2014. Daudt et al excluded the four studies differing between the two reviews as periodontal assessment was based upon radiographs rather than clinical assessments. The review by Watanabe and Cho[42] included 26 articles, of which 14 overlapped with the first review and 16 with the most recent review. They included six publications from 2010 to 2013 that were not contained in the other two reviews. The findings reported in the three systematic reviews were largely in agreement. A summary of the three reviews is presented in Table 1.

TABLE 1 Characteristics of systematic reviews of epidemiologic evidence of metabolic syndrome and periodontitis in adults (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Metabolic syndrome case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Nibali et al[40] UK Association between metabolic syndrome and periodontitis: A systematic review and meta-analysis	Designs: All epidemiologic study designs other case series Sample: Adults Search: MEDLINE, EMBASE, LILACS, Cochrane databases Language: No restrictions Year: Up to including May 2012	Primarily 1 of 3 definitions applied to define metabolic syndrome: Adult Treatment Panel III, National Cholesterol Education Program criteria, or International Diabetes Federation criteria	Minimum 5 different definitions/criteria reported to categorize as periodontal disease. A number set arbitrary thresholds of PPD or CAL averages to define periodontitis	No. of included studies: 20 studies 19 cross-sectional/case-control and 1 longitudinal Meta-analysis: 18 studies Increased odds of the presence of metabolic syndrome in the presence of periodontitis OR 1.71 (95% CI 1.42, 2.03) Meta-analysis of 7 studies reporting a secure definition of periodontitis resulted in higher risk of presence of metabolic syndrome, OR 2.09 (95% CI 1.28, 3.44)	Analysis demonstrates clear evidence of an association between periodontitis and metabolic syndrome, however, the direction and magnitude is unclear.
Watanabe and Cho[42] USA Periodontal disease and metabolic syndrome: A qualitative critical review of their associatio n	Designs: All epidemiologic study designs other than case series Sample: Adults Search: PubMed, SCOPUS, and Cochrane databases Language: English Year: Up to including December 2013	12 definitions used to define metabolic syndrome with varying combinations of metabolic syndrome components	16 different definitions/ criteria reported to categorize as periodontal disease with defined thresholds differing within the named parameter	No. of included studies: 26 studies 21 cross-sectional, 3 case-control and 2 longitudinal Meta-analysis: None All studies showed positive association Difficult to distinguish if periodontitis or metabolic syndrome was the dependent/independent variable in a number of studies OR of primary studies range: 1.52-4.70 Smoking, age, and gender cited as confounders	Because of heterogeneity of study definitions of periodontitis and metabolic syndrome, and lack of longitudinal studies, difficult to conclude the contribution of periodontitis to metabolic syndrome.
Daudt et al[41] BrazilAssociation between metabolic syndrome and periodontitis: a systematic review and meta-analysis	Designs: Observational studies Sample: Adults Search: MEDLINE, EMBASE, Cochrane databases Language: No language restrictions Year: No restriction up to including May 2017	7 definitions applied to determine presence of metabolic syndrome	Full mouth assessment in 17 studies, partial in 16 studies, 18 studies used common definitions while the other 15 varied	No. of included studies: 33 studies 29 cross-sectional, 2 case-control, and 2 cohort Meta-analysis: 26 studies Increased risk of metabolic syndrome in presence of periodontitis with OR 1.38, 95% CI 1.26-1.51 Subgroup analysis of studies reporting full mouth periodontal assessment vs partial mouth assessments resulted in differing ORs: Full mouth assessment OR 1.16, 95% CI 1.08-1.25. Partial mouth assessment OR 1.58, 95% CI 1.38-1.82.	Findings suggest a positive association between metabolic syndrome and periodontitis. Prospective studies indicated to determine cause-and-effect relationship.

Abbreviations: CAL, clinical attachment level; CI, confidence interval; OR, odds ratio; PPD, periodontal probing depth; RR, relative risk.

The earliest systematic review reported coexistence of metabolic syndrome and periodontitis based upon increased odds of the presence of metabolic syndrome in periodontitis patients, with an odds ratio of 1.71 (95% CI, 1.42-2.03).[40] Because of the variability of case definitions of periodontitis, the authors chose to classify the included study populations as either insecure diagnosis of periodontitis or secure diagnosis of periodontitis based upon the reported case definition. Meta-analysis of those studies reporting a secure diagnosis of periodontitis according to the authors' criteria resulted in a higher odds ratio of 2.09 (95% CI 1.28-3.44). The need for longitudinal studies to confirm a temporal association was highlighted.[40]

The subsequent systematic review did not include a meta-analysis as the authors deemed study heterogeneity as too great to support appropriate meta-analysis.[41] The authors noted that in many of the included studies it was unclear as to whether evidence supported periodontitis as contributing to metabolic syndrome or the opposite, that is, the presence of metabolic syndrome contributing to the presence of periodontitis. Odds ratios reported in the included studies ranged from 1.52 to 4.70, although the direction was unclear.[42]

Meta-analysis of 26 studies demonstrated an association between metabolic syndrome and periodontitis with an odds ratio of 1.38 (95% CI, 1.26-1.51).[41] The authors suggested that individuals with metabolic syndrome were 38% more likely to have periodontitis; however, the results of individual included studies sometimes appeared to present the odds of having metabolic syndrome if periodontitis was present. When a subgroup analysis was performed of those studies reporting full mouth periodontal assessment, the odds

ratio was 1.16 (95% CI, 1.08-1.25), while partial mouth examination resulted in an odds ratio of 1.58 (95% CI, 1.38-1.82).

The challenge with the evidence emerging from cross-sectional observational studies is that the direction of the association is difficult to ascertain because of lack of knowledge of the temporal sequence of the conditions. Longitudinal studies are required to determine causality or to define the direction of a proposed association. As mentioned in all of the systematic reviews, longitudinal evidence of the association of the metabolic syndrome and periodontal diseases is minimal. Such studies are very difficult to conduct and require an extensive length of time.

One longitudinal study reported an increased risk of 60% (OR 1.6, 95% CI 1.10-2.20) of reporting at least one metabolic syndrome symptom after 4 years of follow-up if an individual had periodontitis.43 Another longitudinal study tested the relationship between body mass index at baseline and the 5-year incidence of periodontal disease in a sample of 2787 males and 803 females.[44] The hazard ratios for developing periodontal disease after 5 years were 1.30 ($P < .001$) and 1.44 ($P = .072$) in men and 1.70 ($P < .01$) and 3.24 ($P < .05$) in women for those with body mass indexes of 25-30 and ≥ 30, respectively, compared with those with a body mass index of < 22, demonstrating a dose-response relationship between body mass index and the development of periodontal disease. A more recent longitudinal study published subsequent to the three systematic reviews investigated the relationship of toothbrushing with the development of metabolic syndrome using a retrospective 5-year follow-up design.[45] The study included 3722 participants ranging in age from 35 to 64 years with two or less metabolic syndrome components at baseline. During the 5-year follow-up, 11.1% of the participants developed metabolic syndrome. Participants brushing ≥ 3 times per day had a significantly lower risk of developing metabolic syndrome than those brushing their teeth ≤ 1 time per day (OR 0.64, 95% CI 0.45-0.92). Results also showed that participants with periodontitis had 44% higher odds of developing metabolic syndrome than those without periodontal disease (OR = 1.44, 95% CI 1.16-1.77).[45]

Although cross-sectional evidence supports an association between periodontal disease and metabolic syndrome, there is still much to learn. Consideration of the association between the components of metabolic syndrome and periodontitis individually, although not functioning mutually exclusively of each other, have the potential to contribute to the understanding of these complex inflammatory and metabolic conditions.

4.2 | Periodontal disease and hyperlipidemia

Electronic searches of Ovid PubMed, and EMBASE with a focus on epidemiologic evidence resulted in identification of two systematic reviews reporting on the association between periodontitis and serum lipid levels published over the last 5 years.[46,47] The two reviews comprised 22 original articles in total, 19 of which were cross-sectional, and three of which were longitudinal. The review by Lianhui et al[46] included seven articles (six case-control studies and one cohort study) while the most recent review published by Nepomuceno et al[47] summarized 19 articles (16 case-control and three cohort studies). Comparison of the two reviews identified an overlap of four articles, including one of the longitudinal studies. Evidence pertaining to the association of periodontitis and hyperlipidemia showed significant associations between cholesterol, triglycerides, low-density and high-density lipoprotein levels, and periodontal disease. A summary of the two reviews is presented in Table 2.

Results of meta-analysis reported by Lianhui et al[46] showed that the risk of having elevated serum triglyceride or total cholesterol levels was significantly higher in patients with periodontitis than in the periodontally healthy group (OR 4.73, 95% CI 2.74-8.17 and OR 3.62, 95% CI 2.18-6.03, respectively). No significant differences were found for high-density or low-density lipoprotein cholesterol between patients with periodontitis and periodontally healthy patients.[46] The authors concluded that periodontitis is an independent risk factor for hyperlipidemia, in particular serum total cholesterol and serum triglycerides. Results reported by Nepomuceno et al[47] were in agreement with these results in that chronic periodontitis patients demonstrated significantly higher levels of total cholesterol (MD 13.41, $P = .004$) and triglycerides (MD 21.94, $P = .004$) compared with periodontally healthy individuals. In addition, periodontitis patients had higher low-density lipoprotein (MD 11.04, $P = .002$) and lower high-density lipoprotein levels (MD -4.60, $P = .0005$) compared with those without periodontitis.[47] These results suggest that periodontal disease is associated with a reduction in high-density lipoprotein and elevated total cholesterol, triglyceride, and low-density lipoprotein levels. In both reviews, heterogeneity was reported to be high because of differences in the definition of periodontal status.

Longitudinal studies included in the two reviews were few and reported increased odds of development of hyperlipidemia. An additional retrospective cohort study, not included in these reviews, reported that over a 4-year period, individuals with community periodontal index scores of ≥ 3 were 1.9 times more likely to develop atherogenic dyslipidemia than those with lower community periodontal index scores.[43]

4.3 | Periodontal disease and hyperglycemia

The association between periodontal disease and diabetes mellitus is well established with consistent findings across numerous studies. Individuals with diabetes have a higher risk of periodontal disease onset and progression. Electronic searches of Ovid PubMed, and EMBASE with a focus on epidemiologic data resulted in identification of three systematic reviews published since 2013 investigating the association between diabetes mellitus and periodontal disease.48-50 The three systematic reviews comprised 64 original articles in total, 31 cross-sectional, 13 case-control, and 19 cohort studies, and one randomized clinical trial. The review published by

TABLE 2 Characteristics of systematic reviews of epidemiologic evidence of hyperlipidemia and periodontitis in adults (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Hyperlipidemia definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Lianhui et al[46] China Association between chronic periodontitis and hyperlipidemia: a meta-analysis based on observational studies	Designs: All study designs other than case series Sample: Adults Search: PubMed, Cochrane library, EMBASE, CBM, CNKI, Wanfang, and VIP databases Language: English and Chinese Year: Up to and including July 2016	Standard lab definitions of normal used for total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides; however, these varied by country	5 different definitions/ criteria reported to categorise as periodontal disease	No. of included studies: 7 studies (6 case-control, 1 cohort) Meta-analysis: 5-7 studies Serum triglyceride levels higher in periodontitis patients compared with periodontally healthy patients (MD = 50.50, 95% CI 39.57-61.42) as well as serum total cholesterol (MD = 17.54, 95% CI 10.91-24.18). Elevated risk of higher than normal triglyceride level associated with periodontitis (OR 4.73, 95% CI 2.74-8.17) Elevated risk of higher than normal total cholesterol level associated with periodontitis (OR 3.62, 95% CI 2.18-6.03)	A correlation exists between chronic periodontitis and hyperlipidemia and chronic periodontitis. Chronic periodontitis is an independent risk factor for hyperlipidemia (especially total cholesterol and serum triglyceride)
Nepomuceno et al[47] Brazil Serum lipid levels in patients with periodontal disease: A meta-analysis and meta-regression	Designs: All study designs other then case series Sample: Adults Search: PubMed, Web of Science, SCOPUS, EMBASE, Cochrane library Language: Not reported Year: Up to and including February 2016	Standard lab values used for threshold definitions but these varied by study. Some studies reported fasting sample collection and others non-fasting	Approximately 8 different definitions/ criteria reported to categorize as periodontal disease. Studies categorized as secure vs non-secure diagnosis for meta-analysis	No. of included studies: 19 16 cross-sectional, 3 longitudinal Meta-analysis: 19 studies Total cholesterol: Periodontitis cases presented significantly higher serum levels of total cholesterol than periodontally healthy (MD = 13.41, P = .004)	Periodontitis significantly associated with reduction in HDL and elevation of LDL and triglyceride concentrations. Analysis supports that periodontal disease is associated with lipid metabolic control.

Abbreviations: CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MD, mean difference; OR, odds ratio.

Borgnakke et al[48] included 17 articles, while that of Graziani et al[49] covered 20 articles, and the one by Ziukaite et al[50] examined 27 articles. There were no common publications among the three reviews, partially because of year restrictions placed on the electronic searches. All of the reviews addressed the question of the effect of periodontal disease or periodontitis on diabetes or hyperglycemic control. All authors concluded that periodontal disease has adverse effects on diabetes outcomes or glycemic control. One review noted that differences in individual study results differ according to geographic location. A summary of the three reviews is presented in Table 3.

The defined focus of the review by Borgnakke et al[48] was to investigate the effect of periodontitis on diabetes mellitus, therefore eligibility criteria for the systematic review were set to only include studies that permit the determination of directionality of the observed effects. As stated previously, a common source of heterogeneity identified by the various reviews was the difficulty in determining the direction of effect, therefore limiting interpretation of the findings. The authors did not choose to combine data using a meta-analysis but grouped primary studies within the context of common research questions. Describing the results of included studies, summary statements concluded that periodontitis patients have a greater risk of having poorer glycemic control than their counterparts without periodontitis regardless of whether they currently have type 2 diabetes, pre-diabetes, or no diabetes. Furthermore, those with periodontitis and type 1 or type 2 diabetes have a greater risk of diabetes-related complications than those without periodontitis. Lastly, individuals with periodontitis and no diabetes have a greater risk of developing diabetes than periodontally healthy individuals.[48] The recent systematic review conducted by Ziukaite et al[50] was designed to investigate the prevalence and odds of having diabetes in individuals who had been professionally diagnosed with periodontitis. The authors reported that the prevalence of diabetes was 13.1% in individuals with periodontitis compared with 9.6% in those without periodontitis. The prevalence of diabetes within periodontitis patients differed between Asia and Europe with the prevalence in Asian populations reported as 17.2% compared with 4.3% in European populations. The overall odds ratio of patients with periodontitis to have diabetes compared with non-periodontitis patients was 2.27 (95% CI 1.90-2.72). Although periodontitis was professionally diagnosed in the included studies, the authors reported that the presence of diabetes was sometimes based upon self-reporting.[50] The aim of the recent systematic review conducted by Graziani et al[49] was similar to that of Borgnakke et al,[48]-50 that is, a focus on the effect of periodontitis on diabetic control, incidence, and complications. In fact, it was designed as

TABLE 3 Characteristics of systematic reviews of epidemiologic evidence of hyperglycemia and periodontitis in adults (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Hyperglycemia definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Borgnakke et al[48] USA Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence	Designs: All epidemiologic study designs other than case series Sample: Adults Search: MEDLINE, Web of Science, EMBASE, Dentistry and Oral Sciences Source, CINAHL, EBM, SciVerse, LILACS. Language: Restricted to English Year: Up to and including January 2013	Most studies reported HbA1c, plasma glucose level of glucose tolerance test. Some discrepancies of thresholds. Some based upon self-report	Most studies reported full mouth clinical periodontal parameters. However, a variety of case definitions were reported.	No. of included studies: 17 studies 12 cohort, 3 cross-sectional, 2 case-control Meta-analysis: None Periodontitis patients with type 2 diabetes or no diabetes have a greater risk of developing poorer glycemic control. Those with periodontitis and type 1 or type 2 diabetes have a greater risk of diabetes-related complications. Those with periodontitis and no diabetes have a greater risk of developing diabetes.	Evidence suggests periodontal disease has an adverse effect on diabetes outcomes. Further longitudinal studies are needed.
Zuikaite et al[50] The Netherlands Prevalence of diabetes mellitus in people clinically diagnosed with periodontitis: A systematic review and meta-analysis of epidemiologic studies	Designs: All study designs other than case series Sample: Adults Search: MEDLINE, EMBASE, Cochrane Central Language: No language restrictions Year: No restriction up to and including September 2016	Most studies reported HbA1c, plasma glucose level of glucose tolerance test. Some discrepancies of thresholds and some based upon self-report.	Most studies reported full mouth clinical periodontal parameters. Various threshold case definitions reported.	No. of included studies: 27 studies 25 cross-sectional, 1 cohort, 1 RCT Meta-analysis: 16 studies Prevalence of diabetes 13.1% in subjects with periodontitis compared with 9.6% in those without periodontitis. Prevalence of diabetes in periodontitis study populations in Asia was 17.2% compared with 4.3% in periodontitis study populations in Europe. OR for patients with periodontitis to have diabetes was 2.27, 95% CI 1.90-2.72.	Prevalence and odds of having diabetes are higher within patients with periodontitis. Geographic differences of prevalence of diabetes in periodontitis patients with Asia having a higher prevalence than Europe.
Graziani et al[49] Italy A systematic review and meta-analysis of epidemiologic observational evidence on the effect of periodontitis on diabetes	Designs: All study designs other than case series Sample: Adults Search: MEDLINE, EMBASE, Cochrane Central Language: Restricted to English language Year: January 2013 up to January 2017.	Most studies reported HbA1c, plasma glucose level of glucose tolerance test. Some discrepancies of thresholds. Some based upon self-reporting.	Most studies reported full mouth clinical periodontal parameters. Periodontitis case definitions varied.	No. of included studies: 20 studies 3 cross-sectional, 6 cohort, 11 case-control Meta-analysis: None Nondiabetic individuals have poorer glycemic control if they have periodontitis and a higher risk of developing diabetes. Those with diabetes and periodontitis have poorer glycemic control and higher prevalence of diabetes-related complications	Periodontitis has a significant impact on diabetes control, incidence, and complications. Studies have high level of heterogeneity so interpretation with caution is recommended.

Abbreviations: CI, confidence interval; HbA1c, glycated hemoglobin; OR, odds ratio; RCT, randomized controlled trial.

an update to the previous review, and therefore grouped studies according to the same questions posed in the review published in 2013.[48] All 20 included studies were published subsequent to the conduct of the earlier review, therefore resulting in no overlap between the current and the previous review conducted by Borgnakke et al.[48] Based upon the 20 studies published since 2013, results were consistent with those of the previous systematic review. No meta-analysis was conducted; however, concluding statements based upon a summary of the primary study findings were that nondiabetic individuals have poorer glycemic control if they have periodontitis and have a higher risk of developing diabetes. Individuals with diabetes have poorer glycemic control if they have periodontitis and a higher prevalence of diabetes-related complications.[49]

4.4 | Periodontal disease and hypertension

Electronic searches of Ovid PubMed, and EMBASE resulted in identification of one published systematic review and one systematic review abstract on the association between periodontitis and hypertension in the previous 5 years.[51,52] The two reviews comprised 80 original articles in total, of which 59 were cross-sectional, nine were longitudinal, and 12 were intervention studies. All articles reported in the review by Martin-Cebezas et al[51] were included in the subsequent review by Munoz-Aguileira et al[52] with the exception of five publications. The two reviews were in agreement that the presence of periodontal disease was associated with a higher risk of diagnosis of hypertension. A summary of the two reviews is presented in Table 4.

TABLE 4 Characteristics of systematic reviews of epidemiologic evidence of hypertension and periodontitis in adults (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Hypertension definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Martin-Cabezas et al[51] France Association between periodontitis and arterial hypertension: A systematic review and meta-analysis	Designs: All study designs other than case series Sample: Adults Search: MEDLINE, Cochrane Central, Science Direct and Web of Science databases Language: Restricted to English Year: Up to and including June 2016	5 definitions reported to classify patients as hypertensive. Blood pressure recording methods varied across studies.	Approximately 11 definitions/criteria reported to categorize as periodontal disease	No. of included studies: 25 studies 20 cross-sectional, 3 case-control, 2 longitudinal Meta-analysis: 16 studies Moderate-severe periodontitis associated with hypertension with OR 1.50, 95% CI 1.27-1.78. Severe periodontitis demonstrated higher risk with OR 1.64, 95% CI, 1.23-2.19. High heterogeneity	Periodontal diseases are associated with a higher risk of hypertension, especially in the case of severe periodontitis. Longitudinal studies required to test temporal association.
Munoz Aguilera et al[52] UK Periodontitis and its treatment are associated with hypertension. A systematic review and meta-analysis	Designs: All study designs other than case series Sample: Adults Search: MEDLINE, EMBASE, Cochrane Central, LILACS, Web of Science Language: No restrictions Year: Up to and including October 2017	Most studies classified hypertension according to standard SBP/DBP thresholds. Some studies medical records or self-report. Blood pressure recording methods varied across studies.	Approximately 5 different outcome measures reported to categorize as periodontal disease; however, some based on partial mouth and others on full mouth and varying arbitrary thresholds set.	No. of included studies: 62 studies 46 cross-sectional, 9 case-control, 9 cohort, 12 intervention studies Meta-analysis: 21 studies Moderate-severe periodontitis associated with hypertension with OR 1.30, 95% CI 1.14-1.48. Severe periodontitis demonstrated a higher risk with OR 1.54, 95% CI, 1.03-2.03. High heterogeneity	Periodontitis is associated with an increased likelihood of diagnosis of hypertension. Future studies needed to determine nature of association and cause/effect relationship.

Abbreviations: CI, confidence interval. DBP, diastolic blood pressure; OR, odds ratio; SBP, systolic blood pressure.

Meta-analysis of cross-sectional studies showed that the presence of periodontitis was associated with hypertension (OR 1.50, 95% CI 1.27-1.78).[51] A further meta-analysis of a subset of studies selected as those reporting a secure diagnosis of severe periodontitis resulted in increased odds of hypertension associated with periodontitis of 1.64 (95% CI, 1.23-2.19).[51] The subsequent review[52] also reported an association between periodontitis and the presence of hypertension (OR 1.30, 95% CI 1.14-1.48). Meta-analysis based upon studies reporting the presence of severe periodontitis resulted in an increased estimate (OR 1.54, 95% CI 1.03-2.30). Furthermore, a meta-analysis of cohort studies in the review resulted in an odds ratio of 1.41 (95% CI 0.92-2.16) suggesting that periodontitis may be predictive of the development of hypertension, although these results were not statistically significant.

4.5 | Periodontal disease and obesity

Evidence from 14 systematic reviews reporting on the association of periodontal disease and obesity reported on in a recent meta-review suggests a positive association between obesity and periodontal disease onset, progression, and response to periodontal therapy.[54] Ten of these reviews were based upon epidemiologic data. Since then, one additional review has been published.[55] A summary of the 11 reviews is presented in Table 5 (adult populations) and Table 6 (adults, adolescents, or children).

The increased odds of having a form of periodontal disease if an individual is overweight or obese are consistently confirmed in the identified reviews based upon epidemiologic evidence in children, adolescents, and adults. [55-58,61-65] Various individual studies have reported a dose response relationship of the association between obesity and periodontitis with these findings highlighted in the conclusions of five of the systematic reviews.[55-58,60] A noteworthy study conducted in Brazil compared periodontal status based upon full mouth measurements in participants grouped according to World Health Organization body mass index categories reporting odds ratios of 1.20, 1.46, 1.78, and 2.31, respectively, for each body mass index category, inferring a dose-response association.[66] Questions still remain about the role of general obesity vs abdominal obesity in this possible dose-response relationship. A Brazilian study compared abdominal obesity with general obesity and reported no evidence of the effect of the latter on bleeding on probing while the former was linked to periodontal attachment loss and bleeding on probing.[67]

Only five of the identified systematic reviews included longitudinal studies.[56-58,63,65] Longitudinal studies were rare across the reviews but those included reported on the association between obesity and periodontitis progression, with five out of eight supporting a temporal sequence between them. A linear relationship between periodontitis progression and body mass index was reported by Morita et al[44] following a 5-year study of nearly 4000 individuals. Retrospective investigation of US veterans as part of a 40-year health survey demonstrated body mass index, waist circumference, and

TABLE 5 Characteristics of systematic reviews of epidemiologic evidence of obesity and periodontitis in adults (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Overweight/obesity case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Chaffee and Weston56 USA Association Between Chronic Periodontal Disease and Obesity: A Systematic Review and Meta-Analysis	Designs: All study designs other than case series Sample: Adults Search: MEDLINE, SCOPUS, BIOSIS, LILACS, Cochrane, Brazilian Bibliography of Dentistry databases Language: English and Spanish Year: Up to and including July 2010	5 different definitions/ criteria/BMI cut-off points reported to categorize overweight/obesity Measures reported included BMI, WHR	18 different definitions/ criteria reported to categorize as periodontal disease	No. of included studies: 70 studies of 57 study populations, no experimental studies, 2 studies prospective Meta-analysis: 28 studies 41 studies showing a positive association Fixed effect summary association of prevalence of periodontitis and obesity OR: 1.35 (CI 1.23 to 1.47) Greater mean clinical attachment loss among individuals with obesity Higher mean BMI among periodontal patients Trend of increasing odds of PD prevalence with increasing BMI Many potential confounders amongst studies	Evidence of a positive association of obesity and the development or presence of PD. Lack of longitudinal studies so direction of the association is unconfirmed. A higher prevalence of PD is present in obese adults.
Suvan et al57 UK Association Between Overweight/ Obesity and Periodontitis in Adults: A Systematic Review	Designs: All study designs other than case series Sample: Adults Search: MEDLINE, EMBASE, LILACS, SIGLE Language: No restrictions Year: Up to and including December 2009.	8 different definitions/ criteria/BMI cut-off points reported to categorize overweight/obesity Measures reported included BMI, WHR, WC, body fat %	16 different definitions/ criteria reported to categorize as periodontal disease	No. of included studies: 33 1 longitudinal, 32 observational Meta-analysis: Overweight/PD – 7 studies Obese/PD – 12 studies Overweight/Obese/PD – 13 studies Fixed effect summary of prevalence of periodontitis and BMI obese OR 1.81 (1.42, 2.30), BMI overweight OR 1.27 (1.06, 1.51), and obese/overweight combined OR 2.13 (1.40, 3.26).	Evidence of an association between BMI overweight/obesity and periodontitis. Insufficient longitudinal evidence or evidence to advise on management of PD in patients with obesity.
Nascimento et al58 Brazil Is weight gain associated with the incidence of periodontitis? A systematic review and meta-analysis	Designs: Longitudinal studies Sample: Adults Search: MEDLINE, EMBASE, Web of Knowledge, SCOPUS Language: No language restrictions Year: No restriction up to and including February 2015	BMI cut-off points were the WHO's for all studies WC reported in 2 studies with differing cut-off points	4 definitions of periodontal disease 4 definitions of disease progression	No. of included studies: 5 All prospective Meta-analysis: 5 studies Overweight/obese had higher risk to develop periodontitis than BMI normal-weight category Overweight RR 1.13 (1.06, 1.20) Obese RR 1.33 (1.21, 1.47)	Positive association between weight gain and new cases of periodontitis.
Nascimento et al59 Brazil Is there a relationship between obesity and tooth loss and edentulism? A systematic review and meta-analysis	Designs: Observational studies Sample: Adults Search: MEDLINE, Web of Knowledge, SCOPUS, SciELO Language: No restrictions Year: No restriction up to and including July 2015 Aim: To assess the bidirectional association between tooth loss/edentulism and obesity.	Self-reported BMI (1 study) BMI cut-off points combining overweight/obesity (2 studies) BMI WHO Overweight separate from obese (1 study)	Tooth loss cut-off points included: 1-5 missing teeth 6-31 missing teeth Edentulous (1/4 studies) Edentulism (1/4 studies) ≥1 missing teeth (2/4 studies)	No. of included studies: 16 studies but 12 examining impact of edentulism on obesity and 4 considering impact of obesity on edentulism Meta-analysis: 4 studies considering obesity as exposure Obese: OR 1.49 (1.20-1.86) for any tooth loss OR 1.25 (1.10-1.42) for edentulism	Evidence of a bidirectional association between tooth loss and obesity. Studies were of cross-sectional study design limiting inferences on temporality.

(Continues)

TABLE 5 (Continued)

Publication (authors, year, country, title)	Scope of the review	Overweight/obesity case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Martinez-Herrara et al60 Spain Association between obesity and periodontal disease. A systematic review of epidemiologic studies and controlled clinical trials	Designs: Observational and experimental studies Sample: Adults Search: MEDINE and EMBASE Language: Restricted to English Year: Published from 2000 onward Aim: To offer a systematic review of the evidence on the association between obesity and periodontal disease, of the possible mechanisms underlying this relationship	All studies included BMI to define obesity and some additionally included WC, WHR, or percentage of body fat	Definition of PD based upon PPD, CAL, PI, BOP, ABL, self-reporting, and GI with thresholds not reported	No. of included studies: 29 19 observational 9 experimental studies Meta-analysis: None Obese have more PD than normal-weight individuals with a stronger association as obesity level increases. Association between obesity and the development of periodontitis or weight gain and the development of periodontitis.	Consistent association between obesity and periodontitis with pattern of increased risk of periodontitis in overweight or obese individuals.

Abbreviations: ABL, alveolar bone loss; BMI, body mass index; BOP, bleeding on probing; CAL, clinical attachment level; GI, gingival index; OR, odds ratio; PD, periodontal disease; PI, plaque index; PPD, periodontal probing depth; WC, waist circumference; WHO, World Health Organization; WHR, waist/hip ratio.

waist circumference-to-height ratio to be significant predictors of periodontitis progression in men, with those men who gained weight most rapidly presenting with higher levels of periodontal attachment loss.[68] As for the other components of the metabolic syndrome, there is an ongoing need for longitudinal studies to determine a possible cause-and-effect relationship between overweight/obesity and periodontitis. The most recently published systematic review published subsequent to the aforementioned meta-review investigated the association between obesity and periodontitis in individuals aged 13-34 years. Twelve of the 17 included studies showed a positive association between obesity and periodontitis with increased odds ranging from 1.1 to 4.5 for the presence of inflammation or periodontal destruction if an individual was obese. The review assessed a number of clinical parameters indicative of periodontal diseases, including bleeding on probing, probing pocket depth, clinical attachment loss, and community periodontal indices.[55]

Few publications exist suggesting periodontitis to be a risk factor for obesity; however, the effects of periodontitis, such as tooth loss or compromised mastication, have been suggested as associated with obesity. A recently published systematic review investigating the association of mastication or factors affecting masticatory function and obesity reported that poorer mastication was associated with obesity in 12 out of 16 included cross-sectional studies. Five of the 12 studies reported that increasing numbers of missing teeth was associated with higher body mass index, and five showed that a higher number of teeth present was associated with a lower waist circumference or waist-hip ratio.[69]

Aspects of comorbidity of obesity and periodontitis were addressed in an experimental study by Virto et al.[70] Their results suggest that obesity and periodontitis may have a combined or synergistic effect on systematic inflammation resulting in metabolic dysregulation. The effects of a high fat diet fed to Wistar rats with or without periodontitis were investigated compared with those rats fed a standard diet. Lipid profiles, hepatic parameters, glucose levels, cytokines, and adipocytokines were significantly higher in those rats that had the combination of periodontitis and high fat diet compared with the high fat diet and periodontally healthy animals, or the standard diet in both rats with periodontitis or periodontally healthy rats. The authors concluded that these results were indicative of a comorbidity effect on systemic inflammatory and metabolic dysregulation biomarkers.[70]

5 | EVIDENCE OF THE MECHANISMS OF THE ASSOCIATION BETWEEN PERIODONTAL DISEASE AND METABOLIC SYNDROME, AND OBESITY

The aforementioned studies demonstrate that periodontitis is associated with metabolic syndrome and its components. There is good evidence from clinical studies performed in different ethnic and age groups that periodontitis is associated with obesity. Whether the relationship between obesity and periodontitis is of a causal nature has major clinical significance. Furthermore, if the connection between both diseases is indeed causal, the direction of this causality should be clarified. From the current literature it can be speculated that periodontitis and obesity are linked to each other through several pathomechanisms (see below), ie, that a true causal relationship exists. Although it seems likely that obesity increases the risk of periodontitis and that obesity is, therefore, mainly responsible for

TABLE 6 Characteristics of systematic reviews of epidemiologic evidence of obesity and periodontitis in adults/adolescents/children (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Overweight/obesity case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Moura-Grec et al[61] Brazil Obesity and Periodontitis: Systematic Review and Meta-analysis	Designs: All study designs other than case series Sample: Humans aged 15 y and older Search: MEDLINE, EMBASE, LILACS, Cochrane Language: English, Spanish, and Portuguese Year: No restriction up to and including December 2010	8 different definitions/criteria/BMI cut-off points reported to categorize overweight/obesity Measures reported included BMI, WC	16 different definitions/criteria reported to categorize as PD	No. of included studies: 31 All cross-sectional Meta-analysis: 22 studies Positive association of obesity as a risk factor for periodontitis in 25 studies, 6 did not show positive association Compared with normal weight, overweight and obese showed increased odds or PD OR 1.30 (1.25,1.35)	Evidence of an association between obesity and periodontitis, however, the association is confounded by other factors. More research is needed to confirm mechanisms and impact of periodontitis on obesity.
Li et al[62] Hong Kong Anthropometric Measurements and Periodontal Diseases in Children and Adolescents: A Systematic Review and Meta-Analysis	Designs: Observational or longitudinal studies Sample: Children, adolescents Search: MEDLINE, Web of Knowledge, Cochrane, ProQuest, British Nursing Index, ComDisDome, Gender Watch Language: English Year: No restriction up to including December 2014	BMI standard categories adjusted for age, WC	Various periodontal outcomes employed including gingival bleeding, loss of attachment, PI, probing pocket depth, community periodontal index, GI, calculus	No. of included studies: 16 All cross-sectional, 1 on preschool children, 9 on mixed dentition children, 6 on adolescents Meta-analysis: 3 studies Obese compared with nonobese Plaque and obesity OR 4.75 (2.42, 9.34) $P < .001$ BOP and obesity OR 5.41 (2.75, 10.63) $P < .001$ Probing depth > 4 mm and obesity no association Calculus and obesity OR 3.07 (1.10, 8.62) $P < .001$	Obesity is associated with some signs of PD in children and adolescents.
Keller et al[63] Denmark Association Between Periodontal Disease and Overweight and Obesity: A Systematic Review	Designs: Longitudinal (cohort) and experimental studies Sample: Adolescents, adults Search: MEDLINE, Web of Knowledge Language: Not reported Year: No restriction up to including June 2014	Overweight/Obesity definitions/cut-off points not reported Measures reported included BMI, WC	7 different periodontal outcomes reported with PD and CAL most common	No. of included studies: 8 longitudinal studies 5 experimental studies Meta-analysis: None 5/8 longitudinal studies: positive association between degree of overweight/obesity and development of periodontitis	Overweight, obesity, weight gain, and increased WC may be risk factors for development of periodontitis or worsening of periodontal measures.
Akram et al[64] Malaysia Cytokine Profile in Chronic Periodontitis Patients with and without Obesity: A Systematic Review and Meta-analysis	Design: Clinical trials, cross-sectional, observational studies Sample: Adults, adolescents Search: MEDLINE, EMBASE, Science Direct SCOPUS, Web of Knowledge Language: Not reported Year: 1977 up to and including May 2016	Cut-off points used to define obesity in the various included studies not reported in the review	16 different definitions/criteria reported to categorize as PD 4 studies required > 30% of sites to be affected All samples from GCF	No. of included studies: 11 8 cross-sectional, 3 intervention studies (non-RCT) Meta-analysis: Separate for each of cytokines: resistin, adiponectin, TNF-alpha, resistin, leptin, IL-6, IL-8, IL-1beta Obese vs nonobese with chronic periodontitis: TNF-alpha: significant mean difference ($P = .004$) IL-6: no mean difference ($P = .903$) Resistin: significantly higher resistin levels in obese ($P = .02$) Adiponectin: no mean difference ($P = 0.23$) Leptin: no mean difference ($P = .87$) IL-8: no mean difference ($P = .22$) IL-1beta: significant mean difference ($P < .001$)	Level of localized periodontal inflammation may have greater influence on the GCF pro-inflammatory biomarker levels compared with systemic obesity. Unclear evidence of elevated pro-inflammatory GCF biomarker levels in obese patients with chronic periodontitis compared with nonobese with periodontitis.

(Continues)

TABLE 5 (Continued)

Publication (authors, year, country, title)	Scope of the review	Overweight/obesity case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Martens et al[65] Belgium Association between overweight/obesity and periodontal disease in children and adolescents; a systematic review and meta-analysis	Design: Cross-sectional, case-control, cohort Sample: Children, adolescents Search: Cochrane, MEDLINE, Web of Science, SCOPUS, SciELO, LILACS, SIGLE Language: Restricted to English Year: No restriction up to and including September 2015	BMI standard categories adjusted for age WC, waist/hip ratio, body fat percentage, and skinfold thickness	Various periodontal outcomes employed including gingival bleeding, loss of attachment, PI, probing pocket depth, community periodontal index, gingival index, calculus	No. of included studies: 12 11 cross- sectional, 1 longitudinal Meta-analysis: 7 Association between PD and obesity OR 1.46 (1.20, 1.77). Positive association reported between overweight/obesity and calculus deposits, gingivitis, gingival bleeding, GI, periodontal index, BOP, PI, and PPD > 4 mm.	Evidence of a significantly positive association between PD and obesity in children.
Khan et al[55] Australia Is overweight/obesity a risk factor for periodontitis in young adults and adolescents?: a systematic review	Design: Cross-sectional, case-control, or longitudinal studies Sample: Adolescents, young adults Search: Cochrane, MEDLINE, EMBASE, LILACS, DARE, BIOSIS, TRIP, PROQUEST, CINAHL, Google Scholar, WOS Language: Restricted to English Year: January 1990 to August 2016	BMI standard categories for adolescents WC, waist/hip ratio	Parameters of periodontal assessment including gingival bleeding, loss of attachment, radiographic bone loss plaque index, probing pocket depth, community periodontal index, calculus	No. of included studies: 25 18 cross-sectional, 5 case-control, 2 longitudinal Meta-analysis: None 17 studies showed a positive significant association between obesity and periodontitis 8 studies showed no association (including 2 prospective studies) ORs among the reported studies ranged from 1.1 to 4.5 for increased odds of having periodontitis if an individual was obese	Evidence of a positive association between PD and obesity in adolescents and young adults.

Abbreviations: ABL, alveolar bone loss; BMI, body mass index; BOP, bleeding on probing; CAL, clinical attachment level; GCF, gingival crevicular fluid; GI, gingival index; OR, odds ratio; PD, periodontal disease; PI, plaque index; PPD, periodontal probing depth; RCT, randomized controlled trial; WC, waist circumference.

this causal relationship, several mechanisms have also been reported by which periodontitis may affect obesity. Although the current evidence is still limited, it can be assumed that the association between periodontitis and obesity is of causal nature and that this causal relationship is bidirectional. Several potential mechanisms underlying the link between both diseases will be discussed in the following subsections.

5.1 | Potential mechanisms by which obesity may increase the risk of periodontitis

Several mechanisms whereby obesity may add to the risk of periodontitis have been suggested, as depicted in Figure 2. Moreover, some solid evidence that these mechanisms could indeed play a role in the link between obesity and periodontitis have been provided so far.

5.1.1 | Inflammation

Obesity is characterized by excess adipose tissue, in which adipocytes are increased in number and volume. The adipose tissue is not only an energy storage tissue, as previously thought, but also the source of several pro-inflammatory mediators, such as adipokines (eg visfatin, leptin, resistin, and adiponectin).[71,72] Adipokines are cytokines which are produced by the adipocytes themselves but also by the non-adipocyte fraction of adipose tissue. Besides insulin sensitivity and energy expenditure, they also regulate inflammatory and wound-healing processes. Whereas adiponectin possesses anti-inflammatory characteristics, visfatin, leptin, and resistin exert pro-inflammatory effects. Obesity causes an increase in the production of pro-inflammatory adipokines and a decrease in the synthesis of anti-inflammatory adipokines, which results systemically in an imbalance between pro- and anti-inflammatory adipokines and, therefore, in a low-grade inflammatory state.[71,72] There is clear evidence that the levels of pro-inflammatory cytokines are increased in serum but also in gingival crevicular fluid of obese subjects.[73,74] For example, Zuza et al[74] found higher serum levels of interleukin-1beta, interleukin-6, and tumor necrosis factor-alpha in obese subjects compared with individuals of normal weight. Moreover, tumor necrosis factor-alpha was shown to be increased in gingival crevicular fluid of deep sites in obese subjects with periodontitis when compared with periodontitis patients of normal weight.[73] There is also evidence that the plasma and gingival crevicular fluid levels of adipokines are altered in obesity. Elevated plasma and gingival crevicular fluid levels of pro-inflammatory adipokines (leptin, resistin) and decreased

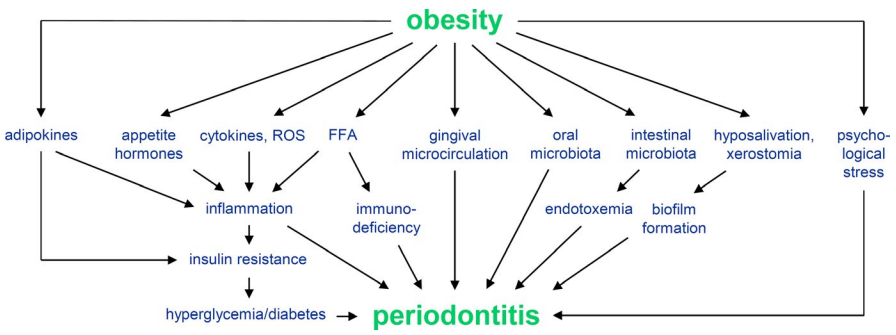

FIGURE 2 Potential mechanisms by which obesity may increase the risk of periodontitis. FFA, free fatty acids; ROS, reactive oxygen species

levels of the anti-inflammatory adipokine adiponectin have been reported.[75-77] These studies demonstrate that the low-grade inflammatory state in obesity is associated with increased levels of pro-inflammatory mediators in the periodontium. Cytokines, such as interleukin-1beta and tumor necrosis factor-alpha, promote recruitment of immunoinflammatory cells, and production of proteases and bone resorption.[78,79] Adipokines, such as visfatin, can also enhance inflammation, for example through CC-chemokine ligand 2, and matrix degradation through matrix metalloproteinase 1.[80] Therefore, it seems reasonable to assume that the systemic inflammation associated with obesity enhances the periodontal inflammatory and destructive processes caused by oral microorganisms.

In addition to the aforementioned adipokine leptin, our appetite is also regulated by the anti-inflammatory hormone ghrelin, which stimulates appetite. Ghrelin, which was originally identified as a hormone secreted mainly by gastrointestinal cells, plays a critical role in the regulation of several physiological processes, such as food intake, energy balance, and body weight, as well as sleep and memory.[81-83] Until now, only a few studies have focused on the role of ghrelin in periodontitis and explored whether it may be involved in the regulation of periodontal inflammatory responses. Ghrelin was found in gingival crevicular fluid and saliva as well as in several cells and tissues of the tooth germ, such as inner enamel epithelium, mesenchymal cells, ameloblasts, odontoblasts, and Hertwig's epithelial root sheath.[84-88] Ghrelin mediates its actions by binding to the growth hormone secretagogue receptor, which has been detected in the hypothalamus, pituitary, pancreas, heart, salivary glands, stomach, and in many other organs.[89,90] Recently, we have shown that the growth hormone secretagogue receptor is also expressed and regulated in periodontal cells.[91,92] Interestingly, the serum level of ghrelin is reduced in obesity, which could result in enhanced periodontal inflammation and destruction in obese individuals.[93]

Furthermore, obesity causes the production of reactive oxygen species and a reduction of the antioxidant capacity. For example, in a study by Tomofuji et al,[94] obesity increased the serum level of reactive oxygen species in rats with and without periodontitis. In addition, the gingival antioxidant level was reduced in the obese rats of both groups. Obesity-associated oxidative stress might therefore be another potential mechanism by which periodontal inflammatory processes are enhanced.

Finally, free fatty acids either derived from adipose tissue or diet are also increased in obese individuals and exert pro-inflammatory effects.[95] Therefore, elevated free fatty acid levels in obesity might also promote periodontal inflammation and destruction.

In addition to this direct stimulatory effect on periodontal inflammation, obesity can also increase the risk for periodontitis through diabetes mellitus, which is a well-established risk factor of periodontitis.[96] Pro-inflammatory mediators, such as tumor necrosis factor-alpha, leptin, and resistin, are elevated in obesity and can inhibit the insulin receptor, which is required for the uptake of glucose from the blood into the cells.[97-99] Consequently, the blood glucose level will increase, which can lead to hyperglycemia or even diabetes mellitus. Several pathomechanisms, such as advanced glycation end products, play a role in the causal relationship between diabetes mellitus and periodontitis. Advanced glycation end products promote the release of pro-inflammatory mediators, cross-linking of collagen, as well as degradation and resorption of periodontal tissues.10-103

5.1.2 | Immunodeficiency

There is also evidence that the immune response to periodontal bacteria is dysfunctional/disrupted in obesity.[14,105] Periodontal bacteria can activate immunoinflammatory cells of the host by binding to toll-like receptors.[106] However, when there is a chronic exposure of these receptors to bacteria, that is, a constant stimulation, the cells develop tolerance.[107] Free fatty acids, which are increased in obesity, can also bind to these toll-like receptors and promote tolerance. As a consequence of the free fatty acid-induced receptor tolerance, there will be no appropriate response of the immunoinflammatory cells to the microbial attack, which again facilitates periodontal destruction.[108-111] Huang et al[111] concluded from a preclinical study that obesity may paralyze the innate immune response of the periodontium via attenuating infiltration and activation of macrophages and, thereby, aggravate periodontal disease.

5.1.3 | Impairment of microcirculation

Although little evidence exists, a study by Lin et al[112] suggests that obesity may also contribute to periodontitis by affecting the gingival vascular supply and the microcirculation. Gingival biopsy specimens from obese and control subjects were studied, and it was found that the basement membrane thickness of the terminal arterioles was

increased in obesity. Furthermore, elevated levels of plasminogen activator inhibitor 1, which inactivates both tissue-type and urokinase-type plasminogen activator and, thereby, prevents fibrinolysis, have been measured in the serum of obese individuals.[113]

5.1.4 | Overgrowth of microbial pathogens

In subgingival biofilms of periodontally healthy/gingivitis individuals, *Tannerella forsythia* was found in greater proportions in those subjects who were obese.[114] Similarly, Al-Rawi and Al-Marzooq[115] found *Tannerella forsythia* as well as *Fusobacterium* spp. and *Porphyromonas gingivalis* in significantly higher quantities in obese individuals compared with nonobese subjects. A different composition of the oral microbiota in obese and nonobese subjects was also demonstrated by Tam et al.[116] If obesity promotes the overgrowth of these or other pathogenic microorganisms and, thereby, periodontal destruction has to be clarified in further studies.

5.1.5 | Intestinal microbiota and permeability

Obesity and overfeeding affect the gut microbiota and gut permeability. Lam et al[117] could demonstrate an increased gut permeability and microbiota change associated with mesenteric fat inflammation and metabolic dysfunction in diet-induced obese mice. In a clinical study by Laugerette et al,[118] overfeeding increased postprandial endotoxemia. Such an endotoxemia would be associated with systemic inflammation and could, thereby, enhance periodontal inflammation. Obesity could therefore render affected individuals more susceptible to periodontal destruction through an altered gut microbiota, increased intestinal permeability, and endotoxemia.

5.1.6 | Hyposalivation/xerostomia

Another mechanism might be hyposalivation/xerostomia, which are more prevalent in obesity and promote plaque accumulation and, thereby, periodontal inflammation.[119,120]

5.1.7 | Impaired emotional well-being

Since distress and inadequate coping behaviors represent a well-established risk factor, weight teasing and a reduced emotional well-being in obesity may also promote periodontal disease.[121-123]

5.2 | Potential mechanisms by which periodontitis may increase the risk of obesity

Several mechanisms by which periodontitis may contribute to obesity have been suggested (Figure 3). Although the evidence for this direction of causality is weak, some mechanisms seem to be at least biologically plausible.

5.2.1 | Inflammation

Periodontitis is a chronic inflammatory disease induced by a complex of microorganisms in the subgingival biofilm, such as *P. gingivalis*, *Tannerella forsythia*, and *Treponema denticola*. Smoking, genetic predisposition, psychological stress, and a number of systemic diseases can contribute to the initiation and progression of periodontitis.[124] The biofilm bacteria interact with infiltrating and resident host cells, which results in the enhanced release of pro-inflammatory cytokines, such as interleukin-1beta, interleukin-6, and tumor necrosis factor-alpha, as well as reactive oxygen species.[125,126] Several studies have shown that the levels of these pro-inflammatory cytokines and reactive oxygen species are not only increased in gingival crevicular fluid and gingiva but also in the serum of periodontitis patients.[53,127] Like adipose tissue, periodontal cells can also secrete pro-inflammatory adipokines, such as visfatin, leptin, and resistin.[128-131] Interestingly, their gingival tissue and gingival crevicular fluid levels are altered in periodontitis, suggesting that they may play a critical role in the etiopathogenesis of periodontitis. Moreover, like in obesity, increased serum levels of visfatin, leptin, and resistin, and reduced serum levels of the anti-inflammatory adipokine adiponectin, have been reported in periodontitis.[132-134] Therefore, like obesity, periodontitis is characterized by a low-grade inflammatory state. The

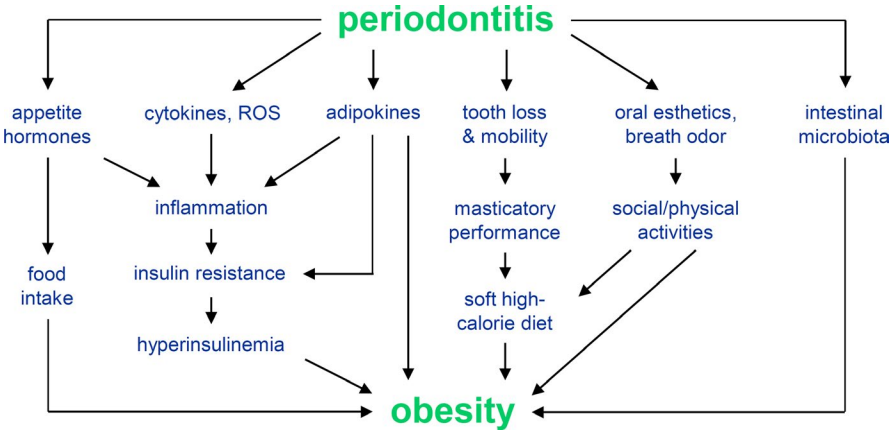

FIGURE 3 Potential mechanisms by which periodontitis may increase the risk of obesity. ROS, reactive oxygen species

periodontitis-associated systemic inflammation can inhibit the insulin receptor and its downstream signaling, thereby promoting insulin resistance. Watanabe et al[135] showed in high fat diet-fed rats that periodontitis could indeed cause a further increase in insulin resistance. Moreover, the association between periodontitis and insulin resistance was also demonstrated in diabetes-free adults.[136] Consequently, the body tries to compensate for the increased insulin resistance by increasing the insulin secretion, which is evidenced by an increased insulin level (hyperinsulinemia) in periodontitis.[137] Since insulin is an anabolic hormone, which promotes glucose uptake and fat storage, hyperinsulinemia promotes obesity. However, further research is needed to confirm that periodontitis contributes to obesity through an elevated level of insulin.[138]

5.2.2 | Food intake

Although few studies exist, it is also conceivable that periodontitis contributes to obesity through increased levels of ghrelin, which stimulates appetite. Yılmaz et al[86] found elevated serum levels of total ghrelin and acylated ghrelin in periodontitis patients compared with periodontally healthy subjects. So it may be that periodontitis stimulates hunger through increased levels of the anti-inflammatory hormone ghrelin.

5.2.3 | Increased tooth mobility and tooth loss

Several studies have shown that the masticatory performance is compromised in periodontitis because of a reduced number of teeth and/or their increased mobility.[139,140] The impaired masticatory function could have a direct effect on the diet selection. It is conceivable that periodontitis patients with a reduced masticatory function will tend to select a soft high-fat/high-calorie diet, which promotes obesity, rather than a hard and healthy diet.[141]

5.2.4 | Compromised oral esthetics

Periodontitis, which may be associated with impaired oral/dental esthetics and/or oral malodor, also has an impact on social life. For example, a study by Durham et al[142] revealed that periodontitis has a negative impact on smiling or laughing, confidence, a carefree manner, and romantic relationships. It is conceivable that such a compromised social life will also affect dietary preferences and physical activities. It can be speculated that periodontitis patients with a compromised social life may eat more high-calorie unhealthy food and may be less physically active, which would increase the risk of obesity.

5.2.5 | Intestinal microbiota

Theoretically, periodontitis might also contribute to an increased risk of obesity by altering/disturbing the gut microbiota. Recently, it has been proven that the gut microbiota is a key determinant of obesity.[143] The gut microorganisms play an important role in nutrient and energy extraction, and energy regulation. However, only a few studies have focused on the effect of periodontitis or its microorganisms on the gut microbiota.[144,145] Oral administration of *P. gingivalis* induced dysbiosis of the gut microbiota, with an increased proportion of phylum bacteroidetes and a decreased proportion of phylum firmicutes, and increased serum endotoxin levels. The investigators suggested that disturbance of the gut microbiota composition by orally derived periodontopathic bacteria may be a causal mechanism linking periodontitis and systemic diseases.[144] However, the *P. gingivalis*-induced dysbiosis of the gut microbiota does not seem to be typical for obesity. Further studies on this emerging topic are needed to clarify the role of this pathomechanism in the link between periodontitis and obesity.

5.3 | Common risk factors for obesity and periodontitis

As described above, the association between periodontitis and obesity seems to be of a causal nature and this causal relationship is probably bidirectional. Nevertheless, there are also some factors which have an impact on both diseases and are discussed in the following subsection (Figure 4).

5.3.1 | Genetic/epigenetic predisposition

There is little evidence to date that there is a common genetic or epigenetic risk factor, even although it cannot be excluded. Yoshihara et al[146,147] have suggested the involvement of beta-3 adrenergic receptor and peroxisome proliferator-activated receptor gamma gene polymorphisms, but further studies are needed to clarify the role of these and other polymorphisms as a common risk factor for periodontitis and obesity. In another approach using Mendelian randomization analyses, Shungin et al[148] investigated causal associations between periodontitis and body mass index. The analysis was based

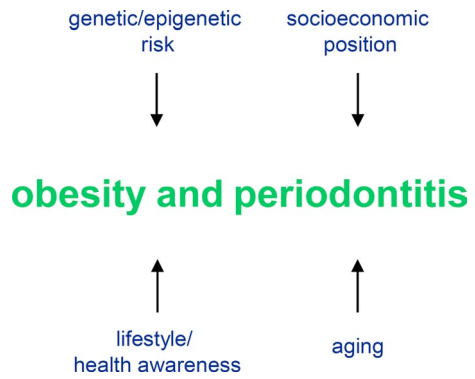

FIGURE 4 Common risk factors for periodontitis and obesity

on almost 50 000 participants with clinically assessed and self-reported periodontitis and genotype data, almost 70 000 participants with body mass index and genotype data, and almost 60 000 participants with data on body mass index and periodontitis. The results of the meta-analyses did not support total adiposity as a causal risk factor for periodontitis.

5.3.2 | Socioeconomic position

In contrast to genetics/epigenetics, a low socioeconomic position has clearly been shown to be a risk factor for both obesity and periodontitis.[149,150]

5.3.3 | Lifestyle/reduced health awareness

Lifestyle, such as alcohol consumption, and a neglectful attitude towards oral and general health, increases the risk of both diseases, as evidenced by several studies in obesity and periodontitis research.[151-154]

5.3.4 | Aging

Aging, with its impact on physical activity, caloric intake, innate immunity, and inflammation, also affects both obesity and periodontitis.[155,156]

Taken together, there is some solid evidence from in vitro, animal, and clinical studies that obesity may contribute to periodontitis by several mechanisms. It is also conceivable that periodontitis increases the risk of obesity by a number of mechanisms, but many of these mechanisms remain speculative even although they are biologically plausible. Last but not least, there are also some common factors which increase the risk of both diseases.

5.4 | Potential pathomechanisms underlying the association of periodontitis with dyslipidemia, diabetes mellitus/hyperglycemia, and hypertension

Like obesity, the other components of the metabolic syndrome (dyslipidemia, diabetes/hyperglycemia, and hypertension) are also linked to periodontitis through a number of pathomechanisms. A recent meta-analysis has demonstrated that periodontitis is associated with a reduction of high-density lipoproteins and an elevation of low-density lipoproteins and triglycerides.[47] A recent cross-sectional study also demonstrated an association of periodontal bacteria with lipid profile alterations.[157] Although the underlying mechanisms are only partly understood, a two-way relationship between periodontitis and dyslipidemia seems to exist. A number of mechanisms by which bacterial infection and, thereby, inflammation can impact on lipid and lipoprotein metabolism have been reported. The infection/inflammation-induced lipid and lipoprotein alterations could result from an increased very low-density lipoprotein secretion, adipose tissue lipolysis, increased de novo hepatic fatty acid synthesis, a suppressed fatty acid oxidation, and a delayed very low-density lipoprotein clearance secondary to decreased lipoprotein lipase and apolipoprotein-E.[158-160] In a combined clinical and in vitro investigation, Nakarai et al[161] found that lipopolysaccharide increased the lipolytic activity of adipocytes in cocultures with macrophages. The authors therefore suggested that periodontal infection promotes lipolysis and subsequent upregulation of circulating triglycerides. In addition to the aforementioned mechanisms, infection and inflammation also induce changes in nuclear hormone receptors, such as peroxisome proliferator-activated receptor, and their target genes involved in fatty acid and triglyceride metabolism. Initially, the lipid and lipoprotein changes under infectious/inflammatory conditions are beneficial to the host and part of the innate immune response. Lipoproteins can neutralize bacterial lipopolysaccharide by accelerating its clearance from the plasma, redirecting it away from monocytes and macrophages, decreasing immune cell activation, and reducing the release of cytokines, thus attenuating lipopolysaccharide toxicity.[162] However, chronic dyslipidemia is deleterious and associated with pathologies.

On the other hand, dyslipidemia can contribute to an increased risk of periodontitis. As mentioned above, fatty acids and lipids can induce secretion of pro-inflammatory cytokines. Moreover, in addition to the activity of high-density lipoproteins in stimulating excess cholesterol efflux from peripheral tissues and transporting it to the liver for excretion, high-density lipoproteins have antimicrobial, antioxidant, and anti-inflammatory properties.[163-165] Therefore, reduced high-density lipoprotein levels and increased triglyceride and low-density lipoprotein levels cause a severe pro-inflammatory state. Moreover, hyperlipidemia causes changes in inflammatory responses to periodontal pathogen challenge.[166] Hyperlipidemia was associated with immune paralysis in the acute phase and accumulation of inflammatory mediators in the chronic period, indicating that hyperlipidemia affects immune functions at different stages via different mechanisms. Lei et al[167] also observed that hyperlipidemia impairs a proper immune response to bacteria challenge, which predisposes the host to periodontitis. Lipids can interfere with cell membrane-bound receptors and enzyme systems, thereby contributing to the development of periodontal diseases. In a recent study, tartrate-resistant acid phosphatase-positive cells were not increased by stimulation with a toll-like receptor-2 ligand alone. However, when the toll-like receptor-2 was combined with oxidized low-density lipoproteins, osteoclastogenesis was significantly promoted.[168] Taken together, several mechanisms have been reported by which periodontitis and dyslipidemia could be linked and these appear to be plausible. Nevertheless, the interactions between infection/inflammation and lipids/lipoproteins are complex, and discrepancies have been reported between rodents and primates.

Like obesity and dyslipidemia, diabetes mellitus is causally connected to periodontitis, and this causality is also bidirectional.[169-171] As mentioned above, diabetes mellitus/hyperglycemia can contribute to periodontitis through the formation of advanced glycation end products.[10-103] Upon binding to advanced glycation end product receptor, advanced glycation end products can induce the release of pro-inflammatory mediators from immunoinflammatory and structural cells of the periodontium and, thereby, enhance periodontal inflammation and destruction. Moreover, advanced glycation end products promote cross-linking of collagen and, thereby, impair the turnover of periodontal tissues. Furthermore, advanced glycation end products stimulate the apoptosis of osteoblastic cells and can, thereby, contribute to alveolar bone loss.[10-103] In addition to advanced glycation end products, glucose itself can exert negative effects on periodontal cells. Diabetes mellitus is also associated with a dysfunctional immune/inflammatory response. For example, chemotaxis and phagocytosis of neutrophils can be compromised and macrophages have been shown to be hyperreactive in diabetes mellitus, which facilitates the microbial invasion and enhances the inflammatory processes within the periodontal tissues.[172-174] On the other hand, periodontitis can contribute to the development of diabetes mellitus through increased levels of pro-inflammatory mediators, such as tumor necrosis factor-alpha, interleukin-6, and resistin, which inhibit the insulin receptor and its downstream signaling, leading to insulin resistance and, thereby, increased glucose levels.[97-99] Insulin resistance in turn promotes the development of dyslipidemia via increased levels of circulating free fatty acids. For a more detailed description of pathomechanisms underlying the association between diabetes mellitus and periodontitis, the reader is referred to the appropriate article on this topic within this volume.

Periodontitis has also been shown to promote atherogenesis.[175-178] Intervention studies have proven that early markers of atherosclerosis, such as endothelial function, intima-media thickness of the *Arteria carotis*, and pulse-wave velocity, can be improved by periodontal therapy.[177,179] Periodontal bacteria, their components and products, and inflammatory mediators derived from the inflamed periodontium can damage endothelial cells and promote atherogenesis and thrombus formation, thereby increasing the risk of cardiovascular diseases and hypertension.[180] Nevertheless, further studies are needed. A more detailed description of this topic can be found in the appropriate article within this volume.

In summary, the aforementioned studies suggest that the relationship between periodontitis and metabolic syndrome, as well as its components, is of a causal nature. Several mechanisms that support causality, often in both directions, have been described (Figure 5). Moreover, the components of the metabolic syndrome themselves are causally connected to each other. However, since common risk factors, such as lifestyle and health awareness, also exist, the relationship between periodontitis and metabolic syndrome is both causal and non-causal. Further studies are needed to better and further define the mechanisms by which periodontitis and metabolic syndrome are linked to each other.

6 | INTERVENTION STUDIES

Several systematic reviews with meta-analyses analyzed the periodontal outcomes of studies that had investigated the response to periodontal therapy (mainly nonsurgical treatment) in patients with periodontitis and obesity.[58,60,63-64,181,182] Only one of these systematic reviews[182] found an inferior response to nonsurgical treatment in obese compared with nonobese patients in five of the eight included intervention studies. The remaining systematic reviews, however, did either not observe a difference in treatment response[58,181] or reported an unclear impact because of inconsistency in the reported findings.[60,63,64] Characteristics of these systematic reviews are presented in Table 7.

It is still unclear whether the relationships between metabolic syndrome, or obesity and periodontal disease, are uni- or bidirectional. Temporality and causality cannot be determined from cross-sectional studies and longitudinal studies are needed. Intervention studies are important to study the direction of the relationship between two conditions and may provide evidence for causality. In this context studies that have either investigated the effect of periodontal interventions on metabolic outcomes, or studies that have investigated the effect of metabolic interventions (such as bariatric surgery and dietary therapy) on periodontal status, are of particular interest.

6.1 | Impact of periodontal therapy on outcomes related to obesity

A few studies reported on the impact of periodontal therapy on parameters related to obesity. Gonçalves et al[77] evaluated the effects of scaling and root planing on local and serum levels of adipokines for up to 12 months in 40 periodontitis patients (20

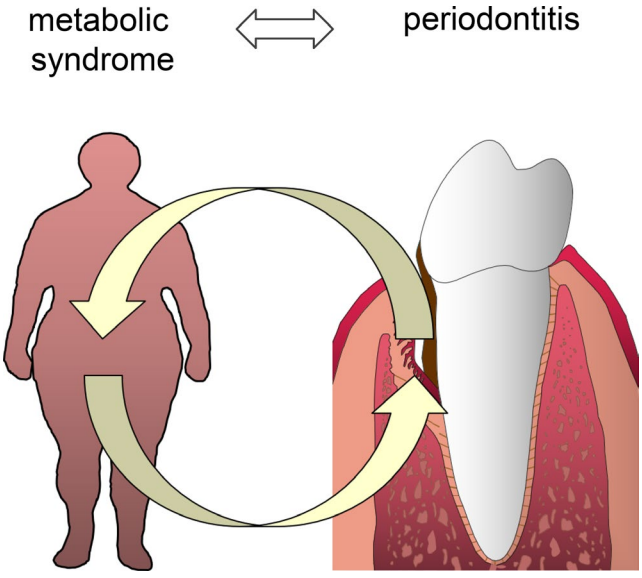

FIGURE 5 Bidirectional relationship between periodontitis and metabolic syndrome

TABLE 7 Characteristics of systematic reviews of treatment response evidence of obesity and periodontitis (in chronological order)

Publication (authors, year, country, title)	Scope of the review	Overweight/obesity case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Gerber et al[182] Switzerland Influence of obesity on the outcome of non-surgical periodontal therapy – a systematic review	Design: Intervention studies Sample: Adults Search: SCOPUS, MEDLINE, Cochrane, CINAHL, BioSIS, Web of Science Language: Restricted to English and German Year: No restriction up to and including January 2016	WHO BMI cut-off points used to define obesity	Intervention in all studies was nonsurgical periodontal therapy using hand and/or ultrasonic instruments including oral hygiene instruction.	No. of included studies: 8 intervention studies Meta-analysis: None 3/8 studies failed to show influence of obesity on pocket depth reduction after nonsurgical therapy 5/8 studies showed a clear negative effect of obesity on the outcome of nonsurgical therapy. Effect noted specially for moderate-to-deep pockets Significant difference in percentage of pocket reduction to <5 mm following therapy as well as lower mean PPD reduction in obese compared with nonobese.	Data support that obesity is not only a factor associated with poorer periodontal health but might also result in inferior response to nonsurgical treatment of periodontitis.
Nascimento et al[59] Brazil Does periodontal treatment have an effect on clinical and immunological parameters of periodontal disease in obese subjects? A systematic review and meta-analysis.	Design: Intervention studies Sample: Adults Search: MEDLINE, EMBASE, SCOPUS, LILACS, Web of Knowledge, SciELO Language: No restrictions Year: No restriction up to and including August 2014	WHO BMI cut-off points used for defining obese	Nonsurgical therapy without adjunctive therapies Test group: obese Control group: nonobese Some studies included smokers and others excluded smokers.	No. of included studies: 5 intervention studies Same studies included as previous review published by Akram et al (2016). Meta-analysis: 3 Same studies included in 1 meta-analysis (3/5 studies) as noted in previous review in this table by Akram et al (2016). Additional meta-analysis of 2/5 studies did not show evidence of a difference between obese and nonobese in terms of clinical parameters. Obese presented with significantly higher levels of circulating pro-inflammatory cytokines than nonobese at baseline. No significant differences were found between groups following periodontal therapy.	Periodontal treatment effective to improve healing in obese individuals. No observed differences on periodontal healing between obese and nonobese subjects, however, only a limited and fragile base of evidence was available for analysis.
Akram et al[64] Malaysia Efficacy of non-surgical periodontal therapy in the management of chronic periodontitis among obese and non-obese patients: a systematic review and meta-analysis	Design: Intervention studies Sample: Adults Search: MEDLINE, EMBASE, Cochrane, SCOPUS, Google Scholar, Web of Knowledge Language: Not reported Year: From 1977 up to and including December 2014	WHO BMI cut-off points used for defining obese	Nonsurgical therapy without adjunctive therapies Test group: obese Control group: nonobese Some studies included smokers and others excluded smokers.	No. of included studies: 5 intervention studies 2/5 studies showed clinical parameters differences statistically significant with nonobese demonstrating better periodontal condition following therapy. Meta-analysis: 3 Only 3/5 studies (2 reporting no difference in clinical parameters between obese and nonobese after treatment and 1 reporting statistically significant difference) reported similar clinical parameters and were combined in meta-analysis; however, heterogeneity was high. No statistically significant difference in clinical parameters (PPD and CAL) between obese and non-obese in overall mean reported in meta-analysis. Biomarkers investigated were Il-6, IL-1beta, IFN-gamma, TNF-alpha, CRP, leptin, and adiponectin: results were variable and inconclusive.	Unclear impact of NSPT on the clinical periodontal outcomes in obese patients vs nonobese patients with chronic periodontitis because of the limited number of selected studies and inconsistency of reported findings.

(Continues)

TABLE 7 (Continued)

Publication (authors, year, country, title)	Scope of the review	Overweight/obesity case definitions or related parameters	Periodontal disease case definition or related parameters	Results	Conclusions
Papageorgiou et al[181] Germany Effect of Overweight/Obesity on Response to Periodontal Treatment: systematic Review and a Meta-analysis	Design: Randomized and non-randomized experimental studies Sample: Adults Search: Databases not reported Language: No restrictions Year: No restriction up to including July 2013	BMI WHO categories Overweight/obese grouped together in some studies or analysis and separated in others	Interventions included: supragingival debridement (1/15) NSPT (8/15) – nonsurgical therapy plus antibiotics (5/15) - nonsurgical plus surgical therapy (1/15)	No. of included studies: 15 4 RCTs, 11 non-RCTs Meta-analysis: 8 studies (with subgroup analysis grouped as nondiabetic or diabetic population samples) analyzing mean difference from baseline. No statistically significant differences between overweight/obese and normal weight found in changes in PPD or CAL between baseline and post-therapy. All therapies grouped together in meta-analysis. Significant differences in inflammatory and metabolic parameters were based upon 1 study where TNF-alpha was found to be higher in overweight/obese individuals prior to treatment and demonstrated greater reduction after treatment compared with normal weight. MD -1.57 pg/ml (-2.61, -0.53 pg/ml)	No difference was found in clinical periodontal parameters; however, significant differences in inflammatory or metabolic parameters were found between overweight/obese and normal-weight patients.
Keller et al[63] Denmark Association Between Periodontal Disease and Overweight and Obesity: A Systematic Review	Designs: Longitudinal (cohort) and experimental studies Sample: Children, adolescents, adults Search: MEDLINE, Web of Knowledge Language: Not reported Year: No restriction up to and including June 2014	Overweight/obesity definitions/cut-off points not reported Measures reported included BMI, WC	7 different periodontal outcomes reported with PD and AL most common All intervention studies reported on nonsurgical periodontal therapy	No. of included studies: 8 longitudinal studies 5 experimental studies Meta-analysis: None 2/5 intervention studies reported better response to therapy in lean patients compared with obese 3/5 intervention studies did not report differences in response to therapy 1/5 showed increased response in bariatric surgery patients compared with controls	Impact of overweight, obesity, weight gain, and increased WC on outcomes of nonsurgical periodontal therapy are unclear.
Martinez-Herrara et al[60] Spain Association between obesity and periodontal disease. A systematic review of epidemiologic studies and controlled clinical trials	Designs: Observational and experimental studies Sample: Adults Search: MEDINE and EMBASE Language: Restricted to English Year: Published from 2000 onward	All studies included BMI to define obesity and some additionally included WC, waist/hip ratio, or percentage of body fat	Definition of PD based upon PPD, CAL, PI, BOP, ABL, self-reporting, and GI with thresholds not reported	No. of included studies: 29 19 observational 9 experimental studies Meta-analysis: None Studies reporting on response to therapy were inconsistent so the effect of obesity on response to periodontal treatment remains unclear.	Although a higher prevalence and severity of periodontitis was noted in obese individuals, response to periodontal therapy remains unclear.

Abbreviations: ABL, alveolar bone loss; BMI, body mass index; BOP, bleeding on probing; CAL, clinical attachment level; GI, gingival index; MD, mean difference; NSPT, non surgical periodontal therapy; OR, odds ratio; PD, periodontal disease; PI, plaque index; PPD, periodontal probing depth; RCT, randomized controlled trial; WC, waist circumference; WHO, World Health Organization.

with and 20 without obesity). Scaling and root planing did not affect the circulating serum levels of adipokines in patients with or without obesity. Akram et al[183] evaluated associations of change in salivary resistin level with periodontal outcomes in 62 obese patients randomly assigned to nonsurgical therapy or no periodontal treatment. Periodontal parameters were significantly improved and resistin levels were significantly decreased in the treatment group. However, salivary resistin level was not associated with improvements in periodontal parameters. Al-Hamoudi et al[184] compared two groups of patients, 70 patients with and 67 without periodontitis. About half of the patients in each group were either obese or nonobese. Scaling and root planing were effective in reducing periodontal inflammation in patients with and without obesity. However, salivary resistin levels were higher in the periodontitis group compared with the non-periodontitis group irrespective of whether obese or nonobese. The authors concluded that periodontitis seems to be the primary factor that influences periodontal status and the expression of resistin and interleukin-6 levels in obese and nonobese patients, and the role of obesity itself is secondary. Suresh et al[185] evaluated the effect

of nonsurgical periodontal therapy on plasma-reactive oxygen metabolite and local and serum resistin levels in 30 obese and 30 normal-weight individuals with periodontitis. Intergroup comparison of periodontal parameters 2 months after therapy showed a significant difference with more improvement in normal-weight than in obese patients. Mean plasma-reactive oxygen metabolite, gingival crevicular fluid, and serum resistin levels at baseline were higher in obese compared with normal-weight patients. Periodontal therapy reduced systemic oxidative stress levels in both groups; however, plasma-reactive oxygen metabolite levels showed a greater reduction in normal-weight individuals than in overweight individuals.

6.2 | Impact of periodontal therapy on outcomes related to metabolic syndrome

Other studies reported on the impact of periodontal therapy on parameters related to metabolic syndrome. In a 2-month pilot study with 31 periodontitis patients (16 with the metabolic syndrome and 15 systemically healthy), Acharya et al[186] assessed the effects of periodontal therapy on measures of systemic inflammation. They detected a significant improvement in periodontal parameters in both groups after therapy and reported significantly decreased levels of high-sensitivity C-reactive protein of total leukocyte counts and of triglycerides, and a significant rise in high-density lipoprotein in patients with the metabolic syndrome . In a 1-year randomized trial, Lopez et al[187] evaluated the effects of periodontal therapy on systemic markers of inflammation in patients with metabolic syndrome and periodontitis. Results showed that elimination of periodontal inflammation by using root planing and systemic antibiotics (group 1, n = 82) or using plaque control and supragingival scaling (group 2, n = 83) significantly decreased C-reactive protein in patients with the metabolic syndrome. Torumtay et al[188] compared the effects of nonsurgical periodontal treatment on inflammatory and oxidative stress markers in 25 patients with the metabolic syndrome and 25 systemically healthy patients. Periodontal treatment decreased oxidative stress and the inflammatory status of patients with the metabolic syndrome and chronic periodontitis. Although similar periodontal improvements were achieved in both groups, the decreases in levels of high sensitivity C-reactive protein and interleukin-6 in the metabolic syndrome group did not reach the levels in the systemically healthy patients. Bizzarro et al[189] investigated the effect of basic periodontal therapy with or without adjunctive systemic antimicrobials on the parameters of metabolic syndrome (waist circumference, systolic/diastolic blood pressure, high-density lipoprotein cholesterol, triglycerides, and glucose). A reduction in systolic blood pressure and triglycerides and a temporary improvement in the whole metabolic status were observed. The adjunctive use of antimicrobials did not yield any additional improvement in the parameters of the metabolic syndrome.

6.3 | Impact of bariatric surgery on periodontal status

Bariatric surgery has been shown to be an effective weight loss strategy and is proposed as a frontline therapy for adult patients with severe obesity.[190] A number of cohort and cross-sectional studies have evaluated the periodontal status of patients who had undergone bariatric surgery, and two systematic reviews with meta-analyses have been published.[191,192] Even although both reviews had a large overlap with regard to the included original studies, their conclusions differed. DeSouza et al,[191] for their meta-analysis, reported no differences in clinical attachment levels, bleeding, and probing depths before and after bariatric surgery. The only significant difference was an improvement in plaque index. By contrast, Fontanille et al[192] observed a significant increase in periodontal inflammation and the percentage of periodontal sites with moderate pocket depth in the first 6 months after surgery. However, at 12 months after bariatric surgery, no significant difference was found for the various periodontal parameters analyzed.

It is noteworthy that patients included in the studies for both systematic reviews presenting with various levels of baseline periodontal health sometimes did not receive periodontal therapy prior to bariatric surgery. A major limitation of the present systematic reviews, acknowledged by the authors, is the low number and the low quality of studies of sufficient quality that could be included in the meta-analyses. There is a paucity of prospective studies available in the literature. Thus, causation cannot be inferred from studies included in the meta-analysis because of their retrospective design.

6.4 | Impact of dietary therapy/weight loss on periodontal outcomes

Weight loss could provide an additional beneficial effect to therapy for periodontitis in obese patients since systemic pro-inflammatory cytokines tend to decrease after weight loss.[9] A few studies have examined the effect of dietary interventions in obese patients or patients with metabolic syndrome with different levels of periodontal health or disease, and have shown positive effects on periodontal parameters.[193-195] Martinez-Herrera et al[196] have recently shown that obese patients present inferior clinical outcomes compared with nonobese subjects 3 months after nonsurgical periodontal therapy, suggesting that obesity has a negative effect on the response to periodontal treatment. In a subsequent study[197] they evaluated whether dietary weight loss intervention would improve the response of obese subjects to periodontal treatment. A total of 78 obese patients received nonsurgical treatment either with or without dietary therapy. At 3 months, patients in the dietary group showed more periodontal improvement and decreased levels of the systemic inflammatory parameters complement component 3 and tumor necrosis factor-alpha compared with the patients without weight loss intervention.

7 | CLINICAL AND PUBLIC HEALTH IMPLICATIONS FOR THE DENTAL TEAM

Obesity is one of a number of noncommunicable diseases referred to by the World Health Organization Director-General as slow motion disasters influenced largely by four behavioral lifestyle factors: tobacco use, unhealthy diet, insufficient physical activity, and the harmful use of alcohol, many aspects of which are embedded in 21st century social determinants. In addition to obesity's direct adverse effects on general health, numerous comorbidities are the focus of scientific investigations, many of which have common risk factors with complex entangled implications for health. The management of obesity and medical care for the obese is therefore no simple matter, requiring the understanding, attention, and efforts of all healthcare professionals and organizations. It is a condition affecting multiple disciplines and will increasingly demand interdisciplinary approaches to maximize the benefits of all efforts. Periodontal diseases are one such group of obesity comorbidities sharing some common risk factors with obesity denoting implications for healthcare professionals involved in obesity management as well as dental professionals managing oral health in the obese. In the past decades, however, dental care and medical care have evolved in separation. Addressing the links between periodontal and other chronic noncommunicable diseases has the potential to improve healthcare and the prevention of chronic conditions. Based on the extensive scientific evidence reviewed in the previous sections, obesity/metabolic syndrome appears to be a promising and necessary area for interprofessional cooperation between medical and dental professionals.

7.1 | CLINICAL IMPLICATIONS

7.1.1 | Access to care

The use of dental services has been reported to be lower among obese than nonobese individuals.[198] A number of factors could explain this finding. Obese individuals may have more important health issues that consume their attention, hence dental visits are low on their list of priorities. Most dental offices do not have facilities to accommodate patients with moderate to severe obesity. Standard dental chairs are commonly rated to accommodate 135 kg static loads without considering the possibility to lift or recline.[199] Higher levels of dental anxiety have been reported to be associated with obesity.[20] Further investigation in this area is needed to better understand the lack of willingness to visit the dentist.

7.1.2 | Medications

An up-to-date record of medications taken by the patient including any changes is essential. As discussed, many obese patients will be taking various medications to enhance metabolic control. Many of these have oral implications, with the most common being reduced saliva flow resulting in a dry mouth. If a patient is taking a medication suspected of altering saliva, they should be asked the listed questions to obtain their subjective assessment of saliva to ascertain if this is potentially affecting their food choices. Subjective assessment of saliva flow is based upon a single positive response to any of the following five questions[21]: (1) Does your mouth feel dry? (2) Does your mouth feel dry while eating? (3) Do you have difficulty swallowing dry foods? (4) Do you sip liquids to aid swallowing? (5) Is the amount of saliva in our mouth too little most of the time? Some patients may report a burning sensation or altered taste associated with the dryness.

7.1.3 | Mouth breathing/obstructive sleep apnea

Simple observation of the patient during consultation can provide clues of possible mouth breathing. Mouth breathing may occur for various reasons, one of which is obstructive sleep apnea. Mouth breathing leads to drying of the anterior oral tissues sometimes resulting in gingivitis and/or mucositis partially because of the drying effect on bacterial plaque accumulations, which tend to be increased. It is often associated with uncontrolled tongue thrust that often obstructs toothbrush placement during oral hygiene self-care. A diligent oral hygiene routine is imperative. Oral appliance therapy for obstructive sleep apnea is often a lifelong treatment that carries the risk of dental side effects .[22] Therefore, these patients should have thorough follow-up.

7.1.4 | Masticatory function

Studies have reported an association between reduced chewing force and higher body mass index regardless of the number of teeth.[23] A study investigating masticatory performance in children found that body mass index-normal children performed better in masticatory performance tests than body mass index-overweight/obese or body mass index-underweight children.[24] Chewing time, cycles, and frequency were compared (using five standard foods) in 44 obese patients scheduled for gastric bypass surgery and 30 nonobese control patients. Results showed higher values in the fully dentate for the morbid obese compared with controls. Furthermore, those who were obese and not fully dentate could not produce a food bolus with the same particle size distribution as the fully dentate obese. The authors suggested this emphasizes the need for dental evaluation including chewing ability for all overweight/obese patients.[25] Comparisons of bolus formation have been assessed before and after surgery demonstrating changes in bolus granulometry were dependent on food and dental status.[26] It may be necessary to recommend increased chewing time to patients according to dental status.[27] Clinicians should consider these aspects during assessment, taking into consideration the number of missing teeth and the location of any gaps. Patients should be asked about their perceptions of their chewing ability: (1) Is the patient aware of difficulties

while chewing on one side of their mouth or the other? Or overall? (2) Do they bite their cheeks or tongue often? (3) Do they avoid or dislike particular foods because chewing seems to take a long time?

7.1.5 | Removable dental prosthesis

Clinicians should consider if the patient has a removable dental prosthesis and, if so, do they wear them to eat or only when going out for social occasions, as is often the case. If they do not wear them, it could be because of the status of the oral tissues, or possibly reduced saliva flow. Prosthetic replacement can be complex because of differing anatomical features in their mouths, including increased cheek and tongue size, therefore, particular modifications may be necessary to facilitate denture retention.[208]

7.1.6 | Oral hygiene

The importance of controlling/removing the dental plaque biofilm remains paramount for all patients and especially for the overweight/obese because of the increased susceptibility for periodontal disease. A number of anatomical factors could negatively influence oral hygiene routines in obese individuals. Large cheeks sometimes obstruct access to posterior teeth. In addition, the forearm and upper arm size may restrict bending and positioning of the arm to a suitable position for brush placement. If placed correctly, movement of the brush can be difficult. Being empathetic with patients and being careful not to undermine their efforts to clean their mouths is vital. Based on the substantial evidence regarding the efficacy of power toothbrushes in plaque removal,[209] it is likely that for most obese patients a power toothbrush would be recommended; however, specific evidence in this area is lacking and oral hygiene devices should always be agreed upon individually with each patient .

7.2 | PUBLIC HEALTH IMPLICATIONS

It is important to enhance public and professional awareness of the interdependence of periodontal health and general health, and the need for specific actions to address common risk factors (eg smoking, malnutrition, sedentary lifestyles, and overweight/obesity) for both periodontitis and other chronic diseases.[1] Obesity is a major health problem increasing the risk of metabolic syndrome, cardiovascular diseases, respiratory disorders, diabetic complications, and certain types of cancers. Obesity, and subsequently many of these other conditions, are preventable. It has been proposed that addressing the obesity epidemic adequately will require the involvement of various healthcare professionals.[210] The World Health Organization has challenged all healthcare providers to contribute to efforts targeting this health issue as part of a global initiative to reduce the incidence of noncommunicable diseases.[6] Scientific evidence indicates associations between sugar consumption and obesity/overweight, between obesity/overweight and oral health, and between sugar consumption and oral health. Given the synergy between the messages needed to increase awareness of these associations, dental professionals may be well positioned to assist in modifying the risk factors for overweight/obesity, through expanding dietary or lifestyle counseling they already are providing to their patients in the context of their oral health.[3,211]

7.2.1 | Role of refined carbohydrates in oral health and metabolic syndrome

The World Health Organization defines free sugars as those added to food and drinks by the manufacturer, cook, or consumer, as well as sugars naturally present in honey, syrups, fruit juices, and fruit juice concentrates.[212,213] The regular consumption of food and drinks high in free sugars is not only associated with caries, gingival inflammation, and obesity, but is also associated with an increased risk of other conditions including type 2 diabetes, cardiovascular disease, gout, fatty liver disease, high blood pressure, some cancers and hyperactivity.[3,214,215] Furthermore, there is no dietary requirement for free sugars for the achievement of health. Food and drinks high in free sugars have been shown to replace more nutrient-dense foods.[216]

A meta-analysis of five trials in adults with ad libitum diets (ie no strict control of food intake) showed that a reduced intake of free sugars was associated with a significant decrease in body weight (0.80 kg; 95% CI: 0.39-1.21).[216] A further meta-analysis of 10 randomized controlled trials showed that an increased intake of free sugars (mostly in the form of sugar-sweetened beverages) was associated with a significant increase in body weight (0.75 kg; 95% CI: 0.30-1.19) compared with those with no increase in sugar intake.216 In 2015, the World Health Organization published new guidelines recommending that free sugars should account for < 10% of the daily energy intake of adults and children. This guideline was based on strong evidence associating free sugars intake with oral health and obesity.[217]

A meta-analysis of eight prospective cohort studies found that individuals consuming 1-2 sugar-sweetened beverage servings per day had a 26% (95% CI: 12-41) and a 20% (95% CI: 2-42) greater risk of developing type 2 diabetes and metabolic syndrome, respectively, compared with individuals consuming ≤ 1 serving per day.[218] Several large randomized control trials have demonstrated that reducing sugar-sweetened beverage consumption significantly decreases weight gain in children and adolescents.[219] Results from other studies have also suggested that reducing sugar-sweetened beverage consumption would not only help to reduce the risk of dental caries but also that of type 2 diabetes and cardiovascular disease by improving insulin sensitivity and reducing blood pressure, inflammation, and visceral adiposity accumulation.[220,221]

A meta-analysis conducted to investigate the association between carbohydrate intake and gingival inflammation demonstrated moderate reduction in carbohydrate intake reduced gingivitis scores on average by one third.[222] Lula et al[223] demonstrated that high frequency consumption of added sugars is associated with periodontal

disease independent of traditional risk factors. Evidence has shown that the prevalence of periodontal disease is associated with higher consumption of carbonated beverages.[224,225] An oral health-optimized diet was shown to be able to reduce gingival and periodontal inflammation in humans.[226] The American Heart Association and the World Health Organization recommended restricting sugar intake in 2015.[227]

7.3 | POTENTIAL ROLE OF THE DENTAL PROFESSIONAL

Consideration of the evidence highlights the necessity for urgent action among healthcare professionals to improve public awareness and curtail uncontrolled levels of obesity, sugar-sweetened beverage consumption, and associated adverse health effects. The interrelationships between obesity, oral diseases, and excess sugar-sweetened beverage intake may provide the dental team with a platform to use healthy beverage discussions as a prelude to communicating healthy weight promotion. Furthermore, dietary similarities between oral preventative advice and healthy weight promotion may aid in enabling patients to understand the importance of healthy lifestyle choices to both oral health and general health. Dental caries and periodontal diseases have been proposed as sensitive warning signs of an unhealthy diet, which predict the future onset of the so-called diseases of civilizations .[215] Periodontitis should be regarded as a "sign post" condition that may indicate malnutrition or that a patient may have an underlying noncommunicable disease.[3]

Dental professionals are currently involved in tobacco and alcohol cessation counseling and oral cancer screening, as well as providing routine dietary and oral hygiene advice in regard to the oral health of their patients. They also assess the body weight of their patients for other purposes, such as administration of local anesthetics for sedation purposes.[228] Therefore, dental health professionals may be in an ideal position to provide broader advice on healthy weight management as it relates to diet since dental care often involves multiple visits, many individuals see their dentist more frequently than their medical doctor, and dental professionals are already educated in discussing healthy diet choices that affect the dentition.[3] In this context it could be concluded that the dental setting allows an opportunity to initiate and reinforce healthy lifestyle choices commensurate with maintaining a healthy diet contributing to healthy weight management. Being healthcare providers, dental professionals should feel confident to screen for overweight/obesity, offer healthy eating advice, and refer to a specialist. This could have a particularly positive impact on children and adolescents, as these groups tend to visit their doctor even less than adults.[228] With regard to healthy aging, it should be communicated that chewing is an essential function to ensure adequate nutrition and is best preserved with natural teeth. Benefits related to retention of healthy dentitions and mastication go beyond oral health, well-being, and self-esteem, as they foster a healthy diet, which is necessary to delay physical decline and loss of independence.[229]

7.3.1 | Role of the dental professional in dietary counseling to reduce sugar consumption

Recent studies of children and adolescents conducted in dental settings have adapted contemporary behavioral change frameworks such as motivational interviewing techniques for the management of body weight/obesity through reducing sugar-sweetened beverage consumptions.[228,230,231] Body mass index screening protocols among children (aged 6-13 years, 2-3 visits over 18 months) promoted obesity risk awareness (food consumption/habits, exercise level), goal-setting, and referral (≥ 85th body mass index percentile) with biannual hygienist interventions. Body mass index screenings were well received and promoted food choice alterations. Dentists' perceptions of regular body mass index screening were influenced by patient/family acceptability, positive effects on oral health, weight status, and minimal costs. Preliminary healthy weight interventions (diet counseling) were well received by both patients (94%) and dentists.[231] The above evidence supports the advantages of introducing healthy weight promotion (including body mass index screening) together with oral health preventative dietary advice in the dental setting.

8 | CONCLUSIONS

A large body of evidence from epidemiologic studies supports the association between periodontitis, metabolic syndrome, and obesity. Extensive research has established plausible mechanisms to explain how these conditions can negatively impact each other. At present there is only limited evidence available from a few intervention studies. Nevertheless, the global burden of periodontitis combined with the obesity epidemic has important clinical and public health implications for the dental team. In accordance with the common risk factor approach for tackling common noncommunicable diseases, a new role for oral healthcare professionals in the promotion of periodontal health and general well-being has been proposed.

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