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The Relationship Between Obesity and Periodontal Disease

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THE RELATIONSHIP BETWEEN OBESITY AND PERIODONTAL DISEASE

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INTRODUCTION.

Obesity rates and its associated health problems have risen to exponential proportions in the United States (U.S.) and globally.[1] Obesity has been targeted as the sixth most significant risk factor worldwide that is known to contribute to both oral and other associated systemic diseases.[2] According to the Centers for Disease Control and Prevention (CDC), the prevalence of obesity among adults in the U.S. is 40% and 18.5% in youth with prevalence higher among middle aged adults (42.8%) than younger adults (35.7%).[3] As of 2016, nearly two billion people worldwide were either overweight or obese.[1] Research indicates accumulated excessive fat from being overweight or obese contributes to serious health impairments.[4] World-wide obesity is associated with increased risk for chronic inflammatory diseases such as arthritis, diabetes, cardiovascular disease, and some cancers.[5,6] Increasing concerns regarding obesity-related health implications include adverse consequences on oral health, in particular periodontal disease.

The World Health Organization (WHO) defines overweight and obesity as "abnormal or excessive fat accumulation that presents a risk to health".[1] Obesity is most commonly determined by calculations based on body mass index (BMI). BMI is calculated by dividing a person's weight in kilograms (kg) by squaring of the height in meters $(kg/m)^2$.[1] For adults, a calculated BMI $\geq 25 kg/m^2$ is considered overweight; while a BMI $\geq 30\ kg/m^2$ is considered obese.[1] For children aged 5-19, overweight is defined as a BMI-for age greater than 1 standard deviation above the growth reference median, and childhood obesity is defined as more than 2 standard deviations above the median.[1] Obesity is also be measured by waist circumference (WC) with ≥ 102 cm and ≥ 88 cm for males and females respectively, indicative of obesity.[7]

Waist circumference correlates with amount of visceral body fat and research suggests a strong correlation with increased disease risk.[8-10] Excess caloric consumption, unhealthy food choices, sedentary lifestyles, genetics, medications, and some diseases contribute to obesity.[1] Brien et al., in a 20-year longitudinal study researched the relationships between physical activity, cardiorespiratory fitness, BMI, and the development of future obesity in 459 Canadian adults with a mean age of 32.8 years and a BMI of 23.2.[11] While controlling for age, sex, smoking, and alcohol use, results revealed deficient levels of physical fitness and a high BMI were strong independent indicators of future obesity.[11] Furthermore, Berrington de Gonzalez et al., researched the relationship of BMI on mortality utilizing 19 prospective studies with over one-million white adults aged 19-84. Results indicate all causes of mortality were lowest when associated with a BMI between 20.0 to 24.9.[12]

Research also suggests obesity has an oral-systemic link, in particular, periodontal disease.[2,4,5,7,9,13] Periodontitis is caused by the interaction of specific periodontal pathogens and the hosts' response resulting in loss of connective tissue attachment and alveolar bone destruction in the mouth.[4] Initiated by bacteria, multiple risk factors contribute to the development and progression of periodontal disease. Several studies have identified both modifiable and non-modifiable risk factors and indicators for periodontal disease, many also common in obesity.[14-19] Factors such as oral biofilm accumulation, smoking, medications, level of education, stress, and nutrition are examples of modifiable risk factors. Non-modifiable factors include past history of periodontitis, genetics, age, gender, ethnicity, and host response as contributors to periodontal disease.[14-17,19,20] In a 5-year longitudinal study in Brazil, Haas et al., followed 697 participants to research the pattern and rate of periodontal attachment loss (PAL) progression related to non-modifiable risk factors and reported PAL progression increased with

age, and PAL progression was significantly higher among males and non-whites.[14] Eke et al., researched the prevalence of adult periodontal disease in the United States among 3,743 participants over the age of 30, including modifiable and non-modifiable risk factors. Results revealed periodontitis was significantly higher overall in males, those with the lowest educational status, current smokers, and more specifically, Mexican American in comparison to all other race and ethnicities studied.[19] Costa et al., in a cross-sectional study of 705 adults, investigated cumulative smoking exposure and duration of smoking cessation associated with periodontitis. Results indicated cumulative smoking exposure correlated with periodontitis and the duration of smoking cessation was inversely associated, independent of age, sex, family income, educational level, alcohol, and other risk-variables evaluated.[18] Moreover, the CDC reports periodontitis increases with age, and is more common among those living below the poverty level, those with less than a high school education, and current smokers.[20] Contributing to disease, both modifiable and non-modifiable risk factors are associated with periodontal disease.

Systemic risk factors largely influence host susceptibility to periodontal disease, and research suggests obesity may be a risk factor. A state of inflammation that results from obesity may increase host susceptibility to periodontal breakdown. A balance between the immune and inflammatory systems play a key role. There is a suggestive association that cardiovascular disease is an independent risk factor for periodontal disease, both Southerland et al., and Dietrich et al., in their recent reviews of epidemiological studies agree there is insufficient evidence to support a strong association.[21,22] However, multiple epidemiological studies conclude there is a positive association between periodontitis and diabetes. Both Salvi et al., and Chávarrya et al., evaluated the relationship between diabetes and periodontitis and concluded Type II diabetes is a

risk factor for periodontitis.[23,24] Research by Zhou et al., examining a bi-directional relationship between diabetes mellitus and periodontitis revealed hyperlipidemia plays an important role in the pathogenesis of diabetes and periodontitis through its effects on insulin secretion and pro-inflammatory cytokines production.[25] The hosts' inflammatory reaction likely plays a significant role in both obesity and periodontitis.[10,26] The following review of the literature will explore the relationship of obesity as a risk factor for periodontal disease.

Oral healthcare providers can benefit from up-to-date knowledge related to the potential association between obesity and periodontal disease. With enhanced knowledge, healthcare providers will be better prepared to educate patients on oral and systemic implications associated with obesity, identify patients with a higher risk of developing periodontal disease, and recognize important treatment outcomes associated with obese patients. The purpose of this paper is to assess current literature to determine the strength of the association between obesity and periodontal disease and review implications for dental hygienists.

Review of Literature

Research will be reviewed in the following areas: adipose tissue, obesity as a risk factor for periodontal disease, and dental hygiene concerns.

Adipose Tissue

Fat, or adipose tissue, is primarily responsible for regulating body energy, and under normal conditions maintains homeostasis of energy storage and exertion. Abnormal or excessive abdominal fat, called visceral adipose tissue, is more highly associated with adverse health conditions than excess subcutaneous fat and contributes to multiple medical conditions.[4,9,10,27,28] Body-shape morphology, indicated by the location of visceral adipose fat deposition, has been

identified as a contributor to adverse health conditions. Proportionally more visceral adipose tissue, evident in an apple-shaped body type, increases the risk of metabolic health conditions, unlike a pear-shaped body type evidenced by excess fat below the waist.[29] Research on the obese (ob) gene, by Zhang et al., revealed visceral adipose tissue, in addition to energy regulation, functions as a complex metabolic endocrine organ with a role in cytokine secretion.[30] Excess visceral adipose tissue can produce unfavorable systemic effects by altering circulating signaling molecules called adipokines that are critical to endocrine function.[31] Research suggests a possible link between obesity and periodontitis related to alterations in the host immune and inflammatory systems associated with both diseases.[5,27,33-36] Research related to the role of these cytokines will be reviewed next, followed by the synergistic effects of oxidative stress.

Adipocytes found in visceral adipose tissue contain activated macrophages that produce various cytokines.[4,6,34-40] Weisberg et al., researched the expression of obesity related macrophages and found a positive correlation between activated macrophages and body mass.[41] Increased macrophage activity leads to increased cytokine secretion that generates an inflammatory response.[42] Skurk et al., researched adipocyte hypertrophy among participants undergoing elective plastic abdominal surgery and results indicated a strong linear correlation of adipokine secretion over time.[43] Leptin, adiponectin, tumor necrosis factor-alpha (TNFα) and interleukin-6 (IL-6) are specialized cytokines that act as inflammatory markers in communication with the immune system and are referred to as adipokines.[36,40,44] Responsible for regulation of inflammation and immunity, research suggests an imbalance of cytokine activity can lead to chronic low-grade systemic inflammation and a modified metabolic and immune response influencing host susceptibility to disease (Figure 1). [4,6,34-36,38-40] Both Defuria et al., and Weisberg et al., researched cytokine changes associated with lean and obese mice, and concurred

that obesity-altered macrophage activity initiates modifications in the regulation of host inflammation and immune reactions.[41,45] Importantly, Weisberg et al., compared results in mice to human subjects, and found similar results.[41] The resultant pro inflammatory state may stimulate pro inflammatory mediators and cytokines which may contribute to periodontal disease.

Adipokines are categorized as either anti-inflammatory or pro-inflammatory according to their role (Table 1). Excessive visceral adipose tissue is associated with increased production of pro-inflammatory cytokines, leptin, TNFα and IL-6. It is also related to a reduction in adiponectin, an anti-inflammatory cytokine. Hence, an exaggerated hyper-inflammatory reaction can be activated and may increase susceptibility to tissue breakdown including tissues of the periodontium.[4,31,36,39,40,46,47] Recent research by Schmidt et al., and Wakkad et al., investigated cytokine levels related to obesity in 117 obese participants and 83 non-obese participants. Results indicated obesity was significantly associated with a change in pro and anti-inflammatory cytokines.[48] Excess visceral adipose tissue can modify cytokine production and create a hyperinflammatory response.

Leptin, a pro-inflammatory cytokine, serves an integral role in the inflammatory process of obesity.[36,40,46,47] Leptin, an endocrine hormone, is primarily responsible for controlling appetite and energy expenditure. Levels of circulating leptin are directly proportional to the amount of adipose tissue mass in the body; and obese individuals have higher levels.[40,47] Numerous health conditions are associated with increased leptin levels including insulin resistance, widely known to be linked to diabetes mellitus, and coronary heart disease disease.[47,49] Kwon et al., researched exogenously administered leptin on mice, and determined it reduced obesity and reversed insulin sensitivity.[31] According to Goncalves et al., and

Zimmermann et al., high levels of leptin initiate macrophage activity that stimulates production of TNFα and IL-6, pro-inflammatory cytokines, thus producing an inflammatory reaction.[36,46] High levels of circulating leptin are associated with an increased production of C-reactive protein (CRP), a chronic inflammatory marker associated with multiple diseases including diabetes mellitus and cardiovascular disease.[40,47] Furthermore, increased leptin production contributes to metabolic changes associated with bone formation and destruction[47], influences oxidative stress, and affects host immunity.[50] Sing et al., researched leptin's role in obesity and found in-vitro, changes in leptin were positively correlated with changes in adiponectin, an anti-inflammatory cytokine.[33] Modified by obesity, increased levels of leptin initiate metabolic and physiologic changes that contribute to a chronic inflammatory reaction and can increase host susceptibility to disease, including periodontal disease.

Like leptin, adiponectin plays an important role in the regulation of appetite and inflammation.[37] Unlike other inflammatory markers produced in adipose tissue, adiponectin is an anti-inflammatory cytokine that also participates in moderating insulin sensitivity.[31,37,40,44] However, it is the reduction of adiponectin that contributes to the inflammatory process in obesity.[36] Produced in adipose tissue, normal adiponectin levels suppress the development of inflammation that contributes to disease progression.[50] Nigro et al., in a recent review of adiponectin's role in obesity concluded the finding that there is a decrease in expression of adiponectin in obese patients, pigs, and rodents.[51] Kwon, et al., in a review of the physiological and molecular effects of adipokines in obesity-induced inflammation and insulin resistance, revealed that adiponectin generates both pro-inflammatory and anti-inflammatory responses.[31] Reduced levels of adiponectin, called hypoadiponectinaemia, produce a metabolic imbalance that facilitates a chronic inflammatory state.[37] Research suggests a decrease in adiponectin in

periodontal patients may induce a worsening of periodontitis.[52] Interestingly, Trujillo et al., in a review of adiponectin as an inflammatory biomarker for metabolic syndrome, concluded that an increase in adiponectin and improved systemic insulin sensitivity was significantly correlated to both diet-induced weight loss and bariatric surgery.[53] According to a critical review of metabolic syndrome and periodontitis by Bullon et al., there may also be a relationship between low levels of adiponectin associated with obesity and oxidative stress.[50] Reduced adiponectin levels create a dysregulation between pro and anti-inflammatory markers that results in a higher expression of pro-inflammatory cytokines.[36] In-vitro research from Brunn et al., on the interaction between adiponectin and other inflammatory cytokines, found an inverse relationship between adiponectin and adipose tissue-derived cytokines, especially IL-6 and TNF.[54] It appears the result of reduced adiponectin associated with obesity, contributes to a hyper-inflammatory state that may both link obesity to host susceptibility to periodontal disease and also propagate progression of the disease.

According to Arner et al., the effects associated with an increase in TNFα and IL-6 are detrimental in the inflammatory process associated with obesity.[56] TNFα, a cell signaling protein, is a pro-inflammatory cytokine produced by white blood cells that contributes to inflammation in the body. IL-6, the initiator of acute phase inflammatory activity, plays a critical role in the pro-inflammatory defense against pathogens. Both TNFα and IL-6 can stimulate further macrophage production and contribute to an acute reaction of C-reactive protein, another important mediator in the inflammatory process.[6,39,57] Research by Hotamisligil et al., to investigate TNFα levels in humans studied 19 obese participants and 18 non-obese participants. Results indicate TNFα levels were two and a half times higher in obese individuals, and a decreased body weight was associated with a decreased level of TNFα.[58] Associated with osteoclastic formation, increased

TNFα can lead to the degradation of the connective tissue matrix resulting in the breakdown of bone. [4,36] In regards to IL-6, Roytblat et al., studied 25 obese participants and 12 non-obese participants and results indicated statistically significant differences in serum IL-6 levels, with the obese participants showing higher levels of IL-6.[59] Overall research suggests there is an increase in TNFα and IL-6 with obesity. Importantly, an increase in these same inflammatory markers are also associated with destruction of connective tissue and bone associated with periodontal breakdown.

Inflammatory marker modifications and overaccumulation of fatty acids in adipose tissue, a result of high caloric diets, can increase the production of reactive oxygen species (ROS) molecules that contribute to a chronic state of oxidative stress.[13,60] Attributable to adverse metabolic conditions, oxidative damage is significantly greater in obese than non-obese individuals. [13,61] According to Dandona and Bullon, the imbalance of adipocytokines related to obesity, is associated with an increase in reactive oxygen species (ROS) molecules, called oxidants or free radicals.[50,61] The imbalance between oxidants and antioxidants results in a damaging state of oxidative stress that can lead to the initiation and progression of many chronic diseases.[62,63] Chen et al., in a case-control study of 72 participants and 105 control group participants researched the relationship between inflammatory markers (CRP, IL-6, and adiponectin) and oxidative stress associated with obesity and metabolic syndrome. Results indicated a significant positive correlation between inflammatory markers and oxidative stress.[64] Similarly, Wang et al., in a progressive cohort study of 305 obese adolescents researched the relationship between inflammation and oxidative stress. Results indicated metabolism, inflammation, and oxidative stress were influenced by adiposity.[65] Importantly, research

suggests obesity may increase reactive oxygen species which may create gingival oxidative damage and could prompt periodontal destruction.

An imbalance of cytokine activity and a state of oxidative stress associated with visceral obesity contributes to systemic inflammation and a modified immune response that results in host susceptibility to disease. As obesity increases circulating reactive oxygen species, it may cause gingival oxidative damage and could prompt periodontal destruction.

Obesity as a Risk Factor for Periodontal Disease

The state of inflammation resulting from dysregulation of cytokine activity and oxidative stress may play a role in the relationship of obesity as a risk factor for periodontal disease (Table 2). Periodontal disease is a chronic inflammatory disease that is initiated by periodontal pathogenic bacteria with host susceptibility determining the course of progression and the severity of the disease.[5,32] According to Muluke et al., the inflammatory host response is crucial in the development and progression of periodontal disease.[32] Research suggests a possible link between obesity and periodontitis related to alterations in the host immune and inflammatory systems associated with both diseases (Table 3).[5,27,33-36] Shah et al., determined the rate of developing periodontitis increases 1.8 times more in obese individuals compared to those with a normal BMI. Similarly, Khader et. al., after adjusting for a plaque index, age, and missing teeth found individuals with a BMI >30 were 3 times more likely to develop periodontitis than those with a normal BMI. [34,35] It is apparent, inflammation associated with obesity has a role in periodontal disease.

Dysregulation of anti-inflammatory and pro-inflammatory adipokines associated with excess visceral fat appears to modulate the development and progression of periodontal disease.[34-36] The first to discover a connection between obesity and periodontal disease, Perlstein

et al., in the 1970's studied the effects of obesity on the periodontium of rats with results revealing that obesity significantly contributed to the severity of periodontal disease.[66] Subsequent research studies have produced similar results. Shah et al., researched the effects of obesity on periodontitis, with 40 obese and 40 non-obese participants, to evaluate the relationship between BMI and WC associated with clinical attachment loss (CAL). Results indicated a significant positive relationship between obesity and both BMI and WC.[35] Martinez-Herrera et al., in a cross-sectional study of 110 obese and 102 non-obese participants found periodontitis is more prevalent in obese participants (80.9%) than lean participants (41.2%), and obese participants risk of periodontitis is six-fold that of lean individuals.[67] Furthermore, Nascimento et al., Suvan et al., and Khader et al., researched the effects of obesity on periodontal outcomes, and results indicated abdominal obesity has a direct effect on unfavorable periodontal outcomes.[34,39,68] For example, Nascimento et al., in a cohort study in Brazil, researched 1,066 participants between the years 2009 and 2012 to determine the controlled direct effect of abdominal and general obesity on periodontal outcomes. Using marginal structural models to control for hypertension, weight loss, weight gain, gender, age, household income, smoking status, alcohol consumption, physical activity, and fatty meat and sugar consumption, the results indicated obesity, particularly abdominal obesity, produced unfavorable periodontal outcomes based on clinical attachment levels and bleeding on probing.[39] Suvan et al., researched 260 adults with severe periodontitis over a 7-year period to assess whether BMI is a predictor of the response to non-surgical periodontal treatment (NSPT). While controlling for baseline status, age, smoking and dental plaque scores, results indicated obese participants had significantly higher mean probing pocket depths after NSPT, than non-obese.[68] Furthermore, Khader et al., researched 340 participants in Jordan to determine the relationship between periodontitis and

overweight/obesity among Jordanians. Results indicated that only 14% of normal weight participants had periodontal disease, while nearly 30% of overweight and nearly 52% of obese participants had periodontal disease.[34] Both Jimenz et al., and Kangas et al., studied non-smoking and non-diabetic participants to examine obesity and its association with periodontal pocketing and periodontitis using WC and waist to height ratio (WHtR). Results revealed a significant association between adiposity and periodontal disease.[10,69] Moreover, Kangas et al., concluded that subjects with the highest WC or WHtR have an increased likelihood, 40-60%, of having periodontal pockets 4 mm or greater.[10] Research supports evidence of a link between obesity and periodontal disease.

Multiple researchers have studied cytokine imbalances in obese and non-obese participants with and without periodontal disease. Research by both Zimmermann et al., and Kose et al., to evaluate circulating levels of adipocytokines in obese and normal weight participants with and without chronic periodontitis, found obese non-periodontitis and obese chronic periodontitis participants had higher levels of TNFα compared to normal weight non-periodontitis and normal weight chronic periodontitis.[46,70] It is well known that high levels of TNFα contribute to periodontal breakdown.[71] Furthermore, Kose et al., found significantly higher levels of IL-6 among obese participants compared to non-obese participants while Zimmermann et al., concluded the highest concentration of leptin was in obese non-periodontitis participants.[46,70] It is evident from this information that inflammatory adipocytokines are associated with obesity, but some results are conflicting in determining a relationship between obesity and periodontal disease. It is possible, however, that high concentrations of leptin in non-periodontitis obese participants will, over time, contribute to the development of periodontal disease as a result of leptin's role in bone metabolism. Buduneli et al., in a cross-sectional, case-

control study of 60 obese and 31 non-obese women researched clinical periodontal measurements and inflammatory biomarker levels. Results indicated clinical attachment levels, and levels of leptin and IL-6 were higher in the obese group compared with the non-obese group.[40] Research by Thanakun et al., to determine effects of inflammatory markers associated with periodontal status and BMI in 109 participants from Thailand where overweight status has a lower designation than the U.S., concluded overweight and obese participants had higher levels of leptin and CRP, and lower levels of adiponectin than normal weight participants without the effect of severe periodontitis.[57] Research suggests there is no relationship between obesity and the severity of periodontitis, however, inflammatory and immune implications associated with obesity, may influence host susceptibility for the development or progression of periodontal disease. Maciel et al., researched the effects of obesity on the subgingival microbiota of chronic periodontitis participants with normal weight compared to those with obesity, and healthy periodontal participants with normal weight compared to obesity. Results from this research indicated obese participants had significantly higher periodontal pathogens than those with normal weight and chronic periodontitis.[27] In addition, *Porphyromonas gingivalis,*(P. gingivalis), a destructive periodontal pathogen, was studied by Amar et al., to determine the effects on the innate immune response in obese and non-obese mice. Suggesting that cytokine dysregulation associated with obesity interferes with the immune's ability to respond to P. gingivalis, results indicated that mice with diet-induced obesity had significantly higher levels of alveolar bone loss than the non-obese control group. More research is needed to determine the full extent of a microbiology association.

In addition to increased periodontal pathogens and implications from macrophage-induced inflammatory markers, a chronic state of oxidative stress associated with obesity has

periodontal implications.[13] According to Ongoz et al., the increased production of reactive oxygen species (ROS) associated with obesity, may have adverse effects on the periodontium.[72] D'Aiuto et al., researched 145 participants with periodontitis and a control group of 56 participants to determine if severe periodontitis was associated with oxidative stress. Results indicated that severe periodontitis was independently associated with increased oxidative stress.[73] Furthermore, Atabay et al., looked at the effects of obesity on healthy and diseased tissue in 48 obese and 45 non-obese participants to determine if gingival crevicular fluid changes were associated with a state of oxidative stress. Results revealed that periodontal destruction and disease severity may be influenced by increased level of oxidative stress associated with obesity.[13] Likewise, Suresh et al., researched whether reactive oxidative metabolite (ROM) levels, by-products of oxygen metabolism, were an indicator of oxidative stress in the body. Sixty participants were divided into four equal groups: obese or overweight with generalized chronic periodontitis, obese or overweight with generalized chronic gingivitis, obese or overweight with healthy periodontium, and non-obese and healthy periodontium. After controlling for plaque and gingival index, probing pocket depth, clinical attachment levels, and blood plasma levels of ROM, the obese participants with periodontitis had more oxidative stress compared to obese subjects with healthy periodontium.[5] Interestingly, 80% of non-obese participants had normal oxidative stress levels.[5] It is evident that the state of oxidative stress from the metabolic imbalance between oxidants and antioxidants, is associated with both obesity and periodontal disease.

Similar to obesity, multiple modifiable and non-modifiable risk factors contribute to the pathogenesis of periodontal disease (Table 4). It is well-known that smoking is one of the most significant contributing modifiable risk factors.[19,74] Obesity has been suggested by some

researchers to be the second.[32,35] Other modifiable risk factors such as oral biofilm accumulation, medications, level of education, stress, and nutrition, as well as non-modifiable factors including past history of periodontitis, genetics, age, gender, ethnicity, and host response are contributors to periodontal disease.[14-17,19,20] In consideration of age, Al-Zahrani et al., researched the relationship between obesity and periodontal disease with 13,665 young, middle-aged, and older adult participants. Controlling for gender, race, smoking, poverty index, education, diabetes, and duration of time since last dental visit, results indicated obesity was significantly associated with the prevalence of periodontal disease in participants aged 18 to 34, but no significant association was found in the older age groups.[75] Unfortunately, the researchers didn't consider age as a risk factor for periodontal disease. Results of the research indicate the prevalence of periodontal disease in obese middle-aged and older aged participants is greater than younger aged participants (1.653% for middle and older-aged participants compared to 1.137% for young participants), but it is difficult to determine whether age or obesity is a confounding factor in those age groups. Additionally, without longitudinal studies, consideration should be given to whether the obese middle-aged and older-aged participants suffered from long-term obesity effects or whether it is a result of the more recent obesity epidemic. Such findings may indicate there is an association between obesity and periodontal disease in older populations. Similar research by H El-Sayed on 380 participants aged 20-26 to assess the relationship between overall and abdominal obesity and periodontal disease, concluded overall and abdominal obesity in young adult females as well as abdominal obesity in young adult males was significantly associated with periodontal disease.[76] Conversely, de Castilhos et al., followed 720 young adult participants, below the age of 24, to determine if there was an association between obesity and periodontal disease and results indicated the presence of periodontal pockets

was not associated with obesity in this age group.[77] It is possible that a lack of association between periodontitis and obesity may be attributed to researchers using only periodontal pocket measurements without considering clinical attachment loss. Of interest, there was an association between gingivitis and obesity, mediated by oral hygiene and systemic inflammation, as well as an association between calculus and obesity suggesting this cohort may be at risk of developing periodontal disease. It is evident that conflicting research warrants further investigation. However, it appears obesity may influence age-related risk factors that contribute to periodontal disease, and the relationship may be more evident in younger age groups that exhibit less comorbidities.

In regards to gender and obesity, Gaio et al., assessed the effects of being overweight or obese on PAL in 755 participants in a 5-year prospective study. Controlling for gender, age, skin color, education, socio-economic status, smoking, and dental care, results indicated obese participants had a significantly higher risk of PAL progression than non-obese participants, and obese females were at a statistically significant higher risk of PAL progression than non-obese females, but the same results were not true for males. [78] These findings are of interest since research generally has found males to have a higher prevalence of periodontal disease than females.

Akman et al., researched blood serum levels including plasma triglycerides, total cholesterol, low and high-density lipoprotein cholesterol, fasting blood glucose, and TNFα, as well as, periodontal parameters including plaque index, probing depth, clinical attachment level, and percentage of sites with bleeding on probing to determine if there was an association between obesity, gender and periodontal disease. In females, the waist-to-hip ration was significantly associated with higher plaque indexes and probing depths, but not in males.[79]

Interestingly, the results may be influenced by the researches' modifications of measured variables. Specifically, different cutoff points were used for males and females, as a result of male participants having had a higher BMI and WHtR score than female participants. Conversely, Gorman et al., researched whether body mass index, waist circumference, and waist circumference to height ratio predicted progression of periodontal disease in 1,038 males between 1969 and 1996. While controlling for age, smoking, education, diabetes, recent periodontal treatment and prophylaxis, and number of filled/decayed tooth surfaces. Results indicated obese males were between 41% and 72% more likely to have periodontal disease progression than non-obese males.[28] Similar results were found by Jimenez et al., in studying 36,910 male participants for 20 years to assess the association between adiposity and risk of periodontal disease. After controlling for age, smoking, race, dental profession, physical activity, fruit and vegetable intake, alcohol consumption, and diabetes status at baseline, results indicated a significant association between central adiposity and the risk of periodontal disease in men.[69] Furthermore, Han et al., in a cross-sectional study of 1,046 Korean participants aged 15 years or older, researched whether obesity was associated with periodontitis. After controlling for age, gender, monthly family income, smoking, drinking, frequency of daily teeth brushing and physical activity, the results indicated obesity was independently positively associated with periodontitis, and, in addition, was associated more in males age 45-54, than any other group.[80] Likewise, Katagiri et al., researched the prevalence of periodontitis in 95 obese and 102 non-obese participants, aged 25-40 years old in Japan. After controlling for gender, decayed, missing, and filled teeth, results indicated there was a significantly higher prevalence of periodontitis among obese female participants, but not males.[81] More research is needed to determine the relationship age and gender has on both obesity and periodontal disease.

Unlike age and gender, behaviors are a modifiable risk factor that may be associated with both obesity and periodontal disease. Ekuni et al., researched effects of BMI and oral health behavior on periodontal status in a cohort of Japanese college students and results indicated elevated BMI was associated with worsening periodontal status, and a lack of interproximal dental cleaning was associated with gingivitis.[82] Park et al., researched 15,666 South Korean adults to assess the relationship between obesity and oral health behaviors including frequency and time of day tooth brushing was performed, and the use of secondary oral products such as dental floss, mouthwash, interdental brushes and electric toothbrushes. Results indicated obese participants had a lower daily frequency of tooth brushing, used fewer secondary oral products than non-obese participants, and that poor oral health behaviors were positively associated with general and abdominal obesity.[83] Prpic et al., in a cross-sectional study, investigated the association between obesity and periodontitis, oral hygiene, and tooth loss in 292 non-smoking, non-diabetic Croatian participants aged 31-75 years. Results indicated the use of interdental brushes/flossing and number of missing teeth were significantly associated with BMI, but results could not validate an association with periodontitis.[84] However, obese participants were less likely than non-obese participants to use interdental brushes and/or floss on a daily basis, and had more missing teeth.[84] In addition, the risk for developing periodontal disease significantly increased in female participants, especially if they were poorly educated or had unsatisfactory oral hygiene habits, defined as a lack of interdental plaque removal. [84] Interestingly, the researchers failed to conclude based on their results that male participants, due to a lack of tooth brushing frequency of less than daily also have a significant increased risk of developing periodontal disease. Clearly, a lack of health awareness can influence both obesity, and oral

health behaviors that stimulate plaque removal, such as tooth brushing, flossing, and the use of interdental appliances.

Dental Hygiene Concerns

As a potential risk factor for periodontal disease, dental hygienists should be aware of dental implications associated with obesity since both have inflammation as a common denominator. Understanding the link between obesity and periodontal disease contributes to patient care in medical, dental, and scientific communities. According to Nascimento et al., Gonvalves et al., and Suvan et al., the success of periodontal therapy may be modulated by the adverse effects of obesity on periodontal tissues.[46,68,85] For example, Goncalves et al., evaluated the effects of scaling and root planing (SRP) on gingival crevicular fluid and adipokine serum levels in 20 obese participants with chronic periodontitis and 20 non-obese participants with chronic periodontitis at baseline, 3, 6, and 12 months post-therapy. Results indicated at 12 months post SRP therapy, concentrations of leptin increased in obese participants in both shallow (5 mm - < 7mm) and deep (≥ 7mm) periodontal pockets when compared to baseline, but not the non-obese participants.[46] Levels of TNFα were also higher in both shallow and deep pockets of the obese, but not the non-obese at 3, 6, and 12 months post SRP therapy.[46] Additionally, at 3 months post SRP therapy, IL-6 was higher in deep pockets of the obese participants in comparison to the non-obese.[46] Suvan et al., researched whether BMI was a predictor of the response to non-surgical periodontal treatment (NSPT) in 93 overweight, 55 obese, and 112 normal weight participants at 2 months post SRP therapy. Results indicated BMI and obesity were independent predictors of a poor response to NSPT with BMI having a statistically significant linear relationship with mean probing pocket depths.[68] Interestingly, for every increase in BMI of 10kg/m^2, the mean number of probing pocket depths >4mm increased by

2.5%.[68] Furthermore, Bouaziz et al., researched 18 obese and 18 non-obese participants in a case-control study to evaluate the association between adiposity and NSPT outcomes in patients with chronic periodontitis. After controlling for gender, age, WHtR, plaque index, bleeding on probing, probing depth, and CAL at baseline and 3 and 6 months after treatment, results indicated a negative association between adiposity periodontal treatment outcomes for moderate-to-deep pockets, defined as pocket depths >5mm.[86] However, unlike other researchers, Duzagac et al., studied the role of obesity on the healing response to periodontal therapy in serum and gingival crevicular fluid in 15 obese participants with periodontitis and 15 non-obese participants with periodontitis. Results indicated that obese participants responded to SRP as well as non-obese participants, but obesity adversely affected the CRP and serum adipocytokine levels in response to therapy.[87] It appears SRP outcomes may not be as effective in obese individuals. Higher levels of inflammatory markers such as leptin, TNFα, IL-6, and even CRP post-treatment, suggest obesity may inhibit positive long-term results. Importantly, obesity seems to complicate outcomes of periodontal treatment and a multi-disciplinary approach between medical and dental professionals may be needed to promote optimal health outcomes.

Interestingly, Lakkis et al., researched whether significant weight loss would improve the response to non-surgical periodontal therapy in obese patients using 15 obese participants with chronic periodontitis that underwent bariatric surgery (BS) for weight loss and 15 obese participants with chronic periodontitis without surgery or weight loss. Probe depths, clinical attachment level, bleeding on probing, gingival index, and plaque index were measured at baseline and at 4 to 6 weeks after periodontal treatment. Results revealed a statistically significant improvement after periodontal therapy in the BS participants compared to the obese group.[88] Similarly, Al-Zahrani et al., studied 2,521 participants to examine if there was an

association between sustained physical activity and periodontitis utilizing the third national health and nutrition examination survey (NHANES III) over a 10-year look back period. The results indicated a strong and statistically significant association between physical activity and periodontitis. For example, participants that were active were 54% less likely to have periodontitis than those participants that were inactive; partially active participants were 35% less likely to have periodontitis than inactive participants.[89] A possible explanation may be the effect physical activity has on insulin sensitivity, thus influencing type II diabetes, a known risk factor for periodontitis. However, another possible explanation may be that physical activity can reduce inflammation, thus supporting the possibility that obesity-related inflammation may play a significant role in the pathogenesis of periodontitis. In a similar study to Lakkis et. al., Sales-Peres et al., in a prospective study of 50 morbidly obese participants, investigated whether significant weight loss as a result of gastric bypass surgery (GBS) would decrease the presence of periodontopathogenic bacteria and periodontal disease, at 12 months post-surgery in comparison to pre-surgery.[90] Interestingly, results indicated that after GBS there was a reduction in some inflammatory biomarkers, but the severity of periodontal disease increased and P. gingivalis was the periodontopathogenic bacteria most associated with the severity of disease. [90] Results suggest that although GBS may decrease inflammatory biomarkers, it does not improve cytokine dysregulation of the immune system to respond accordingly to periodontal pathogens.[90] Such conflicting research warrants further investigation, however, it appears that adverse conditions associated with obesity and periodontal disease are evident.

Inflammatory and immune implications associated with obesity may influence peri-implant health including osseointegration of implants, soft tissue healing, and the longevity of the implant. Elangovan et al., studied the relationship between obesity and inflammatory

markers in tissues surrounding dental implants of non-smoking participants that were on a stable periodontal maintenance program. Twenty-three obese participants and 47 overweight or normal weight participants were examined using BMI, WC, and body fat percentage, as well as, intraoral assessments including plaque index, periodontal and peri-implant comprehensive exams, and peri-implant sulculur fluid collections. Results indicated that although no association was made between BMI, body fat, and inflammatory markers, WC was statistically significantly correlated with inflammatory markers in peri-implant sulcular fluid.[91] Importantly, the participants studied were maintaining a stable periodontal maintenance program suggesting elevated inflammatory markers and dysregulation of the immune system could alter the health of peri-implants in participants with visceral obesity and unstable periodontitis, or those not maintaining a more frequent recall program. Limited research evidence is available relating to the possibility that obesity-induced inflammation could be a risk factor for peri-implantitis. Inflammatory and immune implications associated with obesity could contribute to impaired peri-implant health.

Discussion

Obesity is a risk factor for periodontal disease. Based on findings, no direct cause and effect association could be made between periodontitis and obesity, but the link between the two seems clear. Adipose tissues secrete cytokines such as tumor necrosis factor, interleukin-6 and hormones believed to increase overall inflammation and produce an inflammatory overload. With increased levels of adipose tissue, pro-inflammatory mediators increase while anti-inflammatory mediators decrease. Research indicates such dysregulation of cytokine activity creates a chronic low-grade inflammatory state and modifies metabolic and immune responses that influence host susceptibility to disease. Moreover, modifications in the inflammatory system increases production of reactive oxygen species that results in a chronic oxidative state

and can lead to the initiation and progression of chronic disease. Emerging research suggests increasing levels of inflammatory cytokines in response to obesity, coupled with the presence of periodontal pathogens may increase the risk of periodontal disease; therefore, it is recommended that dental hygienists control oral pathogens and systemic inflammatory markers by non-surgical treatment to reduce the risk of periodontal disease and promote a healthy lifestyle that includes weight control and nutritional counseling. Hopefully, this approach facilitates quality dental hygiene care within the growing overweight population based on current knowledge.

Knowledge of the prevalance of obesity and adverse effects associated with obesity-induced inflammation can provide dental hygienists with an opportuntiy to educate patients about the risk of obesity and periodontitis. However, as obesity is a multifacted and complex issue, coordinated efforts among healthcare providers is essential to help most patients improve weight control. Having regular and frequent contact with patients, dental hygienists are able to recognize and inform patients of health risks associated with obesity and can suggest good nutrition and exercise. Importantly, many dental hygienists already focus on prevention and intervention through behavior modification, smoking cessation, and dietary counseling. Kading et al., investigated dental hygienists' confidence in providing obesity education and counseling, and found that hygienists working in specialty practices were more confident in behavioral counseling than hygienists that work in other settings.[92] Multiple factors may explain this. Perhaps hygienists working in advanced practice offices graduated from 4-year institutions and received more education and training in the treatment of obesity related diseases. It may also be possible that there are more obese patients seeking treatment from advanced practice settings where hygienists have gained more experience and confidence in comparison to general practice settings. Curran et al., researched dentists' barriers in providing obesity counseling for patients.

Results indicate participants feared offending patients, lacked an awareness of an association between obesity and dental disease, lacked education and training, and being obese themselves leads to beliefs of inadequate credibility.[93] Assumably, dental hygienists may face similar barriers.

Results from a study by Essex et al., on California dental hygienists found participants exhibited mildly negative attitudes toward the obese population, and emphasized the importance of the dental hygienist in addressing health effects of obesity.[94] Importantly, dental hygienists must work toward being less judgemental if they are to be successful in motivating obese patients to make positive lifestyle changes. Magliocca et al., researched the knowledge, beliefs, and attitudes of 77 dental hygienists toward obesity. Results indicated almost 40% of participants received 1 hour or less of obesity education in Dental Hygiene school.[95] Interestingly, Divaris et al., in a systematic review to determine dental and dental hygiene schools' intent to address childhood obesity, reported that while the Commission on Dental Accreditation (CODA) standards make sporadic mentions of diet and nutrition, curricula is scant.[96]

Dental hygiene curriculum should be evaluated for development of basic competency skills that ensure graduates are proficient in dietary counseling beyond cavity-producing substances. It is well-known that weight loss and sustained weight maintenance is challenging and will require dental hygienists to be adept in providing dietary counseling to patients. Dental Hygiene CODA standard 2-8b, states "biomedical science content must include content in … nutrition," and standard 2-8d establishes "dental hygiene science content must include oral health education and preventive counseling, health promotion, patient management…[and] legal and ethical aspects of dental hygiene practice.."[97] The growing obesity epidemic necessitates more

fully developing the dental hygiene curriculum in this area and addressing risk factors associated with excess weight. In an already full curriculum, dental hygiene educators should agree that the obesity epidemic is a public health concern and justify the revision of educational requirements.

Similar to dental hygiene smoking cessation education, weight control education could focus on teaching empathy, patient motivation skills, specialized levels of care associated with the 5 A's intervention steps (Ask, Advise, Assess, Assist, and Arrange), and professional intercollaboration. Research supports successful outcomes of patients' smoking cessation with dental hygiene interventions.[98-100] Identification of patients' needs are a significant componenet of the American Dental Hygiene Association (ADHA) dental hygiene clinical practice guidelines and important in promoting patient-centered care and interprofessional collaboration. Dental hygienists should be competent in the management of patients with obesity and be able to convey current research on the link between periodontitis and obesity. Obese patients could benefit through referrals to weight loss centers for weight reduction interventions such as behavioral therapies, surgical options and diet control.

A key component to the dental hygiene process of care is the assessment phase, "the collection and analysis of systematic and oral health data in order to identify client needs". The ability to initiate an open dialogue with patients regarding the latest research on obesity-related health concerns can facilitate awareness for health promotion and disease prevention. In treating obese periodontal patients, dental hygienists should consider more frequent patient recall appointments and early treatment of disease including the use of adjunctive therapies to decrease the host inflammatory burden. In addition, individualized behavioral and dietary counseling should be included in treatment planning for obese patients and those at-risk of obesity. Dental hygienists should closely monitor the periodontal health of obese patients and perform

continuous assessment, education, and dietary counseling for lifestyle changes supported by guidelines for weight loss and weight control. Multiple screenings are utilized in patient assesements including medical and dental health histories, vital signs, oral cancer screenings, and caries risk assessements. Conceivably the addition of a weight assessment screening tool would add value to the dental hygiene assessment with more comprehensive information gathering that could improve oral and systemic health in coordination with other healthcare professionals.

Dental hygienists should be competent in the management of patients with obesity and be able to convey current research on the link between periodontitis, obesity and systemic health. Obese patients could benefit through referrals to weight loss centers for weight reduction interventions such as behavioral therapies, surgical options and diet control.

Continuing education courses for current practitioners may be needed to promote awareness of oral and systemic implications associated with obesity, reduce assessment and treatment plan barriers and improve practitioner confidence when approaching obesity related health topics. Increased knowledge of appropriate caloric intake and physical activity for weight loss and sustainablity, combined with skill development in behavior modifications may promote dental hygienists' role in facilitating positive lifestyle changes for patients. Interprofessional collaboration is important. As part of a multidisciplinary approach to improve health outcomes, dental hygienists are in an ideal position to facilitate referrals to other healthcare professionals including physicians, nutritionists, and behavioral therapists. Obesity is a complex problem and many patients will need counseling to better address the underlying problems involved in this type of disordered eating. Additional collaborations may be needed for encouraging patients to perform physical activities that are appropriate for their situation.

In recognition of periodontal implications associated with obesity, dental hygienists should integrate practice modifications that are based on the latest research. Specifically, dental hygienists can include BMI and waist-to-height ratio calculations as part of the patient assessment in coordination with evaluating medical history risk factors. Such information will enable dental hygienists to identify additional risks associated periodontal disease. The ability to initiate an open dialogue with patients regarding the latest research on obesity-related health concerns can facilitate awareness for health promotion and disease prevention.

Importantly, all dental hygienists should lobby to prioritize obesity as a public health risk factor responsible for multiple diseases. Without awareness of the relationship obesity has on periodontal disease, dental hygienists may not realize the potential role they may serve. With enhanced knowledge, dental hygienists can educate patients on oral and systemic implications associated with obesity, identify patients with a higher risk of developing periodontal disease, and recognize important treatment outcomes associated with obese patients.

Conclusions

People who are obese are likely to have periodontal diseases. The literature reveals no direct evidence of a cause and effect relationship between obesity and periodontal disease; although most studies reviewed, revealed a possible relationship between periodontal disease and obesity. In addition, periodontal bacteria may cause a systemic inflammatory response and coupled with the inflammatory response associated with obesity, increases inflammatory markers leading to periodontal breakdown. Because no studies established a direct relationship between the two diseases, further research is needed to explore the relationships between oral diseases and pathogenesis of obesity. To determine whether obesity causes periodontitis experimental animal studies that initiate and monitor periodontal disease and obesity and longitudinal,

prospective clinical studies measuring periodontal status, obesity, and inflammatory mediators are needed. As long as some studies show that obesity and specific periodontal bacteria and inflammatory mediators are associated, there is an important role for dental hygienists in prevention, early detection and prompt treatment of periodontitis.

Dental hygienists should be competent in the management of patients with obesity and be able to convey current research on the link between periodontitis and obesity. Obese patients could benefit through referrals to weight loss centers for weight reduction interventions such as behavioral therapies, surgical options and diet control. Learning to communicate effectively with overweight patients about their disease risk may facilitate improved oral health for the patient. Continuing education courses for current practitioners and curricula in dental hygiene programs are suggested to facilitate communication and counseling with patients on this often-sensitive subject. Obesity for many is a sensitive subject and may not be easy to bring up. Hence the need for more education. The demand for dental hygienists who specialize in treating patients with obesity may increase as the condition itself is increasing and the link with inflammatory diseases is relevant. Understanding obesity may help the dental hygienist provide quality comprehensive care to those in need.

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Inflammatory Cytokine	Role	Obesity induced modification	Resultant effects
Leptin	Pro-inflammatory	Increased production	➢ Stimulates production of TNFα and IL-6 ➢ Contributes to diabetes mellitus and cardiovascular disease
TNFα	Pro-inflammatory	Increased production	➢ Initiates osteoclastic activity that results in bone and other connective tissue degradation
IL-6	Pro-inflammatory	Increased production	➢ Produces acute and chronic state of inflammation
Adiponectin	Anti-inflammatory	Decreased production	➢ Contributes to metabolic imbalance and oxidative stress

Table 1. Dysregulation of cytokine activity associated with obesity

Inflammatory Markers	**Periodontal disease**	**Obesity**
Leptin	✓	✓
TNFα	✓	✓
IL-6	✓	✓
Adiponectin	✓	✓
Oxidative stress	✓	✓

Table 2. Association of inflammatory markers

Author	*Research results*
Perlstein et al.	Obesity significantly contributed to the severity of periodontal disease.
Shah et al.	BMI and WC were associated with clinical attachment loss.
Martinez-Herrera et al	Periodontitis was more prevalent in obese participants and obese participants risk of periodontitis is six-fold that of lean individuals.
Nascimento et al.,Suvan et al., and Khader et al.	Abdominal obesity had a direct effect on unfavorable periodontal outcomes.
Suvan et al.	Obese participants had significantly higher mean probing pocket depths after NSPT, than non-obese.
Khader et al.	Over 50% of obese participants had periodontal disease.
Jimenz et al.	Significant association between adiposity and periodontal disease.
Kangas et al.	Subjects with the highest WC or WHtR had a 40-60% increased likelihood of having periodontal pockets
Zimmermann et al. and Kose et al.	Obese participants had higher levels of TNFα compared to normal weight participants.
Kose et al.	Significantly higher levels of IL-6 among obese participants compared to non-obese participants.
Zimmermann et al.	Highest concentration of leptin was in obese participants.
Buduneli et al.	Clinical attachment loss, leptin and IL-6 were higher in the obese than the non-obese.
Thanakun et al.	Overweight and obese participants had higher levels of leptin and CRP.
Maciel et al.	Obese participants had significantly higher periodontal pathogens than normal weight, chronic periodontitis participants.
D'Aiuto et al.	Severe periodontitis was independently associated with increased oxidative stress.
Atabay et al.	Periodontal destruction and disease severity might be influenced by increased level of oxidative stress from obesity.
Suresh et al.	Obese participants with periodontitis had more oxidative stress.

Table 3. Summary of research findings

Risk factors	***Periodontal disease***	***Obesity***	
Age	✓	✓	*
Gender	✓	✓	*
Behaviors	✓	✓	
Education	✓	✓	
Genetics	✓	✓	
Nutrition	✓	✓	
Host response	✓	✓	
Smoking	✓		

Table 4. Common risk factors. * Indicates conflicting research

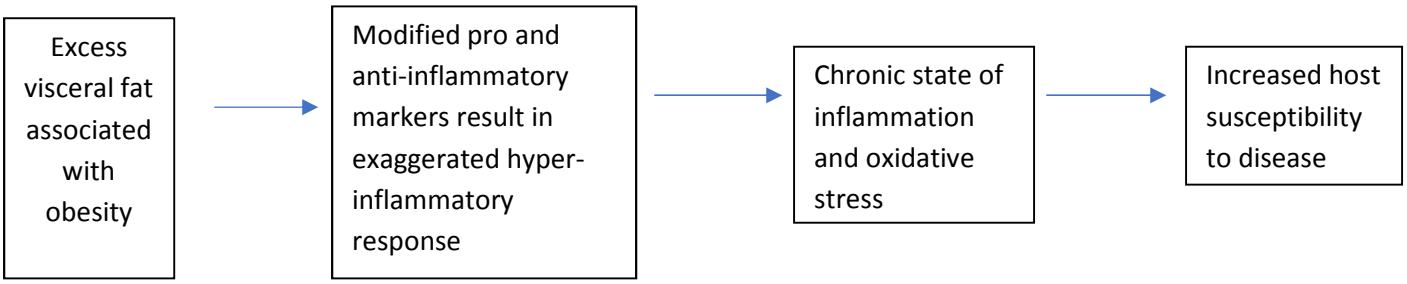

Figure 1. Chain of events associated with the relationship between obesity and disease