Obesity and Periodontitis

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Abstract—*Obesity is a complex multifactorial chronic, inflammatory disease that develops from an interaction of genotype and the environment. The prevalence of obesity has increased substantially and is the result of a number of lifestyle-related factors, including a global shift in diet towards increased energy, fat, and sugar intake, and a trend towards decreased physical activity because of the sedentary nature of modern work and transportation. Besides being a risk factor for cardiovascular disease, certain cancers and type II diabetes, obesity has emerged as one of the risk indicators of periodontal disease. Hence, periodontists need to be aware of the potential problems that obesity can impose on overall as well as oral health. Pro- inflammatory cytokines may be a connecting link among periodontitis and obesity. However, elucidating any physiologic mechanism behind this relationship still requires well designed longitudinal studies. Considering these issues, the article discusses the various forms of obesity, techniques to assess the abdominal fat distribution and obesity related disorders. The article also reviews the relationship between obesity and periodontal disease and the possible role of physicians and periodontists in managing obesity and periodontal disease.*

Keywords*: adipokine; body mass index; leptin; obesity; periodontitis; risk factor*

1. INTRODUCTION

It is evident from the scientific literature that general health has a considerable impact on oral health and vice versa. Many mediators have been postulated for this relationship, namely infection, chronic inflammation, and genetic predisposition. [1] Apart from these mediators, nutrition has been postulated as an alternative mediator. [2] Obesity is a complex multifactorial chronic disease that develops from an interaction of genotype and the environment. [3] The prevalence of obesity has increased substantially, and considerable source of concern given its potential impact on morbidity, mortality and the cost of health care over the past decades in most industrialized countries. [4] The World Health Organization (WHO) estimated that 1 billion people were overweight [body mass index (BMI) > 25] or obese (BMI > 30) in 2005 and the number will increase to 1.5 billion by 2015 if current trends continue. Although obesity was once considered a health problem only in developed countries, the WHO now states that obesity is rising dramatically in developing countries also. This is the result of a number of lifestyle-related factors, including a global shift in diet towards increased energy, fat, and sugar intake, and a trend towards decreased physical activity because of the sedentary nature of modern work and transportation. [5] Besides being a risk factor for cardiovascular disease, certain cancers and type II diabetes, obesity might also pose an increased risk for periodontal disease. [6] The adipose tissue secretes several cytokines and hormones, involved in inflammatory processes, suggesting that similar pathways are involved in the pathophysiology of obesity and periodontitis. [7]

2. DEFINITION AND FORMS OF OBESITY

Obesity, defined as a body mass index (BMI) >30.0 kg/m^2 is characterized by the abnormal or excessive deposition of fat in the adipose tissue. [8] Two distinct patterns:

Abdominal obesity: K/as *central, visceral, android obesity*, defined as fat accumulation around the viscera and inside the intraabdominal solid organs.

Subcutaneous obesity: K/as *peripheral, gynoid, gluteofemoral obesity.* The typically female (or gynecoid) pattern of body fat distribution around the hips, thighs, and buttocks, is subcutaneous fat, and poses less of a health risk compared to visceral fat.

3. ASSESSMENT OF ABDOMINAL FAT DISTRIBUTION

ANTHROPOMETRIC TECHNIQUES

Body Mass Index (BMI):(BMI, also called Quetelet Index), which is the ratio of body weight (in kg) to body height (in m) squared. [1]

Waist Hip Ratio (WHR): The waist-hip ratio measured in a standing position is the most widely used index of regional adipose tissue distribution. Waist circumference is minimal circumference measured at the navel, and the hip circumference is the widest circumference measured at the hips and buttocks. [8]

Waist Circumference: The measurement of the body circumferences at the abdomen or "waist"/, measured at the midpoint between the lower border of the rib cage and the iliac crest has been reported to be more closely correlated with the

level of abdominal visceral adipose tissue and associated metabolic variables than the WHR in both sexes. [9,10,11,12]

Abdominal Sagittal Diameter: Abdominal sagittal diameter is derived either from a CT abdominal scan or by using a carpenter's spirit level placed over the abdomen perpendicular to the length axis of the trunk at the iliac crest level when the subject is placed on a firm examination table. [9] The sagittal diameter is measured with a ruler as the vertical distance from the horizontal spirit level to the examination table after a normal expiration. [14]

4. IMAGING TECHNIQUES

Computed Tomography *(*CT*)*: CT can be considered the gold standard; not only for adipose tissue evaluation but also for multicompartment body measurement. [14]

Magnetic resonance imaging (MRI): MRI demonstrated good reproducibility for total and visceral adipose tissue volumes [17]

Dual-energy X-Ray Absorptiometry (DEXA): This technique can be also used to accurately measure total body fat and regional fat distribution. DEXA is more accurate than anthropometric measures and more practical and cost effective than CT or MRI scans.

Ultrasound (US)*:* Abdominal ultrasonography has been proposed as a suitable technique for intraabdominal fat measurement in research and clinical settings. [18,19,20,21,22,23]

5. CLASSIFICATION OF OVERWEIGHT AND OBESITY ACCORDING TO BMI, WAIST CIRCUMFERENCE AND ASSOCIATED DISEASE RISK

			Disease risk* relative to normal weight and waist circumference	
	BMI (kg/m²)	**Obesity class**	**MEN ≤102 cm(≤40in) WOMEN ≤88 cm (≤35 in)**	**>102 cm (>40 in) >88 cm (>35 in)**
Underweight	<18.5			
Normal	18.5 – 24.9			
Overweight	25.0 – 29.9		Increased	High
Obesity	30.0 – 34.9 35.0 – 39.9	I II	High Very high	Very high Very high
Extreme obesity	≥40	III	Extremely high	

* Disease risk for type 2 diabetes, hypertension, and CVD.
Source (adapted from): Preventing and Managing the Global Epidemic of Obesity. Report of the WHO Consultation of Obesity, Geneva, June 1997.

6. DISEASES RELATED TO OBESITY:

Cardiovascular Diseases: About 10 – 15% of all cases of cardiovascular diseases are related to overweight and obesity. Obese person have 1.5 times increased risk for coronary heart disease and cerebrovascular disease (18).

Hypertension: Overweight and obesity have long been recognized as important determinants of elevated blood pressure levels (19). Compared with normal-weight individuals, obese persons have reported about 5 times higher risk of hypertension, and up to 2/3 of cases of hypertension can be attributed to excess weight (20).

Type 2 Diabetes Mellitus: Obese individuals have 10 times more risk of developing type 2 diabetes mellitus. Interaction between insulin resistance and beta cell failure leads to the development of type 2 diabetes mellitus. (21)

Osteoarthritis: In people with severe OA, synovial fluid leptin concentrations are greater than serum concentrations and are significantly correlated with BMI [21–23]. Similarly, leptin gene expression is correlated with BMI in severely arthritic cartilage [23]. Joint leptin levels are also greater in women, consistent with their higher risk of developing OA with increasing age [22].

Respiratory disorders: Development of obstructive sleep apnea and obesity hypoventilation syndrome. Studies have shown an increase in self-reported dyspnea and wheezing at rest and on exertion in obese compared with lean individuals.[10,11,13]

Metabolic syndrome: Persistent obesity dysregulates metabolic processes including action of insulin on glucose-lipid-free fatty acid metabolism and severely affects processes controlling blood glucose, blood pressure, and lipids. Thus begins a cluster of conditions; dysglycemia, dyslipidemia, hypertension, and procoagulant state, known as the metabolic syndrome (3). Data suggest that the obesity and the metabolic syndrome are immediate precursors of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) (4, 5, 6, 7).

7. PERIODONTITIS: A DISEASE ENTITY

Periodontal disease refers to the process of destruction of the peri-tooth structures that support the teeth. These are composed of the gingiva, the periodontal ligament, the cementum, and the alveolar bone. The chronic destruction of these supporting tissues leads to the eventual loss of teeth and hence partial or complete loss of teeth which is known as periodontitis.

Periodontitis must be distinguished from gingivitis (inflammation of the gum tissue), which is a term used to describe a non-destructive periodontal disease [4]. Epidemiologically, gingivitis is the most common form of periodontal disease. From a prognostic point of view, in the absence of treatment, gingivitis may progress to periodontitis,

which is a destructive form of periodontal disease [4], but in some sites or individuals, gingivitis never progresses to periodontitis [5]. Although periodontal pathogens such as Porphyromonas gingivalis, Prevotella intermedia, Tannarella forsythia, and Aggregatibacter actinomycetemcomitans, cause plaque-induced inflammatory periodontal disease, the progression and clinical characteristics of these diseases are influenced by both acquired and genetic factors that can modify susceptibility to infection.

Susceptibility to periodontitis is highly variable and depends on host responses to periodontal pathogens. The initial increased presence of neutrophils at the site is followed by the release of cytokines by neutrophils and macrophages; the chemical mediators released include tumor necrosis factor alpha (TNF-α), interleukin-1 (IL-1), and prostaglandins. The inflammatory process includes the stimulation of fibroblasts by IL-1 and the secretion of matrix metalloproteinases (MMP), of which collagenase is the most prominent, by polymorphonuclear neutrophils. MMPs are responsible for increased collagen breakdown and TNF-α is primarily responsible for increased osteoclast activity resulting in bone resorption. T-lymphocytes secrete receptor activator of nuclear factor kappa-B ligand (RANKL), which is involved in osteoclast activity and, therefore, bone resorption.

Periodontitis has also been associated with elevations in circulating levels of IL-6. IL-6 is an important proinflammatory cytokine involved in the regulation of host response to tissue injury and infection. It is produced by a variety of cells, such as monocytes, fibroblasts, osteoblasts, and vascular endothelial cells, in response to inflammatory challenges. In addition, a significant overexpression of IL-21, IL-1β, IL-17, and IL-23p19 has been detected in tissues affected by periodontal disease compared with healthy gingival tissues.

8. OBESITY AND PERIODONTAL DISEASE

Recently, obesity has emerged as one of the risk indicators of periodontal disease. Various cross sectional and case control studies have indicated a close correlation of obesity with periodontal disease (table 2). Recent studies have demonstrated how normal weight persons who participate in sports and physical activity show a decreased incidence of periodontal disease [40-43].

Table 2: Studies showing correlation between obesity and periodontitis

Author	Study Design	No. of Subjects	Criteria for Periodontitis	Result
Nishimura et al. (27)	Case-series	N = 79 Subjects with NIDDM	Max. probing depth ≥4 mm (CPI)	BMI was associated with periodontitis in NIDDM patients
Saito et al. (31)	Cross-sectional	N = 643 (512 females,131 males) 19–79 years	Max. probing depth ≥4 mm (CPI)	WHR, BMI, and body fat were associated with periodontitis
Wood et al. (47)	Cross-sectional	NHANES III N = 8842	Percent sites with Attachment loss ≥3 mm	WHR and BMI were associated with attachment loss nonlinearly
Al-Zahrani et al. (1)	Cross-sectional	NHANES III N = 13665 18–90 years	Attachment loss ≥3 mm and probing depth ≥4 mm	BMI ≥ 30 and high waist were associated with periodontitis, especially in younger adults (18-34yrs)
Buhlin et al. (7)	Case–control	N = 96 50 periodontitis and 46 periodontally healthy subjects, 36–70 years	Seven or more sites with ≥6 mm of attachment loss	BMI > 26 in men and >25 in women was associated with periodontitis
Torrungruang et al. (40)	Cross-sectional	N = 2005 50–73 years	Mean attachment loss	BMI and waist were not associated with periodontitis
Alabdulkarim et al. (3)	Case–control	N = 400 200 obese (BMI ≥30) 200 non-obese (BMI < 25), ≥18 years	Alveolar bone score <60	Obesity (BMI ≥30) was associated with alveolar bone loss, especially in young adults (<40 years)
Saito et al. (32)	Cross-sectional	Community Women, N = 584, 40–79 years	Upper 20th percentile of mean probing depth and mean attachment loss	BMI, body fat, and WHR were associated with deep pockets, adjusted for OGTT

Nishida et al. (26)	Cross-sectional	N = 372, 20–59 years	Upper 20th percentile of % probing depth ≥3.5 mm	BMI > 26 was associated with periodontitis
Reeves et al	case-control	NHANES III N=2452 nonsmokers, 13 - 21 years	≥ 1 periodontal sites with loss of tissue attachment ≥3 mm and probing depth≥3 mm	Total body weight and waist circumference were associated with periodontitis, but the association varied by age.
D'Aiuto et al	Cross-sectional	NHANES III N = 13,994, > 17 years	Gingival bleeding, mean pocket depth and attachment loss	Severe periodontitis was associated with metabolic syndrome in middle-aged individuals
Khader YS et al	Cross - sectional	N = 340, 18 - 70 years	≥4 teeth with ≥1 sites with probing pocket depth ≥ 4 mm and clinical attachment loss ≥3 mm.	BMI-defined obesity, high WC, and high fat per cent were significantly associated with increased odds of having periodontitis.
Hans DL et al	Cross-sectional	N = 1046, ≥ 15 years	Max. probing depth ≥4 mm (CPI)	Obesity was associated with periodontitis. VFA was the most suitable indicator of obesity in relation to periodontitis.
Pataro AL et al	Cross sectional	N = 594, women	bleeding on probing, probing depth and clinical attachment level ≥ 4 mm	Periodontitis was positively associated with obesity, and this association was more evident as obesity levels increases.

Studies have also demonstrated how individuals with normal weight showed a lower prevalence of periodontitis and decreased plasma levels of inflammatory markers. The first report on the relationship between obesity and periodontal disease appeared in 1977, when Perlstein *et al.* observed histopathologic changes in the periodontium in hereditary obese Zucker rats (27, 28). Using ligature induced periodontitis; they found alveolar bone resorption to be greater in obese animals compared with non-obese rats (28).

In 1998, Saito *et al.* analyzed 241 healthy Japanese individuals and showed, for the first time, an association between obesity and periodontal disease in humans (29). They applied the community periodontal index of treatment needs (CPITN) and estimated, based on their cross sectional analysis, that the relative risk for periodontitis after adjustment for confounders such as age, gender, oral-hygiene status, and smoking was 3.4 in persons with BMI of 25 to 29.9 kg/m², and 8.6 in those with BMI above 30 kg/m²(29).

9. MECHANISM CONNECTING OBESITY WITH PERIODONTAL DISEASE

For many years, adipose tissue was considered as an inert organ that stored triglycerides. It is now clear that adipose tissue is a complex and metabolically active endocrine organ that secretes numerous immunomodulatory factors and plays a major role in regulating metabolic and vascular biology. Adipose cells, which include adipocytes, preadipocytes, and macrophages, secrete more than 50 bioactive molecules, known collectively as adipokines. Some of these adipokines act locally, whereas others are released into the systemic circulation where they act as signaling molecules to the liver, muscle, and endothelium. (fig.1)

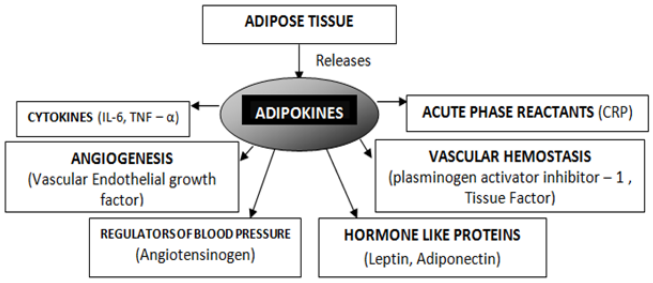

Fig. 1: Adipocytokines: bioactive substances secreted from adipose tissue. TNF-a, tumor necrosis factor-alpha; CRP, C - Reactive peptide.

The path physiologies between obesity and periodontitis are not well-known; however, adipose-tissue-derived cytokines and hormones (adipokines) may play a key role in modulating periodontitis. These are:

1. TNF-α. TNFα mRNA in fat tissue (subcutaneous abdominal fat studied) is more in obese person as compare to lean persons (34,35), with a significant correlation between

TNFα mRNA and BMI. Studies have shown the local action of the cytokine, and other additional local factor, which limits the entrance of fatty acids via LPL and the subsequent hypertrophy of the adipocyte. TNFα not only decreases the activity of LPL, also decreases the expression of glucose transporter GLUT 4 (36) and an increase in hormone-sensitive lipase (37).

2. INTERLEUKIN-6. Since the plasma concentration of interleukin-6 is proportional to the fat mass (39), the adipose tissue could become an important source of that cytokine. Both interleukin-6 as well as TNFa reduces the expression of LPL, it could have a local role in the regulation of the uptake of fatty acids by the adipose tissue. In effect, TNFα produces a 60-fold increase in interleukin-6 production in differentiated 3T3-L1 adipocytes (40).

3. LEPTIN: Leptin is a pleiotropic cytokine, secreted by adipocytes, which is involved in a variety of biological processes, including energy metabolism, endocrine functions, reproduction, and immunity(44). Leptin is thought to act as a "lipostat" that regulates adipose tissue mass. As a negative feedback mechanism, elevated leptin concentrations result in increased energy expenditure, decreased food intake, and a negative energy balance (45,46).

4. ADIPONECTIN: Adiponectin is a circulating hormone, that is involved in glucose and lipid metabolism, secreted by adipose tissue, accounts for about 0.05% of total serum proteins(48,49). Compare to other adipose-derived hormones, adiponectin levels are reduced in persons with obesity, insulin resistance, or type 2 diabetes (48,49).

In periodontitis sites, adiponectin could exert an anti-inflammatory effect and thereby have a negative influence over the onset and progression of periodontitis (Yamaguchi *et al.*, 2007). In humans, two recent studies (Furugen *et al*., 2008; Saito *et al*., 2008) have found that serum adiponectin levels tended to decrease in Japanese persons with periodontitis, albeit not significantly. Moreover, adiponectin levels were negatively correlated with mean attachment loss, but not mean probing depth or percentage of sites bleeding on probing. Another study(Iwamoto *et al.*, 2003) found that serum adiponectin levels did not change significantly after periodontal therapy.

5. PLASMINOGEN ACTIVATOR INHIBITOR – 1 (PAI – 1): PAI-1 is an adipokine which generates agglutination of blood and raises the risk of ischemic vascular disease and gingival inflammation. PAI-1 may decrease blood flow in the periodontium of obese patients and promotes development of periodontitis.[15,16]

7. CHEMERIN: Chemerin is a recently identified adipokine that is highly expressed in liver and adipose tissue and is associated with adiposity. Importantly, chemerin is thought to regulate adipogenesis and metabolic homeostasis in murine and human adipocytes.

Furthermore, an overgrowth of Tannerella forsythia in the subgingival biofilms of periodontally healthy overweight and obese individuals, which was reported by Haffajee & Socransky (2009), has also been suggested to be a possible link between body weight and periodontal infection.

Obesity affects host immunity (24, 33, 36). It has been reported that obese-hypertensive rats are more likely to have periodontitis than normal rats and that the periodontal blood vessels of these rats show intimal thickening, indicating diminished blood flow (30). A high-cholesterol diet has been associated with the proliferation of junctional epithelium, with increasing bone resorption in rat periodontitis (38). As a high-cholesterol diet leads to fat accumulation directly, an elevated serum cholesterol level may be a reason for the relationship between obesity and periodontal disease.

10. ROLE OF PHYSICIANS AND PERIODONTISTS IN MANAGING OBESITY AND PERIODONTAL DISEASE

Physicians should be aware of the signs and symptoms of periodontal disease that includes gingival bleeding, reddish or bluish discoloration and puffiness of gingiva, halitosis, feeling of itching in gums, sensitivity to hot and cold, toothache in the absence of caries, and mobility, extrusion or migration of teeth. In such conditions the patient should be referred to a dentist or a periodontist.[25] Physicians may also play an important role in educating patients with obesity, diabetes and coronary heart disease, about the importance of good oral hygiene and how poor oral hygiene adversely affects the general health.

Periodontists may wonder what their role should be in the management of obesity and obesity-related diseases like diabetes and atherosclerosis. The diagnosis of such patients is in the realm of physicians. But a periodontist can evaluate patients for signs and symptoms of obesity-related diseases. They should refer their overweight and obese periodontal patient for weight reduction interventions like diet therapy, behavioral therapy, pharmacotherapy and surgical procedures, so that they can have better control over periodontal inflammation. In the future, if obesity is to be acknowledged as a multiple-risk-factor syndrome for overall and periodontal health, general and oral risk assessment in the dental office should include the evaluation of BMI on a regular basis.

11. CONCLUSION

Obesity is a complex multifactorial chronic disease that develops from an interaction of genotype and the environment, and its relationship to oral status has been realized by the scientific community in recent years. Various cross sectional and case control studies have indicated a close correlation of obesity with periodontal disease. Hence, periodontists need to be aware of the potential problems that obesity can impose on overall as well as oral health. Pro- inflammatory cytokines

may be a multidirectional link among periodontitis, obesity, and other chronic diseases. (4)

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