

Metabolic Syndrome and Periodontitis



Dental Science

KEYWORDS: metabolic syndrome, obesity, chronic periodontitis, peri-implantitis

Eser Elemek

PhD, DDS, Marmara University Faculty of Dentistry, Department of Periodontology/Private Practice, Istanbul/Turkey

ABSTRACT

There is only little evidence about the possible relationship between Metabolic Syndrome (MetS) and periodontitis. The contribution of systemic conditions and diseases in onset and exacerbation of periodontal disease is very well known. Because both periodontitis and metabolic syndrome are associated with systemic inflammation, these two diseases may be linked through common pathophysiological pathway. To prevent formation of metabolic syndrome, weight loss and physical activity is the initial step. In addition, to prevent inflammation, periodontal treatment is a high priority in patients with poor oral hygiene. More studies are needed to clarify possible link between metabolic syndrome and peri-implantitis which is inflammation of peri-implant mucosa and bone around dental implants.

Definition of Metabolic Syndrome:
Metabolic syndrome (MetS) has existed in various forms and definitions. In 1999, WHO [1] and European Group for the Study of Insulin Resistance [2] have formulated definitions. They both included glucose intolerance, obesity, hypertension and dyslipidaemia to define metabolic syndrome. However, criteria for these definitions were different. One of the major problems was difference in criteria used to define obesity and overweight between Asian people and other populations. International Association for the Study of Obesity with the support of WHO redefined overweight as body mass index >23 and obesity as >25 in Asians [3].

A global definition has been proposed by International Diabetes Federation (IDF) and American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI), joined by the World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity [4](Table 1). Metabolic syndrome is widely accepted concept that identifies the centrally obese patient with increased risk for cardiovascular disease and diabetes [5].

Table 1: Criteria for defining Metabolic Syndrome

	Categorical cutpoints
Increased waist circumference	Population specific and country specific definitions
Increased triglycerides	≥150mg/dL(1.7 mmol/L)
Reduced HDL cholesterol	<40mg/dL(1.0 mmol/L) in men; <50mg/dL(1.3 mmol/L) in women
Increased blood pressure	Systolic ≥130 and/or diastolic ≥85mmHg
Increased fasting glucose	>100mg/dL(5.5 mmol/L)

Pathophysiology of Metabolic Syndrome and Its Relation to Periodontitis:

There is only little evidence about possible relationship between MetS and periodontitis. One of the most accepted underlying mechanisms of metabolic syndrome is insulin resistance. Although exact causes of insulin resistance are not completely understood, scientists think major contributors as excess weight and physical inactivity. Excessive accumulation of fatty acids in circulating blood contributes to development of insulin resistance. Factors associated with increased risk of insulin resistance are family history of diabetes, impaired glucose metabolism, obesity and increased body mass index(BMI). Because both periodontitis and MetS are associated with systemic inflammation and insulin resistance, these two diseases may be linked through a common pathophysiological pathway. Prevalence of MetS was found to be 18%, 34% and 37% among individuals with mild, moderate and severe periodontitis, respectively [6].

Obesity is a multifactorial condition with a wide range of etiological factors including genetic, biological, social and behavioral factors. It

is characterized by abnormal or excessive deposition of fat in adipose tissue and is the second major contributor to metabolic syndrome. Contribution of systemic conditions and diseases in the onset and exacerbation of periodontal disease is very well known. Being overweight or obese has also been associated with an increased risk for periodontal disease. It causes an increase in oxidative stress, leading to endothelial dysfunction. Thus, increase in proinflammatory cytokines is seen and the function of periodontal tissues is affected negatively. Obesity may be a significant predictor of periodontitis and insulin resistance mediates this relationship, as it is associated with high plasma levels of tumor necrosis factor alpha(TNF-α) [7]. TNF-α is the best candidate connecting higher periodontal disease with obesity and MetS. TNF-α levels are systemically elevated in both obesity and metabolic syndrome [8]. TNF-α was also reported to induce insulin resistance in both diabetes and obesity [9].

Tumor necrosis factor-alpha is an early inflammatory cytokine in periodontal disease. TNF-α induces alveolar bone resorption by stimulating formation of osteoclasts [10]. It also regulates matrix metalloproteinases, which are capable of degrading connective tissue. The second candidate explaining mechanism for higher prevalence of periodontal disease in obesity or metabolic syndrome is interleukin 6(IL-6). It is produced by macrophages, neutrophils and endothelial cells. Systemic and gingival crevicular levels of IL-6 were found to be increased in periodontal disease [11].

In obesity, subclinical inflammatory response is observed, characterized by increased levels of acute phase proteins, proinflammatory cytokines and leukocytes [12]. Periodontitis is an inflammatory disease associated with activation of polymorphonuclear leukocytes which in turn may generate reactive oxygen species [13]. Reduction of body fat causes a reduction in formation of oxidants [14].

A significant difference in mean proportions of Tannerella forsythia, a periodontal pathogen, between both obese and non-obese males and females was observed having the highest values in obese, younger individuals [15]. This microorganism was in greater proportions in gingival sulci in periodontally healthy/gingivitis subjects who were obese, potentially increasing their risk of developing periodontitis. In a recent study, among 419 participants, 14.08% found to have severe periodontitis which was associated with MetS [16]. Severe periodontitis, high CRP levels and body mass index were associated with MetS as well [17]. Individuals with MetS had greater probing depths and clinical attachment levels [18]. In another study, chronic periodontitis was also found to be associated with MetS [19]. All these studies suggest that MetS and chronic periodontitis may be bidirectional.

The relation between insulin resistance and hypertension must be considered as well. Insulin is a vasodilator when given intravenously to people of normal weight [20]. In the presence of insulin resistance,

vasodilatory effect of insulin can be lost [21]. Fatty acids themselves can mediate relative vasoconstriction [22].

Management of Metabolic Syndrome:

Presence of metabolic syndrome carries high risk for developing cardiovascular disease and type-2 diabetes. There are underlying risk factors such as being overweight or obese, physical inactivity, total cholesterol, HDL cholesterol. Management of metabolic syndrome should first aim to eliminate these risk factors.

Weight loss and physical activity is the initial step to prevent formation of metabolic syndrome and so as type-2 diabetes. The goal must be to reduce bodyweight by about 7-10% over 6-12 months followed by maintenance of increased physical activity [23].

There is a general agreement that people with metabolic syndrome should adhere to a set of dietary principles: low intakes of saturated fats, trans fats and cholesterol, reduced consumption of simple sugars and increased intakes of fruits, vegetables and whole grains [24]. Mild elevation of blood pressure can often be controlled with lifestyle changes, but if hypertension persists despite such therapies, antihypertensive drugs are usually required [25].

Effect of the metabolic control of diabetes on periodontal disease and effect of periodontal treatment on metabolic control in diabetic patients remains controversial. Reduction of periodontal inflammation either with root planing and systemic antibiotics or with plaque control and subgingival scaling significantly reduces CRP levels after 9 months in patients with MetS [26]. In another study, patients who had no treatment for MetS had more severe periodontal diseases than patients who were diagnosed as healthy [27]. In general, however, periodontal treatment is high priority in patients for whom periodontal disease may pose a health risk. Peri-implantitis is also an inflammatory disease occurring around dental implants due to poor oral hygiene. Inflammation of peri-implant mucosa and resorption of bone are observed in peri-implantitis lesions. Interleukin 1 β and tumor necrosis factor- α were also found higher in crevicular fluid of implants with peri-implantitis [28, 29]. More studies are needed to clarify possible link between MetS and peri-implantitis.

References:

- Alberti, K.G. and P.Z. Zimmet, Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*, 1998, 15(7): p.539-53.
- Balkau, B. and M.A. Charles, Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). *Diabet Med*, 1999, 16(5): p.442-3.
- Redefining Obesity and its Treatment. WHO /IASO /IOTF, 2000.
- Alberti, K.G., et al., Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*, 2009, 120(16): p.1640-5.
- Eckel, R.H., et al., The metabolic syndrome. *Lancet*, 2010, 375(9710): p.181-3.
- D'Aiuto, F., et al., Association of the metabolic syndrome with severe periodontitis in a large U.S. population-based survey. *J Clin Endocrinol Metab*, 2008, 93(10): p.3989-94.
- Genco, R.J., et al., A proposed model linking inflammation to obesity, diabetes, and periodontal infections. *J Periodontol*, 2005, 76(11 Suppl): p.2075-84.
- Gregor, M.F. and G.S. Hotamisligil, Inflammatory mechanisms in obesity. *Annu Rev Immunol*, 2011, 29: p.415-45.
- Hotamisligil, G.S. and B.M. Spiegelman, Tumor necrosis factor alpha: a key component of the obesity-diabetes link. *Diabetes*, 1994, 43(11): p.1271-8.
- Kobayashi, K., et al., Tumor necrosis factor alpha stimulates osteoclast differentiation by a mechanism independent of the ODF/RANKL-RANK interaction. *J Exp Med*, 2000, 191(2): p.275-86.
- Nibali, L., et al., Interleukin-6 in oral diseases: a review. *Oral Dis*, 2012, 18(3): p.236-43.
- Bisrian, B., Systemic response to inflammation. *Nutr Rev*, 2007, 65(12 Pt 2): p.170-2.
- Canakci, C.F., Y. Cicek, and V. Canakci, Reactive oxygen species and human inflammatory periodontal diseases. *Biochemistry*, 2005, 70(6): p.619-28.
- Dandona, P., et al., The suppressive effect of dietary restriction and weight loss in the obese on the generation of reactive oxygen species by leukocytes, lipid peroxidation, and protein carbonylation. *J Clin Endocrinol Metab*, 2001, 86(1): p.355-62.
- Haffajee, A.D. and S.S. Socransky, Relation of body mass index, periodontitis and *Tannerella forsythia*. *J Clin Periodontol*, 2009, 36(2): p.89-99.
- Gomes-Filho, I.S., et al., Severity of Periodontitis and Metabolic Syndrome: Is There an Association? *J Periodontol*, 2016, 87(4): p.357-66.
- Thanakun, S., et al., Inverse Association of Plasma IgG Antibody to Aggregatibacter actinomycetemcomitans and High C-Reactive Protein Levels in Patients with Metabolic Syndrome and Periodontitis. *PloS one*, 2016, 11(2): p.1-18.
- Shimazaki, Y., et al., Relationship of metabolic syndrome to periodontal disease in Japanese women: the Hisayama Study. *J Dent Res*, 2007, 86(3): p.271-5.

- Kumar, N., et al., Association of chronic periodontitis with metabolic syndrome: A cross-sectional study. *J Indian Soc Periodontol*, 2016, 20(3): p.324-9.
- Steinberg, H.O., et al., Insulin-mediated skeletal muscle vasodilation is nitric oxide dependent. A novel action of insulin to increase nitric oxide release. *J Clin Invest*, 1994, 94(3): p.1172-9.
- Tooke, J.E. and M.M. Hannemann, Adverse endothelial function and the insulin resistance syndrome. *J Intern Med*, 2000, 247(4): p.425-31.
- Tripathy, D., et al., Elevation of free fatty acids induces inflammation and impairs vascular reactivity in healthy subjects. *Diabetes*, 2003, 52(12): p.2882-7.
- Eckel, R.H., S.M. Grundy, and P.Z. Zimmet, The metabolic syndrome. *Lancet*, 2005, 365(9468): p.1415-28.
- National Cholesterol Education Program Expert Panel on Detection, E. and A. Treatment of High Blood Cholesterol in, Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*, 2002, 106(25): p.3143-421.
- Chobanian, A.V., et al., Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*, 2003, 42(6): p.1206-52.
- Lopez, N.J., et al., Effects of periodontal therapy on systemic markers of inflammation in patients with metabolic syndrome: a controlled clinical trial. *J Periodontol*, 2012, 83(3): p.267-78.
- Thanakun, S., et al., Association of untreated metabolic syndrome with moderate to severe periodontitis in Thai population. *J Periodontol*, 2014, 85(11): p.1502-14.
- Yaghobee, S., et al., Assessment of interleukin-1 β and interleukin-6 in the crevicular fluid around healthy implants, implants with peri-implantitis, and healthy teeth: a cross-sectional study. *J Korean Assoc Oral Maxillofac Surg*, 2014, 40(5): p.220-4.
- Duarte, P.M., et al., Could cytokine levels in the peri-implant crevicular fluid be used to distinguish between healthy implants and implants with peri-implantitis? A systematic review. *J Periodontol Res*, 2016, 51(6): p.689-98.