Association of Metabolic Syndrome and Periodontal Disease in an Indian Population

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Abstract

Background: Metabolic syndrome, the whole of interconnected factors, presents with local manifestation, such as periodontitis, related by a common factor known as oxidative stress. The aim of the present study was to assess the association between metabolic syndrome and periodontal disease in an Indian population.

Methods: Clinical criteria for metabolic syndrome included: 1) abdominal obesity; 2) increased triglycerides; 3) decreased high-density lipoprotein cholesterol; 4) hypertension or current use of hypertension medication; and 5) high fasting plasma glucose. Serum C-reactive protein (CRP) levels were also measured. Periodontal parameters including gingival index (GI), average and deepest probing depth (PD) and clinical attachment level (CAL) were recorded on randomly selected quadrants, one maxillary and one mandibular. Based on the presence or absence of metabolic syndrome, individuals were divided into two groups.

Results: The periodontal parameters PD, CAL and GI differed significantly between the two groups. The GI values in Group 1 (2.06 ± 0.57) were greater than in Group 2 (1.79 ± 0.66; $p = 0.0025$). Similarly PD and CAL values in Group 1 (4.58 ± 1.69 and 2.63 ± 1.61 mm) were significantly greater ($p < 0.001$) than in Group 2 (3.59 ± 1.61 and 1.61 ± 1.40 mm, respectively). Also, three metabolic components and serum CRP correlated with average PD, and the strength of the correlation was medium in Group 1 as compared to Group 2, in which it was weak.

Conclusion: The association between metabolic syndrome and periodontal disease was significant, and abdominal obesity appeared to be the most important contributing metabolic factor to periodontal disease

Key words: Metabolic syndrome, periodontal disease, obesity

Introduction

Obesity, hypertension, impaired glucose tolerance, and abnormal lipid metabolism have received a great deal of attention as risk factors for arteriosclerotic diseases, including coronary artery disease. The term "metabolic syndrome" is commonly used to refer to a condition in which several such components are present in an individual (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001).

The prevalence of metabolic syndrome is increasing worldwide (Cameron *et al.*, 2004). Although each component of metabolic syndrome independently increases the risk for cardiovascular disease (McGill *et al.*, 2002; Eberly *et al.*, 2003), many studies have reported that an accumulation of these components significantly enhances the risk of death from all causes and cardiovascular disease (Lakka *et al.*, 2002).

Many studies have reported that periodontitis is more prevalent in persons with diabetes (Soskolne and Klinger, 2001), and that individuals with periodontitis have abnormal lipid metabolism (Loesche *et al.*, 2000). However, it is unclear whether the accumulation of the components of metabolic syndrome increases the risk of periodontal disease.

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A significant association exists between metabolic syndrome and periodontal disease (Han *et al*., 2010). Metabolic syndrome was found to be associated with the extent of severe periodontitis in a Gullah population with type 2 diabetes mellitus (T2DM; Sora *et al*., 2013). Also, increased severity of periodontitis was correlated with significantly increased prevalence of metabolic syndrome in the middle-aged and aged population of a community in Beijing (Yu *et al*., 2012).

Cytokines have been suggested to have a role in the pathogenesis of several diseases, such as diabetes mellitus (Stumvoll *et al*., 2005) and obesity (Ziccardi *et al*., 2002), as well as in the pathogenesis of periodontitis (Saxlin *et al*., 2009).

Metabolic syndrome is a primary risk factor for cardiovascular disease and is associated with a proinflammatory state. Periodontal disease is related to biomarkers of endothelial dysfunction and dyslipidemia such as CRP, t-PA, and LDL-C, which are known risk factors for cardiovascular disease (Joshipura *et al*., 2004). C-reactive protein is an acute-phase reactant synthesized by the liver in response to inflammatory cytokines such as IL-6, IL-1 and tumor necrosis factor-alpha (TNF-α). Circulating CRP levels are a marker of systemic inflammation and are associated with periodontal disease (Noack *et al*., 2001).

To date, no study has examined the association between metabolic syndrome and periodontal disease in an Indian population. In this study, we aim to examine the relationship between periodontal disease and the components of metabolic syndrome, singly and in combination, through a community-based health examination.

Materials and Methods

Subjects

In this case-control study, 100 subjects with metabolic syndrome (Group 1) and 100 age- and sex-matched controls without metabolic syndrome (Group 2) were included. Patients were selected from the population referred to the Department of Periodontics, Government Dental College and Research Institute (GDCRI), Bangalore. It was made clear to the potential subjects that participation was voluntary and written informed consent was obtained from those who agreed to participate. Ethical clearance was obtained from the institutional ethical committee and review board of the Government Dental College and Research Institute, Bangalore.

Inclusion criteria were age 40-79, ambulatory subjects who were fit to participate in the study, and, for Group 1, subjects with metabolic syndrome. According to The National Cholesterol Education Program (NCEP), the definition of metabolic syndrome requires the presence of three or more of five components: abdominal obesity (waist circumference (WC) > 88 cm); triglycerides (TG) > 150 mg/dL; decreased serum high-density lipoprotein (HDL) cholesterol (< 50 mg/dL); systolic blood pressure (SBP) > 130 mmHg or diastolic blood pressure (DBP) > 85 mmHg; fasting plasma glucose > 110 mg/dL (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001). Group 2 subjects met the above criteria but did not have metabolic syndrome.

Exclusion criteria were age < 40 or > 79 years, any kind of periodontal treatment within the previous 6 months back, severe or terminal illness, or smoking.

Subjects were selected based on the inclusion criteria and categorized into two groups based on the presence (Group 1) or absence (Group 2) of metabolic syndrome.

General examination

Blood pressure was measured three consecutive times, after participants rested for at least 5 minutes, by means of a standard mercury sphygmomanometer, with the participants in the sitting position, and the average value was used for the analysis. A blood sample was collected from the antecubital vein the morning after an overnight fast and analyzed for serum cholesterol, triglycerides, and fasting plasma glucose. Trained nurses measured the participants' waist circumference at the level of the umbilicus. The measurement was taken after the participants exhaled. Each participant completed a self-administered questionnaire in advance that included a medical history of diabetes, hypertension, smoking, and medication use. Trained nurses checked the questionnaires.

Oral examination

A periodontal examination was performed on randomly selected quadrants, one maxillary and one mandibular. Probing depth (PD), clinical attachment levels (CAL) and gingival index (GI) measurements were made using a University of North Carolina (UNC-15) periodontal probe on six sites per tooth: mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual. The probe was inserted parallel to the long axis of the tooth on the buccal and lingual surfaces. Interproximally, the probe was placed with slight angulation, as close to the contact area as possible. The clinical examiner, who was blinded to the groups (NK), recorded the average and deepest sites.

Measurement of Serum CRP

The plastic vials containing serum were transferred to the laboratory for immunoturbidimetric analysis. Samples were reacted with a buffer and anti-CRP-coated latex. Latex particles coated with antibody specific to human CRP aggregate in the presence of CRP from the sample, forming immune complexes. The immune

complexes cause an increase in light scattering that is proportional to the concentration of CRP in the serum. The light scattering was measured by reading turbidity (absorbance) at 570 nm. The CRP concentration was then determined from a calibration curve developed from CRP standards of known concentration.

Statistical analysis

Comparisons between metabolic syndrome components and the periodontal parameters between the two groups were performed using the unpaired *t*-test. Three components of metabolic syndrome, i.e., WC, serum TG and average SBP, were correlated with the average PD using the Pearson correlation coefficient test. Serum CRP levels were also tested for any correlation with average PD. All statistical analyses were performed using SPSS 10.0 statistical software.

Results

Table 1 shows the demographic characteristics of the study population. A total of 100 age- and gender-matched individuals in each group were evaluated. Group 1 consisted of 48 males and 52 females while Group 2 had 50 males and 50 females. The mean age in Group 1 was 53.79 ± 5.00 years and in Group 2 it was 50.84 ± 5.22 years. Differences in various components of the metabolic syndrome, such as WC, serum TG, HDL, low-density lipoprotein (LDL), systolic and diastolic BP, were found to be significant between the two groups. The periodontal parameters such as PD, CAL and GI also differed significantly between the two groups. The GI values in Group 1 (2.06 ± 0.57) were greater than in Group 2 (1.79 ± 0.66). Similarly, PD and CAL values in Group 1 (4.58 ± 1.69 and 2.63 ± 1.61 mm) were significantly greater ($p < 0.001$) than in Group 2 (3.59 ± 1.61 and 1.61 ± 1.40 mm, respectively).

Table 2 demonstrates the correlation, if any, among three components of the metabolic syndrome (TG, WC and systolic BP) and serum CRP with average PD in the two groups. Serum TG, CRP and systolic BP correlated positively with the average PD in Group 1; the strength of correlation was medium. The correlation between WC and average PD was found to be weakly positive. On the other hand, in Group 2, the correlation of these parameters with average PD was negative, but the correlation was weak and almost negligible. If the correlation coefficient (r) < 0.05, it is concluded that no correlation exists between the two variables (Loesche *et al.*, 2000).

Table 1. Demographic characteristics of the population and the mean ± SD values and *p* values showing the comparison between the various components of metabolic syndrome and periodontal parameters between the two groups

Parameter	Group 1 (Subjects with metabolic syndrome)	Group 2 (Subjects without metabolic syndrome)	*p* - value
Age (years)	53.79 ± 5.00	50.84 ± 5.22	<0.0001*
Waist circumference (cm)	123.45 ± 19.88	81.06 ± 9.23	<0.0001*
Serum triglycerides (mg/L)	185.37 ± 27.09	119.66 ± 14.30	<0.0001*
High density lipoprotein (mg/l)	43.33 ± 6.00	66.98 ± 6.23	<0.0001*
Avg systolic blood pressure (mmHg)	128.42 ± 8.26	123.20 ± 4.16	<0.0001*
Diastolic blood pressure (mmHg)	83.36 ± 3.71	80.63 ± 2.42	<0.0001*
Fasting blood glucose (mg/L)	140.00 ± 22.10	86.10 ± 6.00	<0.0001*
Gingival index	2.06 ± 0.57	1.79 ± 0.66	0.0025*
Deepest probing depth (mm)	7.45 ± 2.56	5.84 ± 1.97	<0.0001*
Avg probing depth (mm)	4.58 ± 1.69	3.59 ± 1.61	<0.0001*
Greatest clinical attachment loss (mm)	5.79 ± 3.16	3.35 ± 2.83	<0.0001*
Avg clinical attachment loss (mm)	2.63 ± 1.61	1.61 ± 1.40	<0.0001*
C-reactive protein (mg/L)	4.8 ± 1.0	1.9 ± 1.2	<0.0001*

*statistically significant

Table 2. Correlation coefficient (r) values obtained using Pearson correlation coefficient test applied to components of metabolic syndrome and average probing depth (PD)

Correlation	Group 1 (Subjects with metabolic syndrome)	Group 2 (Subjects without metabolic syndrome)
Triglycerides and average PD	0.16	-0.078
Systolic blood pressure and average PD	0.23	-0.01
Waist circumference and average PD	0.35	-0.08
C-reactive protein and average PD	0.22	-0.02

Discussion

The present case control study was designed to assess whether or not any association exists between metabolic syndrome and periodontal disease. Although there are studies that have suggested an association between metabolic syndrome and periodontal disease, this is the first study of this kind in an Indian population. We measured various components of metabolic syndrome and divided the subjects into two groups: one with metabolic syndrome and one without. It was generally found that individuals who met the criteria for metabolic syndrome were more likely to have periodontal disease and thus an association exists between metabolic syndrome and periodontal disease.

Early identification, treatment, and prevention of the metabolic syndrome present major challenges for health care professionals who are facing an epidemic of overweight and sedentary patients. Hyperlipidemia and hyperglycemia are major risk factors for cardiovascular disease. In recent years, some evidence has been presented that periodontal disease is associated with an increased risk of cardiovascular disease (Cohen *et al*., 1988).

A study by Pozharitskaia *et al.* documented an aggressive course of chronic generalized periodontitis (CGP) in patients with metabolic syndrome as compared to CGP in patients showing no components of this syndrome (Pozharitskaia *et al*., 2004). Nishimura *et al.* have introduced the inclusion of this oral disease as one of the components of metabolic syndrome (Nishimura *et al*., 2005).

High-sensitivity C-reactive protein (hsCRP) has been reported to be elevated in patients with metabolic syndrome (Ishikawa *et al*., 2007). At a local level, CRP is also known to contribute to periodontal tissue destruction and bone resorption (Howells *et al*., 1995). In the present study also, serum CRP levels were found to be highly elevated in metabolic syndrome patients as compared to the control group. This could offer a possible explanation for the higher values of periodontal parameters such as PD, CAL and GI in the metabolic syndrome group, as the higher CRP levels could also cause periodontal destruction locally.

Metabolic syndrome seems to induce a pro-oxidative state in periodontal tissue, altering anti-oxidant defense mechanisms. This adversely affects the tissue response against bacterial plaque (Marchetti *et al*., 2012).

The biological mechanisms that may explain the nature of the association between metabolic syndrome and periodontal disease are not well known (Andriankaja *et al*., 2010). However, of the five metabolic components, this study concluded that abdominal obesity plays the most significant role in the association between metabolic dysfunction and periodontal disease, as apparent from the highest correlation coefficient value between WC and average PD in *Table 1*.

In contrast to a previous study by Andriankaja *et al.,* who found that the association between two or more metabolic components with females to be highly significant as compared to males, our study found no such difference between males and females. This could be due to the small sample size evaluated in the current study.

Smokers were excluded from the study, as smoking is a well-established potential risk factor for periodontal disease development, greatly multiplying the chance of developing periodontal disease (Rivera-Hidalgo, 2000) and could have acted as a confounder.

Metabolic syndrome may, however, also be an independent risk factor for periodontal disease. Given its hyperinflammatory characteristics, it is plausible that metabolic syndrome could interact with periodontal disease in a negatively synergistic manner, leading to the onset of many systemic diseases (Rivera-Hidalgo, 2000).

To conclude, we hypothesized that metabolic syndrome is a possible independent risk factor for periodontal disease in an Indian population. We believe that the findings in the present study support this conclusion. Although there have been studies and surveys conducted to test this association previously, this is the first study of this kind in an Indian population. Long-term multicenter longitudinal trials or surveys with a larger sample size may be required to confirm these findings in an Indian population.

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