Original Article

Association of Periodontitis With Metabolic Syndrome: A Case-Control Study

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ABSTRACT

Aim: This study was undertaken to assess the association between periodontitis and metabolic syndrome. **Materials and Methods:** A case-control study was designed among 100 cases as patients with metabolic syndrome aged 35–74 years, and age- and sex-matched 100 controls as apparently healthy relatives or friends accompanying the cases visiting the diabetic outpatient department at Victoria Hospital, Bengaluru, Karnataka, India, using convenience sampling method. Information related to diabetes, hypertension, and oral hygiene practices was collected. Periodontal health status was measured using community periodontal index. Metabolic syndrome was diagnosed based on the criteria of National Cholesterol Education Program Adult Treatment Panel III. Chi-square test and logistic regression were used for analysis. **Results:** Significantly more number of cases had shallow pockets 4–5 mm, deep pockets ≥ 6 mm, and also more number of loss of attachment code 1, code 2, code 3, and code 4 compared to controls. Bivariate analysis showed significant association between metabolic syndrome and body mass index, smoking, and tobacco chewing. The association between periodontitis and metabolic syndrome was significant with increased risk of developing metabolic syndrome among the subjects with community periodontal index code 3 and code 4 (odds ratio [OR] = 17) and among the subjects having loss of attachment code 1, code 2, code 3, and code 4 (OR = 12). Association remained significant even after adjustment with other variables (adjusted OR = 6). **Conclusion:** This study showed significant association between periodontitis and metabolic syndrome. Further prospective and randomized control trials are recommended to assess causal association between these two diseases.

KEYWORDS: *Association, chronic periodontitis, metabolic syndrome, periodontal diseases, periodontitis*

INTRODUCTION

Metabolic syndrome (MetS) is defined as the combination of three out of five of the following interrelated conditions: increased plasma glucose,

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hypertension, dyslipidemia (elevated triglycerides and low levels of high-density lipoprotein [HDL]), and/or elevated abdominal circumference.[1] Abdominal obesity, hypertension, and hyperglycemia are the most frequently occurring components of MetS.[2] MetS is multifactorial disorder, also known by other names such as Reaven's syndrome, insulin resistance syndrome, plurimetabolic syndrome, syndrome X, and the deadly quartet.[3]

There has been an increase in the global prevalence of MetS.[4] It has been reported to affect 10%–84% of the population worldwide and around 25% of the population in developed countries.[5] Prevalence of MetS is high among Asians including Indians and is rising, particularly with the adoption of modernized lifestyle.[6] Risk factors for MetS besides age include genetic predisposition, race, low household income, weight, particularly abdominal obesity, smoking, alcohol consumption, post-menopausal status, carbohydrate-rich diet, physical inactivity, stress, and lifestyle.[3,7]

MetS is likened to an epidemic gripping the modern civilization. MetS has attracted immense clinical significance since the last two decades.[3] It is a high-risk factor for several systemic diseases.[4] MetS consists of such conditions that expose an individual to an elevated risk for development of cardiovascular disease (CVD) and type 2 diabetes mellitus and also claimed as risk factor for atherosclerotic CVD. These risk factors for CVD in MetS profoundly attribute to mortality worldwide.[1]

Periodontal disease is a common, chronic, low-grade inflammatory disease of microbial origin, affecting humans and resulting in the destruction of tooth-supporting apparatus, and affects up to 90% of the global population.[3,4]

Periodontal diseases, considered as inflammatory diseases, have proved to have a spectrum of systemic implications. Periodontitis is a known risk factor for the deterioration of glycemic control over time.[2] Periodontitis is becoming an important public health concern with different severity rates in individuals, synchronizing with other systemic conditions.[1]

MetS and periodontitis are linked through common risk factors and pathways, sharing inflammation and oxidative stress/mitochondrial dysfunction mechanism as a common link.[1,8] Thus, chronic systemic inflammation accelerates an individual with periodontitis to develop MetS or vice versa.[1] However, other studies reported different strengths of association, including tobacco, gender, and age as confounding factors while evaluating the association between MetS and periodontitis. A very little information is available on the association between periodontitis and MetS as a sole clinical entity in Indian population.

Thus, this study is justified by supplementary clarifications needed on the association between periodontitis and MetS in Indian population. The null hypothesis for this study is no association of periodontitis with MetS. Thus, the aim of this study was to examine the association between periodontitis and MetS in Bengaluru city, Karnataka, India.

MATERIALS AND METHODS

SETTING AND DESIGN

A case-control study was designed with cases as patients with MetS and age- and sex-matched controls as apparently healthy relatives or friends accompanying the cases visiting the diabetic outpatient department at Victoria Hospital, Bengaluru, from August to September 2013. Ethical clearance was obtained from Institutional Ethical Committee and Review Board of Government Dental College and Research Institute, Bengaluru. (GDCRI/ACM/PG/Ph.D./10/2013–2014, 06/08/2013). All participants voluntarily participated and submitted a written informed consent.

SAMPLING CRITERIA

A pilot study was conducted to check the feasibility of the study and to obtain an estimate for sample size determination. The prevalence of periodontitis was 95% with 80% of statistical power and 95% confidence interval; the sample size was calculated by: $n = (Z\alpha/2 \times p \times q)/d^2$ where n = sample size, Z = standardized normal deviate (Z value), α = 5%, Zα/2 = 1.96, p = prevalence of periodontitis = 95%, q = 100 − p = 100 − 95 = 5%, d = precision (allowable error) = 4, n = [(1.96)2 × 95 × 5]/4^2 = 100.

On the basis of the pilot study, the total sample size for the study was calculated to be 100 cases and 100 controls. The subjects who qualified the inclusion/exclusion criteria and who were present on the day of the study were included in the sample. A prestructured proforma was designed to record the information regarding all the variables namely sociodemographic status, general and oral health-related behaviors, diet, and oral health status.

Inclusion criteria were patients with presence of at least three of the following five criteria: increased waist circumference, elevated plasma triglycerides, reduced HDL cholesterol, high blood pressure and elevated fasting glucose suggestive of MetS, minimum of 20 natural teeth during examination, patients with

age group 35–74 years, and patients giving consent to participate in the study. Controls were selected without any syndrome with aforementioned other criteria.

Exclusion criteria were patients who have undergone periodontal therapy/oral prophylaxis past 6 months; the use of any antibiotics for >1 week in the last 6 months; diagnosis of cardiovascular, cerebrovascular, or kidney disease; or any known condition for which a prophylactic antibiotic treatment is required.

STUDY METHOD AND OBSERVATIONAL PARAMETERS

Cases were diagnosed with MetS based on the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).[9]

According to the definition proposed by NCEP ATP III, MetS is defined as the presence of at least three of the following five criteria: waist circumference >80 cm in men and >90 cm in women, elevated plasma triglycerides >1.7 mmol/L (150 mg/dL), reduced HDL cholesterol below 1 mmol/L (40 mg/dL) in men and 1.3 mmol/L (50 mg/dL) in women, high blood pressure >130/85 mm Hg or antihypertensive drug treatment, elevated fasting glucose >5.5 mmol/L (100 mg/dL), or hypoglycemic drug treatment.

Individuals' medical data (NCEP ATP III criteria) were collected from medical records. Eligible individuals for cases consist of 35- to 74-year-old 100 subjects from both genders with an existed diagnosis of MetS. Eligible individuals for control consist of 100 subjects from both genders without MetS.

Periodontal status was assessed using a Community Periodontal Index (CPI) given by World Health Organization 1994.[10]

One trained and calibrated dentist examined the periodontal status of all study participants.

The inter-rater reliability of the CPI index between two raters was kappa index of 0.82. The sample used was a convenient sample between August 2013 and September 2013. In this study, confounding was noted with respect to smoking and tobacco chewing habit. This was adjusted in analysis by doing logistic regression analysis. There was no drop out of study noted.

STATISTICAL ANALYSIS

Descriptive analysis was carried out. The chi-square test was used to assess the association between categorical variables. A value of $P < 0.05$ was accepted as indicating statistical significance. The sociodemographic and oral health variables were expressed as an odds ratio

(OR) with a 95% confidence interval. To check the relationship between periodontitis, as independent variable, and other variables with MetS, a logistic regression analysis was performed. Data were entered in a standard Microsoft Excel 2007 sheet (Microsoft Corporation, Redmond, Washington, DC) and analyzed using SPSS, version 16.0, statistical package (SPSS Inc., Chicago, IL).

RESULTS

Cases and controls included in this study were matched for age and gender. In this study, the age of study subjects ranged from 35 to 74 years with a mean age of 50.49 ± 8.85 among cases and 50.50 ± 8.88 among controls. The study group consisted of 50% males and 50% females in cases and control group, respectively.

There was a significant difference observed among the study groups with respect to the mean number of the sextants with CPI score 2, score 3, and score 4 ($P < 0.05$) [Table 1].

There was a significant difference observed among the study groups with respect to the mean number of the sextants with loss of attachment (LOA) score 0, score 1, score 2, and score 3 ($P < 0.05$) [Table 2].

In this study, there was statistically significant association between MetS and body mass index

Table 1: Distribution of the study subjects according to the mean number of sextants affected per person as per CPI codes

CPI codes	Cases	Controls
0	0	0
1	0	0
2	0.62 ± 1.33*	2.73 ± 2.54
3	3.89 ± 1.99*	2.26 ± 2.33
4	1.20 ± 1.89*	0.69 ± 1.65
X	0.29 ± 0.977	0.34 ± 1.05

*$P < 0.05$

Table 2: Distribution of the study subjects according to the mean number of sextants affected per person as per LOA codes

LOA codes	Cases	Controls
0	2.12 ± 2.60*	4.87 ± 2.30
1	1.87 ± 2.22*	0.37 ± 1.30
2	1.13 ± 1.74*	0.33 ± 1.19
3	0.47 ± 1.16*	0.11 ± 0.51
4	0.12 ± 0.49	0.04 ± 0.28
X	0.29 ± 0.97	0.28 ± 0.93

*$P < 0.05$

(BMI), smoking, and tobacco chewing. Preobese subjects were 30 (OR) times and obese were 85 (OR) times higher risk of developing MetS compared to normal subjects. Subjects with smoking were 6.7 (OR) times whereas subjects with tobacco chewing were 3 (OR) times higher risk of developing MetS compared to nonsmokers and non-chewers, respectively [Table 3].

In this study, there was statistically significant association found between MetS and tooth mobility, CPI codes 3 and 4, and LOA codes 1, 2, 3, and 4. Strong association was found between subjects having periodontitis; that is, subjects with shallow pockets 4–5 mm and deep pockets ≥6 mm (CPI code 3 and code 4) had 17 (OR) times higher risk of developing MetS. Whereas among the subjects with LOA code 1, code 2,

Table 3: Bivariate association between metabolic syndrome and risk factors of metabolic syndrome

Variables	Cases (%)	Controls (%)	Crude OR (95% CI)	*P* value
Age				
<50 years	58	58	1	
>50 years	42	42	1 (0.57–1.75)	1.00
Gender				
Male	50	50	1	
Female	50	50	1 (0.58–1.74)	1.00
Diet				
Vegetarian	41	54	1	
Mixed	59	46	1.69 (0.97–2.95)	0.06
BMI				
Normal	4	68	1	
Preobese	36	20	30.60 (9.84–95.11)	0.00001*
Obese	60	12	85.00 (26.25–275.20)	0.00001*
Smoking				
No	78	96	1	
Yes	22	4	6.77 (2.25–20.35)	0.00001*
Tobacco chewing				
No	63	84	1	
Yes	37	16	3.02 (1.50–6.10)	0.00020*

CI = confidence interval

*P < 0.0

Table 4: Bivariate association between oral health variables and metabolic syndrome

Variables	Cases (%)	Controls (%)	Crude OR (95% CI)	*P* value
No. of teeth present				
20–25 teeth	11	8	1.75 (0.64–4.82)	0.27
25–28 teeth	53	46	1.47 (0.81–2.65)	0.19
>28 teeth	36	46	1	
Tooth mobility				
No	54	70	1	
Yes	46	30	1.99 (1.12–3.54)	0.0200*
Missing teeth				
No	30	25	1	
Yes	70	75	0.77 (0.41–1.44)	0.42
CPI codes				
Periodontitis absent code 0, 1, 2	2	26	1	
Periodontitis present code 3, 4	98	74	17.22 (3.99–74.29)	0.00001*
LOA codes				
Code 0	25	80	1	
Code 1, 2, 3, 4	75	20	12.00 (6.18–23.30)	0.00001*
CPI codes				
Code 0, 1, 2	2	26	1	
Shallow pockets 4–5 mm code 3	61	57	14.16 (3.25–61.69)	0.00001*
Deep pockets ≥ 6 mm code 4	37	17	28.29 (6.13–130.53)	0.00001*

CI = confidence interval

*P < 0.05

code 3, and code 4, risk of developing MetS was almost 12 (OR) times higher compared with the subjects having LOA code 0. Strength of association increased with increasing level of severity of periodontitis. Risk was 14 (OR) times higher among the subjects having shallow pockets 4–5 mm (CPI code 3) whereas risk was 28 (OR) times higher among the subjects having deep pocket ≥6 mm (CPI code 4). We also found significant association between mobile teeth and MetS with strength of association being 1.9 (OR) [Table 4].

Variables that showed statistically significant results were considered for logistic regression analysis. Model showed that subjects with shallow and deep pockets (CPI codes 3 and 4) had 6.34 (OR) times and obese subjects had 37 (OR) times higher risk of developing MetS compared to subjects without periodontitis and nonobese, respectively. Subjects with mobile teeth had 0.2 (OR) times higher risk of developing MetS compared to subjects without mobile teeth (P <0.05), whereas among the subjects with LOA more than 3 mm (LOA codes 1, 2, 3, and 4) had almost 1.4 (OR) times increased risk of developing MetS compared to subjects with no LOA (P < 0.05) [Table 5].

DISCUSSION

In this study, the CPI index was used as a measure of periodontal disease status.

Most of the studies have considered a wide age group ranging from 18 to 90 years.[1,4-9,11-18] There was no difference among cases and controls regarding age as control group was matched for age, whereas Abdalla-Aslan *et al*.[7] reported that patients with MetS were significantly older than without MetS. Han and Park[11] showed that MetS increases with age; the association between periodontitis and MetS became higher in

adults aged 45–49 years compared to younger adults aged 30–44 years (OR = 1.9).

In this study, cases and controls were matched for gender. This was similar to the previous studies.[6] Kim *et al*.[12] reported that severity of periodontitis in male patients with MetS was higher compared to that of females. Abdalla-Aslan *et al*.[7] reported that males in the periodontitis group presented with OR of being diagnosed with MetS of 2.25. Tegelberg *et al*.[5] reported that females in the periodontitis group showed greater ORs of 2.8 of being diagnosed with MetS, whereas males in the periodontitis group presented with ORs of being diagnosed with MetS of 1.6. Kim *et al*.[4] reported that the prevalence of MetS was 44.3% in the male group and 36.9% in the female group.

A statistically significant difference was observed between cases against controls with regard to tobacco chewing and smoking. With its potential pathogenic properties, smoking is a risk factor for both CVD and periodontal disease. The results have shown that smokers are not significantly associated with MetS risk with an OR of 0.67. These results are similar to studies by Pham.[8] Tegelberg *et al*.[5] also found no significant association between smoking and MetS. However, Abdalla-Aslan *et al*.[7] (OR = 3.05), Campos *et al*.[1] (OR = 2.19), Kim *et al*.[4] (OR = 1.35), and Jaramillo *et al*.[13] (OR = 1.72) observed a significant association between smoking and MetS. In this study, tobacco chewing exhibited no significant association with MetS with an OR of 0.38. These results are similar to studies by Kumar *et al*.[6] (OR = 1.30) who also found no significant association between tobacco chewing and MetS.

There was a significant difference observed among the study groups regarding BMI. This was in line with the

Table 5: Logistic regression analysis for study variables and metabolic syndrome							
Variables	Cases	Controls	Level	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Periodontitis CPI code 3, 4	2	26	No	1	0.00001*	1	0.04*
	98	74	Yes	17.22 (3.99–74.29)		6.34 (1.06–37.82)	
LOA code 1, 2, 3, 4	25	80	No	1	0.00001*	1	0.37
	75	20	Yes	12.00 (6.18–23.30)		1.41 (0.66–3.05)	
Tooth mobility	54	70	No	1	0.0200*	1	0.03*
	46	30	Yes	1.99 (1.12–3.54)		0.20 (0.05–0.87)	
Smoking	78	96	No	1	0.00001*	1	0.63
	22	4	Yes	6.7 (2.25–20.35)		0.67 (0.13–3.49)	
Tobacco chewing	63	84	No	1	0.00020*	1	0.14
	37	16	Yes	3.0 (1.50–6.10)		0.38 (0.11–1.37)	
BMI	4	68	Normal	1	0.0000*	1	0.0000*
	96	32	Obese	51 (17.23–150.91)		37.03 (12.06–81.69)	

CI = confidence interval. Adjusted OR obtained after adjusting the other variables presented in the table
*P < 0.05

previous studies.[1,8] Obese subjects were higher risk of developing periodontitis compared to normal subjects. This was in line with the previous studies.[11,19]

There was no significant difference observed among the study groups regarding number of teeth present. Also number of teeth present was not significantly associated with MetS. There was almost 1.47 (OR) times increase in risk of developing MetS among subjects with 25–28 teeth compared to subjects with more than 28 teeth present. And subjects with 20–25 teeth had 1.75 (OR) times greater risk of developing MetS. Campos *et al.*[1] showed that subjects with ≤14 teeth had 1.78 (OR) times greater risk of developing MetS.

Missing teeth exhibited no significant association with MetS in this study with OR of 0.36 whereas Musskopf *et al.*[14] showed that MetS was associated with tooth loss (≥6 teeth) with OR of 1.23.

Patients with MetS had poor periodontal health compared to controls (periodontitis was present among 98% of the cases and 74% in controls). Results are in accordance with the findings of Han and Park[11] (prevalence for periodontitis was 33.7%), Campos *et al.*[1] (prevalence for periodontitis was 54.6%), and Nascimento *et al.*[15] (prevalence for periodontitis was 14.3%), whose studies have also found periodontitis to be more common in patients with MetS compared to controls.

The significant crude OR for periodontitis (periodontal status index score 3 and 4) was 17, whereas the significant adjusted OR for periodontitis (periodontal status index score 3 and 4) was 6. Reports of study by Campos *et al.*[1] (OR = 2.02), Kim *et al.*[4] (OR = 1.42), Koo and Hong[16] (OR = 1.12), Musskopf *et al.*[14] (OR = 1.17), Jaramillo *et al.*[13] (OR = 2.72), Pham[8] (OR = 3.68), Nascimento *et al.*[15] (OR = 0.11), Kumar *et al.*[6] (OR = 2.64), and Tegelberg *et al.*[5] (OR = 1.8) are comparable with this study results. Adachi and Kobayashi[17] showed that there was no association between periodontitis and development of MetS. Gomes Abreu *et al.*[18] concluded that the chronic inflammation is an important factor in the physiopathology underlying to these conditions and that local and systemic alterations initiated by the periodontal disease may contribute to a chronic inflammatory state, increasing the probability of developing MetS and CVD.

There was significant association between LOA code and MetS. Risk of developing MetS was 12 (crude OR) times higher among the subjects having LOA code 1, code 2, code 3, and code 4 compared to subjects having LOA code 0. These associations were found to be statistically significant, whereas the adjusted OR for LOA (LOA code 1, code 2, code 3, and code 4) was 1.4 compared to LOA code 0. These associations were not statistically significant. The study conducted by Musskopf *et al.*[14] observed a significant association between LOA and MetS with an OR of 1.47 for mean attachment loss ≥2 mm, and Pham's[8] OR of 4.55 mean clinical attachment loss ≥3.66 can be comparable with our results.

Thus, this study shows the significant association between periodontitis and MetS. Hence, we reject null hypothesis.

A majority of the studies in this analysis indicated an elevated risk of MetS associated with periodontitis. The effect seems to be maintained even after controlling for other risk factors.

With both these diseases posing a major threat to health, it is only imperative that we prevent this web of causation by delinking this chain of events. With the fact that periodontal disease is a highly prevalent disease in community, if an increased risk of MetS is attributable to periodontal disease, then a substantial proportion of population will be at risk, with its implication for clinical practice.

Dental health measures have been focusing mainly on preserving the teeth and supporting structures or reducing further disease occurrences. The benefits of periodontal health in reducing the risk of MetS could be used as a potent additional motivating factor for some patients.

Although the current therapies used to manage periodontitis may be adequate to simultaneously manage systemic sequelae, dentists will need to assume a larger responsibility for the overall health of patients and eventually periodontal care may become a medical necessity.

Thus the following recommendations can be made based on this study:

- Regular periodontal health check-up is required for individuals with MetS.
- Screening and referral for patients with periodontitis and MetS in dental and health care settings, respectively, can help to improve the oral health as well as general health of patients.
- Additional large-scale longitudinal and interventional studies are needed to establish whether periodontal disease is a contributing factor to or a result of MetS.
- Future studies preferably longitudinal aimed at establishing the underlying causal factors.
- Randomized controlled trials are required to determine whether treatment of periodontal disease reduces the risk of the MetS.
- Oral health is determined by many factors such as dietary practices, oral hygiene practices, and habits such as smoking, alcohol, and stress. As these

factors are common to a number of chronic diseases, adopting a collaborative approach is more rational than one that is disease specific. This common risk factor approach can help in further integration of the medical and dental fields.

CLINICAL SIGNIFICANCE

Patients with MetS seem to have a higher risk for periodontitis and should be screened for periodontal disease. Oral health professionals in India should recognize the association between periodontitis and MetS, and the risk factors related to MetS. This study highlights for oral health professionals the clinical evidence of association between periodontitis and MetS. The prevention and treatment of periodontal disease that oral health professionals provide for patients may help reduce the risk or adverse effects of MetS. MetS must be taken into account by the oral health professionals when evaluating risk factors for periodontitis. Most of the medical health professionals are unaware of the consequences of periodontal disease on other systemic conditions. Medical health professionals can provide proper education and guidance in collaboration with the oral health professionals to contribute for oral health and eventually for the overall health of the patients.

LIMITATIONS

Other confounding variables, for example, genetics, socioeconomic status, and hereditary, were not included in the study. The design of the study is such that the causal relationship between MetS and periodontitis cannot be identified.

CONCLUSION

Overall this study suggested an association between periodontitis and MetS. This association was strong and significant. Thus, the study further supports the concept that chronic inflammatory conditions such as periodontal disease may have a significant role in MetS.

CONFLICTS OF INTEREST

There are no conflicts of interest.

AUTHORS CONTRIBUTIONS

All authors listed have significantly contributed to the development and the writing of this article.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

The study was approved by the Government Dental College and Research Institute, Bangalore. Registered in August 2013 with number GDCRI/ACM/PG/Ph.D./10/2013–2014, 06/08/2013 and all the procedures have been performed as per the ethical guidelines laid down by Declaration of Helsinki (2000).

PATIENT CONSENT STATEMENT

Consent was obtained from the patients who were included in the study. As we have not included minor patients so there is no consent from the parents.

DATA AVAILABILITY STATEMENT

The entire data have been submitted to the journal in the form of tables and statistical evaluation in the article.

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