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Research Article

Association of Periodontal Disease, Oral Candidal Carriage, and Salivary pH in Patients with Metabolic Syndrome

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Abstract

Background: Periodontitis is an immunoinflammatory disease and it induces a systemic low-grade inflammation. Metabolic syndrome (MetS) is a complex collection of components involving hypertension, abnormal glucose and lipid metabolism. Proinflammatory cytokines may act as a multidirectional link between periodontitis and MetS. MetS components such as obesity, hyperglycemia and hypertension affect the properties of saliva and microbial colonisation. The aim of this study was to find out the association between MetS and periodontitis, pH of saliva, and Candidal carriage.

Method: This cross sectional study consists of 95 patients with MetS (MetS group) and 80 healthy adults [MetS (-)] group. All subjects were assessed for periodontal parameters [gingival index (GI), plaque index (PI), simplified oral hygiene index (OHI-S) and percentage of sites with bleeding on probing (BOP), probing pocket depth (PPD),clinical attachment loss (CAL)] and systemic parameters (waist circumference, blood pressure, lipid profile, FBS, PPBS). Salivary pH and Candidal carriage were also assessed.

Results: GI, PI, OHI-S and percentage of sites with BOP were significantly higher in MetS group. The mean PPD, and CAL were significantly higher in MetS group (3.04 ± 0.44, 3.29 ± 0.68) as compared to MetS (-) group (2.33 ± 0.43, 2.54 ± 0.60). The occurrence and severity of periodontitis were significantly higher in MetS patients. In MetS group significantly low salivary pH and higher Candidal carriage was observed.

Conclusion: The occurrence and severity of periodontitis were higher in Metabolic syndrome. Low salivary pH, higher Candidal carriage and presence of periodontitis can worsen the systemic status in metabolic syndrome. Therefore, MetS patients should undergo routine periodontal therapy, Candidal carriage detection, anticandidal treatment.

Keywords: *Metabolic Syndrome; Periodontitis; Diabetes; Candidal Carriage*

Introduction

Periodontitis is an immunoinflammatory disease and the periodontopathic gram-negative bacteria activate the host immune response significantly and have actions beyond periodontal tissues. Pro-inflammatory cytokines, such as IL-1, IL-6, C-reactive protein, TNF-α

and MMP's are significantly elevated during the destructive phase of periodontitis and it induces asystemic low-grade inflammation [1]. These inflammatory mediators act as a risk factor for a variety of systemic diseases/conditions, including coronary artery disease, atherosclerosis, stroke, diabetes mellitus and metabolic syndrome etc [2].

Metabolic syndrome (MetS) comprises of a complex collection of components like abdominal obesity, hypertriglyceridemia, reduced high density lipoprotein cholesterol, hypertension and impaired fasting glucose. Among the five components, minimum of three should be present to confirm MetS. The adipose tissues are a large reservoir of biologically active mediators such as TNF -α, IL-6 and adipokines [3]. Proinflammatory cytokines may act as a multidirectional link between periodontitis and MetS. In obesity increased production of inflammatory mediators like interleukins (IL-1, IL-6 and TNF-α) and adipokines may contribute to increased destruction in periodontitis [4]. Hyperglycaemia induce excessive AGE accumulation, triggers connective tissue degradation and aggravate periodontitis. On the other hand Inflammatory mediators released in periodontitis increase insulin resistance and leads to hyperglycaemia.

MetS components, such as obesity, hyperglycemia and hypertension affects the properties of saliva [5-7]. The salivary flow rate is a modulator of salivary pH. At low flow rate, less bicarbonate is released, and pH decreases [8]. Thus, the defence mechanism against pathogenic microorganism is affected, which predispose the host to Candida colonization and subsequent infection. Candida can coaggregate with bacteria in subgingival biofilm and adhere to epithelial cells. Such interactions are associated with the capacity of Candida species to invade gingival tissue and may be important in the microbial colonization that contributes to progression of oral alterations caused by diabetes mellitus and MetS [9].

Studies linking the association between MetS and periodontal disease, salivary pH and Candidal carriage are scarce in the literature. So, this study was carried out to find out the association between MetS and periodontitis, pH of saliva, and Candidal carriage.

This study assessed the occurrence and severity of periodontitis in subjects with MetS and determined the severity of periodontitis in different MetS component combinations (3, 4 and 5 components). Secondary objectives of this study were to assess the salivary pH and Candidal carriage in MetS subjects.

Materials and Methods

This cross sectional study was conducted by the department of Periodontics, Govt. Dental College, Kozhikode in collaboration with Department of Internal Medicine, Govt. Medical College, Kozhikode. This study was approved by the Institutional Ethics Committee (IEC no- 26/2013/DCC) Govt Dental College Kozhikode and approved by the clinical trial registry of India (Reg No: CTRI/2014/12/005291). Informed consent was obtained from all study subjects and the study was conducted in accordance with the Helsinki declaration of 1975, as revised in 2000. MetS group was recruited from the out-patient wing of Department of Internal Medicine, Medical College, Kozhikode after clinical diagnosis of metabolic syndrome based on the revised national cholesterol education program adult treatment panel III definition [10]. Among the following five components of MetS, minimum of three should be present to confirm MetS: 1) central obesity (waist circumference ≥ 90 cm for males and ≥ 80 cm for females-Asian Indian population), 2) high blood pressure (systolic blood pressure ≥ 130 mm of Hg or diastolic blood pressure ≥ 85 mm of Hg), 3) low serum high density lipoprotein (HDL) cholesterol (< 40 mg/dl for males and 50 mg/dl for females), 4) hypertriglyceridemia (triglyceride ≥ 150 mg/dl), and 5) high plasma glucose (fasting plasma glucose ≥ 100 mg/dl).

MetS (-) group were selected from the healthy bystanders of the patients from Department of Internal Medicine, Medical College, Kozhikode. 100 MetS patients and 90 MetS (-)s were randomly selected. The eligibility criteria for the selection of MetS and MetS (-) were subjects within the age group of 30 - 60 yrs and with minimum of 20 teeth. Exclusion criteria were patients with known systemic disease and condition (other than type II diabetes mellitus, hypertension, dyslipidemia) such as cardiovascular disease, renal disease, rheumatoid arthritis, liver and pancreatic disease, Patients with acute condition that contraindicate a periodontal examination and patients who received periodontal therapy for the past one year. Five patients from the MetS group and ten subjects from the MetS (-)

group were excluded. The study population included 175 subjects, of which 95 subjects with metabolic syndrome formed the MetS group, 80 clinically healthy subjects formed MetS (-) group. The duration of the study was six months from January 2015 to June 2015. The patient characteristics included age, sex, religion, family income, education status, occupation, diet, oral hygiene practice, family history of diabetes, hypertension, and previous drug allergy.

All subjects underwent a comprehensive general and biochemical examination [height, weight, waist circumference, blood pressure (BP), fasting plasma glucose (FPG), total cholesterol, triglycerides (TG), high- density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol, haemoglobin (Hb) level, total leukocyte count (TLC) and ESR]. Periodontal and oral examination were done and recorded for all study participants. Periodontal parameters like plaque index (PI), gingival index (GI), bleeding on probing (BOP), probing pocket depth (PPD) and clinical attachment level (CAL) were recorded. The pH of the unstimulated saliva was measured with HANNA HI 99104 pH Meter (USA) and a 4 cm Micro pH electrode tip with a pH range of 0.00 to 14.00 and a resolution of 0.01 pH.

Candidal carriage was assessed for all participants by taking Candidal smear from tongue, buccal mucosa and periodontal pocket followed by Gram staining.

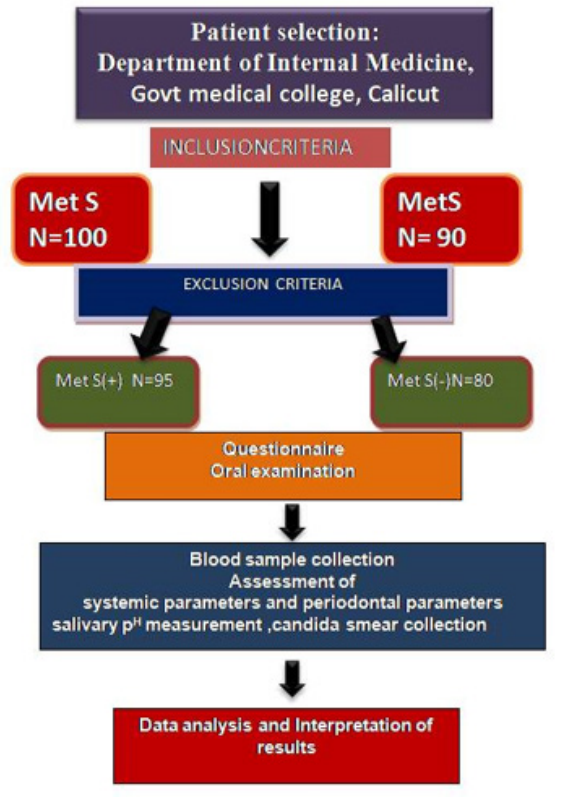

Figure 1: *Flow chart.*

Statistical analyses

Means (± SD) was calculated for quantitative variables and frequency was calculated for qualitative variables. X^2 test was performed to compare the characteristics like gender, family income, Candidal carriage between MetS and MetS (-). For quantitative variables independent t test was used to compare the difference in means. The α value was set at 0.05.

Results

In this study, more females were in the MetS group as compared to MetS (-) group (p = 0.002) (Table 1). The systemic parameters like waist circumference, systolic B.P, diastolic B.P, HDL cholesterol, triglycerides, fasting plasma glucose, Hb level, Total leukocyte count (TLC) and ESR were significantly different between the groups (p < 0.05). The periodontal parameters (mean gingival index, plaque index and simplified oral hygiene index, Percentage of sites with bleeding on probing, mean probing pocket depth, mean clinical attachment level) were significantly higher in MetS group (p < 0.05) (Table 2). The occurrence of periodontitis in MetS group was 100% and in MetS (-) group it was 58.8%. MetS group consisted of 5.3% of mild periodontitis, 38.9% moderate periodontitis and 55.8% severe periodontitis. In MetS (-) group, 41.3%, 11.3%, 40% and 7.5% had no periodontitis, mild, moderate, and severe periodontitis respectively. In the distribution of severity of periodontitis significant difference was observed between groups (Table 3). When the study subjects were categorized according to the number of MetS components, patients with 3 components of MetS 43.8% had moderate periodontitis and 56.3% had severe periodontitis. In patients with 4 components of MetS 4.1% mild periodontitis, 36.7% moderate, and 59.2% severe periodontitis were observed. Distribution of mild, moderate, and severe periodontitis were 10%, 40% and 50%respectivelyin patients with 5 components (Figure 2).

Sociodemographic Characteristics		MetS n = 95	MetS(-) n = 80	p value
Age (years; mean ± SD)		52.07 (5.81)	50.90 (5.25)	0.167
Gender (% within the group)	Male	33.7	56.2	0.002*
	Female	66.3	43.8	
Family income (% within the group)	APL	30.5	33.8	0.745
	BPL	69.5	66.2	

Table 1: *Sociodemographic Characteristics of MetS and MetS (-) group.*

**p < 0.05.*

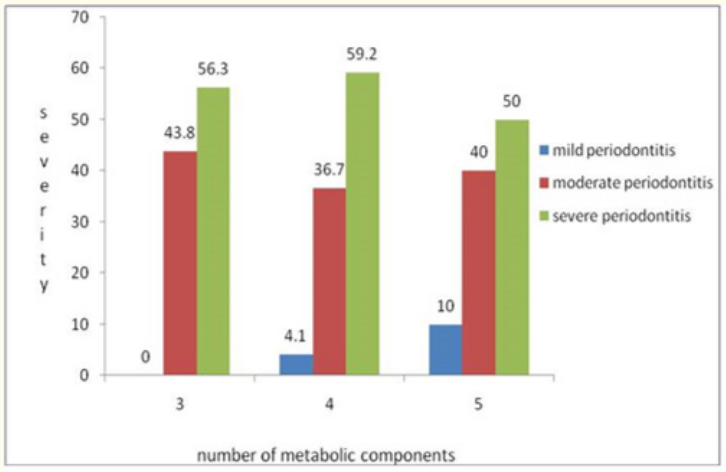

Figure 2: *Distribution of severity of periodontitis (Revised CDC criteria 2012) according to the number of components of metabolic syndrome.*

Systemic and Periodontal Parameters	MetS (+) Case Group Mean ± SD	MetS (-) Control Group Mean ± SD	p value
Waist Circumference (cm)	96.93 (4.14)	83.05 (4.83)	0.001*
Systolic B.P (mm of Hg)	147.35 (11.95)	121.25 (7.71)	0.001*
Diastolic B.P (mm of Hg)	90.72 (4.68)	74.19 (5.36)	0.001*
HDL cholesterol (mg/dl)	42.45 (8.53)	49.70 (11.89)	0.001*
Triglycerides (mg/dl)	162 .47 (91.30)	114 .54 (49.43)	0.001*
Fasting Plasma Glucose (mg %)	158.99 (40 .98)	94.55 (15.95)	0.001*
Hb (g/dl)	12.69 (1.18)	13.37 (0.82)	0.001*
TLC (cells/mm^3)	8126.95 (1492.44)	7707.50 (812.52)	0.026*
ESR (mm/hr)	32.17 (12.40)	11.40 (2.95)	0.001*
MGI	1.24 (1.03)	0.84 (0.32)	0.001*
PI	1.06 (0.16)	0.86 (0.22)	0.001*
OHIS	2.51 (0.66)	1.74 (0.72)	0.001*
BOP (%)	39.11 (12.88)	24.11 (10.86)	0.001*
PPD (mm)	3.04 (0.44)	2.33 (0.43)	0.001*
CAL (mm)	3.29 (0.68)	2.54 (0.60)	0.001*

Table 2*: Distribution of Systemic and periodontal Parameters among MetS and MetS (-) Group.*

**p < 0.05.*

Occurence and Severity of Periodontitis		MetS(+) n = 95 (%)	MetS (-) n = 80 (%)	p value
Occurence of periodontitis		100	58.8	0.001*
Severity of Periodontitis	No periodontitis	0.0	41.3	0.001*
	Mild periodontitis	5.3	11.3	
	Moderate periodontitis	38.9	40.0	
	Severe periodontitis	55.8	7.5	

Table 3: *Occurrence and severity of Periodontitis In MetS and MetS(-) Groups.*

** p < 0.05.*

The mean salivary pH of MetS and MetS (-) group was 6.41 ± 0.16 and 7.05 ± 0.17 respectively and there was a statistically significant difference between the groups (p value < 0.05). A significant difference was observed in the DMFT score of the MetS group (11.01 ± 2.90) and MetS (-) group (8.11 ± 2.87), (p < 0.05). The Candidal carriage was positive in 69.5% of the MetS group, whereas in MetS (-) group it was 36.2%. The Candidal carriage in tongue, periodontal pocket and tongue, and buccal mucosa, tongue and periodontal pocket for MetS group was 8.4%, 32.6%, 28.4% respectively. There was a significant difference in the distribution of Candidal carriage between MetS and MetS (-) groups (Table 4).

Parameter		MetS(+) Mean ± SD	MetS(-) Mean ± SD	p value
Salivary pH		6.4 1 (0.16)	7.05 (0.17)	0.001*
Caries Experience (DMFT score)		11.01 (2.90)	8.11 (2.87)	0.000*
Candidal Carriage		69.5%	36.2%	0.001*
Distribution of Candidal carriage	Tongue	8.4	17.5	0.001*
	Tongue + Pocket	32.6	18.8	
	Tongue + Buccal Mucosa + Pocket	28.4	0	

Table 4: *Mean Salivary pH, Caries Experience and Candidal Carriage in MetS and MetS(-) Groups.*

** $p < 0.05$.*

Discussion

The inflammatory response in Periodontal disease is characterised by dysregulated secretion of host-derived inflammatory mediators resulting in inflammation and immune reaction in host and an ultimate systemic inflammatory burden. Obesity, dyslipidemia and hyperglycaemia associated with metabolic syndrome can affect the immunoinflammatory status by cytokines (IL-1, IL-6 and TNF-α), adipokines and prostaglandins. A multidirectional link exists between periodontitis and MetS via proinflammatory cytokines. MetS can influence the pathogenesis of periodontitis and periodontitis can affect the MetS components.

We have used the Revised CDC criteria (2012) for population based surveillance to assess the periodontal disease severity [11]. In our study population the mean age was comparable between MetS and MetS (-) group with more females in the MetS group. These findings were in accordance with the study conducted by Hajieh Shahbazian., *et al.* in 2013, they concluded that the prevalence of MetS increases with increasing age and women are at higher risk for MetS than men [12].

In our study total leukocyte count and ESR were higher in MetS group than MetS (-) group, which may be due to an increased inflammatory status in MetS group. Andreas Festa., *et al.* opined that chronic subclinical inflammation is a part of insulin resistance syndrome, associated with high levels of inflammatory markers and leukocytes [13]. Genel SUR., *et al.* in 2014 observed an increase in CRP, and leukocytes in MetS and concluded that inflammation in these patients depends on the number of MetS components [14]. In this study, we did not assess the level of inflammatory markers, otherwise more confirmatory results would have obtained regarding the inflammatory status in these patients.

In our study the periodontal parameters like mean gingival index, plaque index, simplified oral hygiene index and percentage of sites with bleeding on probing were higher in patients with MetS. The high scores of these indices might be explained by inadequate oral hygiene maintenance, frequency and nature of the food intake. Metabolic components might also have influenced the oral hygiene status of these patients.

In the present study, mean probing pocket depth, and mean clinical attachment level and occurrence of periodontitis were higher in patients with MetS. A high proportion of periodontitis observed in this study was not only due to high plaque score, but also due to the effect of different components of MetS. Saito T., *et al*. in 2007 and D'Aiuto., *et al*'s in 2008 reported that patients with MetS, were associated with deep pocket depth [15,16]. In accordance with our study Peng Li., *et al*. in 2007 reported that patients with MetS had poor periodontal conditions and periodontal disease was associated with MetS, independent of other risk factors [17]. Shimazaki., *et al.* in 2007 were in the opinion of increased risk for periodontitis in MetS and reported that persons exhibiting more components of MetS had significantly higher odds ratios for greater pocket depth and clinical attachment loss [15]. In contrast, the data of Borges., *et al.* 2007 did not support an association between MetS and periodontitis [18].

An interesting observation of this study was severe periodontitis is associated with MetS irrespective of its components. In MetS groups (Mets with 3 component, 4 components and 5 components) the percentage of severe periodontitis is high as compared to mild and moderate periodontitis. In accordance with our study, P. M. Pozharitskaia., *et al.* in 2004 and Yousef Khader., *et al.* in 2008 reported that MetS patients displayed more severe and extensive periodontal disease [19,20].

Saliva plays a great role in the homeostasis of the oral cavity, because it stabilizes the ecosystem of the oral cavity. The saliva flow rate is a modulator of salivary pH. At low flow rate, less bicarbonate is released, and pH decreases [21]. In our study the salivary pH was found to be lower in patients with MetS as compared to healthy subjects. The low salivary pH may also be due to the effect of components of MetS. In accordance with our study, Monique Tremblay., *et al.* in 2013 reported an association between salivary pH and MetS in women and they observed that the mean pH level decreased as the number of MetS components increased [8]. In diabetes, decreased salivary flow and higher glucose levels, results in a more acidic environment. Dyslipidemia and hypertension also associate with decreased salivary flow [7,22]. Prathibha KM., *et al.* in 2013 showed a significant decrease in pH in diabetics in comparison with that in non diabetic subjects [23]. Acidic pH was also observed in diabetic subjects by M E Lopez., *et al.* in 2003, and they opined that this was attributed to either the microbial activity or a decrease in bicarbonate, which had occurred along with low flow rate [24].

Quantitative and/or qualitative changes in salivary flow and salivary pH lead to local problems, including caries, oral mucositis, halitosis, Candidiasis etc [25-27]. MetS group exhibited high DMFT score in this study. Poor oral hygiene, low salivary pH and the influence of different components of MetS contributed to the statistically significant DMFT score. Miki Ojima., *et al*. in 2015 opined that tooth decay was significantly related to MetS components [28]. Cao., *et al.* in an observational study conducted in 13998 participants, noticed a higher prevalence of MetS in participants with severe caries [29].

In the present study, patients with MetS had higher Candidal carriage. It may be due to the decreased salivary flow and low pH that predispose the host to Candida colonization and subsequent infection. Influence of metabolic components and impaired host defense mechanism in these patients can also contribute to higher Candidal carriage. Thanakun., *et al.* in 2015 studied the prevalence of oral manifestations in patients with MetS and observed 9.2% of oral Candidiasis [30].

Candida can coaggregate with bacteria in subgingival biofilm and adhere to epithelial cells [9]. The ability of the Candidal coaggregation in periodontal pockets may be important in the microbial colonization that contributes to progression of oral alterations caused by diabetes mellitus and MetS [31]. Sultan Al Mubaraka., *et al*. in 2012 observed increased frequencies of Candida infections among subjects with high blood sugar levels and increased pocket depths [32]. On the other hand, RM Bremenkamp., *et al.* detected no differences in colonization of Candida species in oral isolates from type 1 and type 2 diabetes [33].

The higher Candidal carriage observed in our study may be due to decreased salivary flow, low salivary pH, increased occurrence of periodontal disease, influence of metabolic components and impaired host defense in these patients. Candidal culture and species identification was not evaluated in our study. These tests could have offered a better understanding about the association of Candida species in MetS.

Conclusion

In this study an association between periodontitis and MetS is observed and occurrence and severity of periodontitis is higher in patients with MetS. MetS patients had low salivary pH and higher Candidal carriage as compared to healthy subjects. This has an important clinical impact as periodontitis and Candidal infection can worsen the glycemic control of MetS patients, by increasing insulin resistance. Therefore, MetS patients should undergo routine periodontal examination, Candidal carriage detection, anticandidal treatment and periodontal therapy. A better understanding of the association between MetS and periodontitis among the medical and dental fraternity will help in delivering improved treatment options for these patients.

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