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The Potential Effect of Periodontal Disease on the Development of Metabolic Syndrome: A 10-Year Observational Study in a Thai Adult Cohort

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ABSTRACT

Aim: As data are sparse on the long-term association between periodontal diseases and development of metabolic syndrome (MetS), we investigated their relationship in a Thai cohort over a 10-year observational period.

Methods: Medical records and data on periodontal assessments of 2161 employees of the Electricity Generating Authority of Thailand collected at two time points, 2003 and 2013, were used. Experienced periodontists used standard national and international criteria to define periodontitis and MetS. The impact of baseline periodontitis on subsequent MetS incidence and its components was evaluated using regression analyses.

Results: The severity and extent of periodontitis significantly predicted MetS incidence over a decade, with a higher incidence of MetS in individuals with poorer periodontal health. A single percentage increase in the periodontitis extent raised the risk of MetS incidence by 0.4% and the risk of developing individual components of MetS by 0.2%. Independent of periodontal health, age of an individual emerged as a factor impacting MetS development.

Conclusion: This study highlights the potential effect of the severity and extent of periodontitis on the increased incidence and progression of MetS. Hyperglycaemia and hypertension were the two MetS components most significantly affected by the existence of periodontitis.

1 | Introduction

Periodontitis, a chronic inflammatory response to periodontal infection, affects a major portion of the population worldwide during their lifespan (Eke, Thornton-Evans, et al., 2012). Numerous studies have shown that periodontal disease is associated with systemic inflammation (Loos et al. 2000; Nibali et al. 2007; Tonetti et al. 2013), as evidenced by elevated C-reactive protein (CRP), interleukin-6 (IL-6) and leukocytes, suggesting a very strong link between periodontitis and atherosclerotic vascular disease, type 2 diabetes mellitus (T2DM), adverse pregnancy outcomes and many other systemic affections.

Metabolic syndrome (MetS) comprises a cluster of conditions that significantly increase the risk of cardiovascular disease (CVD), and as per the definition of NCEP ATP III (National

Cholesterol Education Program-Third Adult Treatment Panel) criteria, MetS is diagnosed when any three of the following five specific conditions co-occur: high plasma glucose, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), abdominal obesity and hypertension (Expert Panel on Detection and Treatment of High Blood Cholesterol in 2001). Klein, Klein, and Lee (2002), for instance, noted that an increased count of MetS components substantially elevated the risks for CVD and T2DM, with the presence of four or more components raising such risk by 35-fold.

Periodontal disease is known to increase the risk of complications in people with T2DM and negatively impact metabolic control. A number of cross-sectional surveys (Fukui et al. 2012; Han et al. 2010; Khader et al. 2008), including a US study (D'Aiuto et al. 2008), have associated periodontitis severity with increased MetS prevalence. MetS-induced animal models further demonstrated the interplay between periodontal infection, systemic inflammation and metabolic disturbance (Y. Li et al. 2015). Shared risk factors such as genetics, smoking, diet and socioeconomic status are also posited as common links between periodontitis and MetS (Nibali et al. 2013). We have recently reported the potential association between periodontal disease and MetS in a Thai cohort (Suwanprasit et al. 2021). The evidence clearly suggests a bidirectional relationship between periodontal disease and MetS. One possible explanation for this association is the systemic inflammation that arises from periodontal infection, leading to an imbalance in metabolic regulation. Chronic inflammation can trigger insulin resistance, disrupt lipid metabolism and promote the development of MetS (Bullon et al. 2009; Lamster and Pagan 2017).

Although multiple cross-sectional studies have examined the relationship between MetS and periodontal disease, data on the long-term relationship between periodontal conditions and the development of MetS are sparse. Only four longitudinal studies (Adachi and Kobayashi 2020; Morita et al. 2010; Saito et al. 2024; S. I. Sakurai et al. 2019) have demonstrated the influence of periodontitis on the development of MetS. All of these studies were conducted in Japanese population. A 4-year cohort study by Morita et al. (2010) found a significant association between the presence of periodontal pockets and the incidence of hypertension and lipid abnormality. A 2-year observational study by S. I. Sakurai et al. (2019) found that the prevalence of positive MetS components was increased in individuals with persistent or progressive periodontitis. Among the MetS components, only hyperglycaemia and hypertension were found to be correlated with periodontitis (S. I. Sakurai et al. 2019). An 8-year study by Saito et al. (2024) found a significant link between the presence of deep periodontal pockets and the onset of MetS, with abdominal obesity and hyperglycaemia being the only associated components. Conversely, Adachi and Kobayashi (2020) found no association between periodontitis and MetS, which is in contrast to the aforementioned studies. The presence of conflicting data necessitates further longitudinal studies. Therefore, in the present study we investigated the impact of periodontitis on the incidence and progression of MetS over an extended observation period of 10 years. The data for the study were extracted from a continuing longitudinal study of employees of the Electricity Generating Authority of Thailand (EGAT), which permitted the identical cohort to be evaluated over a period of a decade in 2003 and 2013 in successive examinations (Charupinijkul et al. 2022; Vathesatogkit et al. 2012). We believe that ours is the first study with such an extensive long-term observational period examining the association between periodontitis and MetS, in a single cohort.

2 | Materials and Methods

2.1 | Study Population

The subjects of this study were employees of EGAT, working at hydroelectric plants in Thailand. All participants provided written informed consent before enrolling in the EGAT cohort studies. The study protocol was approved by the Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand (HREC-DCU 2021-021).

The cohort design of the EGAT studies allowed for the same participants to be contacted for subsequent examinations. The data from the EGAT investigations in 2003 (EGAT 2/2), 2008 (EGAT 2/3) and 2013 (EGAT 2/4) were used for analysis in the current study. These are detailed in our previous studies (Charupinijkul et al. 2022; Vathesatogkit et al. 2012).

The inclusion criteria stipulated that only individuals who had registered and completed both medical and periodontal examinations were eligible for study analysis. Participants were excluded from longitudinal analyses if they were unable to undergo the periodontal examination (such as those in a high-risk group for infective endocarditis as defined by the American Heart Association, or those requiring antibiotic prophylaxis prior to a periodontal examination), if they had fewer than two teeth or if they presented with all components of MetS at baseline in 2003.

In the initial phase of the study, in 2003, questionnaires were used to gather demographic information, such as age, gender, educational level, alcohol consumption and smoking habits. Family history of cancer or CVD and personal medical history involving diagnosis of conditions such as CVD, stroke, DM, hypertension and dyslipidaemia were documented.

2.2 | Physical Examination

General health examination was performed by trained personnel from the Ramathibodi hospital, Thailand. Measurements of blood pressure, heart rate, height, weight, waist and hip circumstance were obtained as described in our previous studies (Suwanprasit et al. 2021; Vathesatogkit et al. 2012). For laboratory testing, fasting blood samples were collected, and the concentrations of glucose, total cholesterol, low-density lipoprotein (LDL), HDL and triglyceride (TG) were evaluated.

The criteria of the NCEP ATP III (Expert Panel on Detection and Treatment of High Blood Cholesterol in 2001)—with adjustments to the waist circumference cut-off point for Asian populations—were applied for the diagnosis of MetS (Alberti et al. 2009; Tan et al. 2004). According to these updated joint

statement criteria of 2009 (Alberti et al. 2009), a diagnosis of MetS would be made if an individual presented with any three of the following five conditions: hyperglycaemia (fasting plasma glucose [FPG] ≥100 mg/dL), hypertriglyceridemia (serum TG ≥150 mg/dL), low HDL-C ([HDL-C] <40 mg/dL in men or <50 mg/dL in women), visceral obesity (waist circumference [WC] ≥90 cm in men or ≥80 cm in women) and hypertension (blood pressure [BP] ≥130/85 mmHg).

2.3 | Periodontal Examination

The periodontal examination was carried out by six periodontists from the Department of Periodontology, Faculty of Dentistry, Chulalongkorn University. To ensure consistency, all examiners underwent a calibration process before conducting the examinations. The weighted kappa coefficients, indicating agreement within ±1 mm, ranged from 0.77 to 0.89 for probing depth (PD) and from 0.67 to 0.94 for clinical attachment level (CAL). The repeatability of measurements within each examiner yielded kappa values ranging from 0.87 to 0.91 for PD and from 0.90 to 0.96 for CAL (Suwanprasit et al. 2021).

The periodontal health of all fully erupted teeth, with the exception of third molars and retained roots, was examined. Periodontal parameters recorded included the number of missing teeth, plaque score, recession (RE) and PD. Both RE and PD were measured and rounded to the nearest millimetre using a UNC-15 periodontal probe at six sites per tooth: mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual and disto-lingual. The CAL at each site was determined by adding the values of PD and RE. To evaluate the extent of periodontitis, the percentage of sites with a CAL ≥3 mm was calculated for each individual. The CDC/AAP periodontal case definitions were then applied to classify the presence and severity of periodontal disease as follows:

- Severe periodontitis: ≥2 interproximal sites with CAL ≥6 mm (not on the same tooth) and ≥1 interproximal site with PD ≥5 mm.
- Moderate periodontitis: ≥2 interproximal sites with CAL ≥4 mm (not on the same tooth) or ≥2 interproximal site with PD ≥5 mm (not on the same tooth).
- Mild periodontitis: ≥2 interproximal sites with CAL ≥3 mm and ≥2 interproximal sites with PD ≥4 mm (not on the same tooth) or one site with PD ≥5 mm.
- No periodontitis: no evidence of mild, moderate or severe periodontitis.

2.4 | Data Collation

All collected data were uploaded into EpiData 3.1, a software designed for data collection. To minimize errors during the data entry process, a double entry method was employed by a group of periodontists and dental assistants. EpiData 3.1 was subsequently used to compare the two sets of identical data to verify their accuracy. If any discrepancies or mismatched data were identified, a re-evaluation was undertaken to correct such discrepancies.

2.5 | Statistical Analyses

The CDC/AAP case definition (Eke, Page, et al., 2012) was used to assess the presence and severity of periodontitis. Based on their periodontal status in 2003, subjects were categorized into one of three groups: no/mild periodontitis, moderate periodontitis or severe periodontitis. The incidence of MetS and the changes in the number of MetS components from 2003 to 2013 were determined as previously outlined (Expert Panel on Detection and Treatment of High Blood Cholesterol in 2001). The baseline characteristics of the subjects are summarized in Tables 1 and 2.

A two-model analysis was used in the study. The first model examined the incidence of MetS in the cohort with the exclusion of those with MetS in 2003. The second model focused on the increase in the number of MetS components from 2003 to 2013. Participants who had all five metabolic components at baseline were excluded from this part of the study.

To examine the relationship between periodontitis status and the development of MetS, as well as other cofactors (Table 3), a univariate regression analysis was conducted (Table S1). Poisson regression analysis was used to calculate the relative risk (RR) with a 95% confidence interval (CI), adjusting for covariates (as indicated in Tables 4–7). Moreover, because of the high prevalence of periodontitis, quantile stratification was adopted to segment the continuous data of baseline periodontal parameters, including mean PD, mean CAL and the extent of periodontitis (the percentage of sites with a CAL ≥3 mm), into four quartiles to represent varying degrees of periodontitis severity and extent. Additionally, the association between baseline periodontitis and the incidence of each component of MetS was further clarified using the same multivariate regression analysis. All statistical analyses were performed using SPSS version 22.0 (SPSS Inc, Chicago, IL, USA). A *p*-value of less than 0.05 was considered statistically significant.

3 | Results

3.1 | Incidence of MetS Over 10 Years and the Presence of Periodontitis

In total, 1616 participants were included in this analysis, after exclusion of those with MetS in 2003 (Figure S1). The mean age of the participants in 2003 was 46.9 ± 4.5 years (range 38.7–65.3 years) with a corresponding 10-year age increment in 2013. Sixty percent of participants were aged between 45 and 60 years, and 68% were males. More than half of the participants had a moderate income and performed regular exercise, while 46% had a higher education level and the majority were neither current smokers nor drinkers (Table 1).

Regarding the periodontal components, the survey data indicated that over 80% of the participants had moderate to severe periodontitis; the extent of periodontitis expressed as mean % sites of CAL ≥3 mm was 43%, while the mean PD and CAL were 2.3 ± 0.6 and 2.6 ± 0.9 mm, respectively. Approximately, one-quarter of the cohort (25.4%) had MetS at baseline as per NCEP

TABLE 1 | Baseline demographic data of the participants included in the analysis.

Characteristics	Incidence of MetS in 2013, *n* (%)	Increase in number of MetS components in 2013, *n* (%)
Age		
Mean ± SD (year)	46.9 ± 4.5	47.2 ± 4.6
Age group		
<45 years	650 (40.2)	825 (38.2)
45–60 years	965 (59.7)	1334 (61.7)
>60 years	1 (0.1)	2 (0.1)
Gender		
Male	1105 (68.4)	1550 (71.7)
Female	511 (31.6)	611 (28.3)
Incomes		
<600 USD/month	160 (9.9)	245 (11.4)
600–1600 USD/month	845 (52.4)	1137 (52.7)
>1600 USD/month	608 (37.7)	774 (35.9)
Education		
Lower than high school	344 (21.3)	527 (24.4)
High school—bachelor's degree	526 (32.5)	716 (33.1)
Higher than bachelor's degree	745 (46.2)	917 (42.5)
Smoking		
Never smoker	941 (58.2)	1194 (55.3)
Former smoker	363 (22.5)	529 (24.5)
Current smoker	312 (19.3)	437 (20.2)
Alcohol consumption		
Never drinker	830 (51.4)	1049 (48.5)
Former drinker	125 (7.7)	178 (8.2)
Current drinker	660 (40.9)	933 (43.3)
Exercise		
None	449 (27.8)	621 (28.7)
1–2 times/week	445 (27.5)	585 (27.1)
≥3 times/week	722 (44.7)	955 (44.2)

Abbreviations: MetS, metabolic syndrome; *n*, number of participants; SD, standard deviation.

ATP III criteria (Table 2). In 2008 and 2013, 21.6% of the participants (349 out of 1616) developed MetS. Most of them developed at least one MetS component, while only 159 participants showed no increase in the number of MetS components. Baseline data of control participants without MetS or any increase in MetS component in 2008 and 2013 are summarized in Tables S2 and S3.

The multivariate regression analysis indicated a 43.2% increased risk of MetS development and severe periodontitis, with an $RR_{adjusted} = 1.432$ (Table 4). Regarding the extent of periodontitis, each percentage increase in its extent corresponded to a 0.4% rise in the risk of MetS incidence ($RR_{adjusted} = 1.004$) (Table 5). Notably, individual in the highest quartile of the extent of periodontitis showed a substantially (33.6%) heightened risk for MetS. Moreover, a significant correlation was observed between mean CAL and MetS incidence after adjusting for all covariates (Table 6). For each millimetre increase in mean CAL, there was an 11.9% increase in the risk of developing MetS (with $RR_{adjusted} = 1.119$, 95% CI: 1.012–1.236) (Table 6). These data emphasize the influence of periodontal severity on MetS development. Additionally, various influencing factors in the multivariate model, such as age, gender, low income, low education level and current drinking status, showed statistically significant effects on the incidence of MetS, with corresponding $RR_{adjusted}$ values ($p < 0.05$) (Tables 4 and 5).

TABLE 2 | Baseline data of MetS and periodontal condition of the participants included in the analysis.

MetS and periodontal data	Incidence of MetS in 2013, *n* (%)
Hyperglycaemia	
Mean ± SD (glucose, mg/dL)	91.7 ± 16.8
No	1448 (89.6)
Yes	168 (10.4)
Hypertriglyceridemia	
Mean ± SD (triglyceride, mg/dL)	119.8 ± 74.0
No	1264 (78.2)
Yes	352 (21.8)
Low HDL-C	
Mean ± SD (HDL-C, mg/dL)	56.8 ± 13.9
No	1454 (90.0)
Yes	162 (10.0)
Hypertension	
No	1181 (73.1)
Yes	435 (26.9)
Obesity (waist, cm)	
No	1186 (73.4)
Yes	430 (26.6)
Number of MetS component	
0	556 (34.4)
1	573 (35.5)
2	487 (30.1)
3	—
4	—
5	—
MetS diagnosis	
No	1616 (100.0)
Yes	—
Number of teeth	
Mean ± SD (*n*)	26.2 ± 4.3
Severity of periodontitis	
No/mild	315 (19.5)
Mean PD ± SD 1.73 ± 0.27 (1.047, 2.746[a])	
Mean CAL ± SD 1.85 ± 0.28 (1.065, 2.786[a])	
Moderate	851 (52.7)
Mean PD ± SD 2.13 ± 0.32 (1.288, 3.246[a])	
Mean CAL ± SD 2.40 ± 0.40 (1.413, 5.050[a])	
Severe	450 (27.8)
Mean PD ± SD 2.92 ± 0.66 (1.375, 6.460[a])	
Mean CAL ± SD 3.57 ± 1.09 (1.888, 8.733[a])	
Extent (%site with CAL ≥3 mm)	
Mean ± SD (%)	43.0 ± 28.8
Mean PD	
Mean ± SD (mm)	2.3 ± 0.6
Mean CAL	
Mean ± SD (mm)	2.6 ± 0.9

(Continues)

TABLE 2 | (Continued)

MetS and periodontal data	Increase in number of MetS components in 2013, *n* (%)
Hyperglycaemia	
Mean ± SD (glucose, mg/dL)	95.8 ± 24.0
No	1741 (80.6)
Yes	420 (19.4)
Hypertriglyceridemia	
Mean ± SD (triglyceride, mg/dL)	147.0 ± 108.1
No	1361 (63.0)
Yes	800 (37.0)
Low HDL-C	
Mean ± SD (HDL-C, mg/dL)	53.8 ± 14.2
No	1704 (78.9)
Yes	457 (21.1)
Hypertension	
No	1336 (61.8)
Yes	825 (38.2)
Obesity (waist, cm)	
No	1277 (59.1)
Yes	884 (40.9)
Number of MetS component	
0	556 (25.7)

(Continues)

TABLE 2 | (Continued)

MetS and periodontal data	Increase in number of MetS components in 2013, *n* (%)
1	573 (26.5)
2	487 (22.5)
3	341 (15.8)
4	204 (9.5)
5	
MetS diagnosis	
No	1616 (74.7)
Yes	545 (25.3)
Number of teeth	
Mean ± SD (*n*)	26.2 ± 4.4
Severity of periodontitis	
No/mild	392 (18.1)
Mean PD ± SD 1.73 ± 0.27 (1.047, 2.746[a])	
Mean CAL ± SD 1.85 ± 0.28 (1.065, 2.786[a])	
Moderate	1139 (52.7)
Mean PD ± SD 2.14 ± 0.32 (1.288, 3.246[a])	
Mean CAL ± SD 2.41 ± 0.39 (1.413, 5.050[a])	
Severe	630 (29.2)
Mean PD ± SD 2.95 ± 0.68 (1.375, 6.460[a])	
Mean CAL ± SD 3.60 ± 1.10 (1.888, 8.733[a])	
Extent (%site with CAL ≥3 mm)	
Mean ± SD (%)	44.5 ± 28.9
Mean PD	
Mean ± SD (mm)	2.3 ± 0.6
Mean CAL	
Mean ± SD (mm)	2.7 ± 0.9

Abbreviations: CAL, clinical attachment loss; HDL-C, high density lipoprotein cholesterol; MetS, metabolic syndrome; *n*, number of participants; PD, pocket depth; SD, standard deviation.
[a]Minimum and maximum observed values for each quartile.

3.2 | Increment in the Number of MetS Components Over 10 Years and Baseline Periodontal Status

From the initial 2686 participants, 410 were excluded because of incomplete periodontal records or loss to follow-up, and another 115 were excluded as they had all five MetS components in 2003. This led to a total of 2161 individuals for the final analyses (Figure S1). The average age of the latter group was 47.2 ± 4.6 years (range 38.7–65.3 years), and the majority were males, with a moderately high income relative to the general populace and with a regular exercise routine. Approximately 43% had education beyond a bachelor's degree, and most were neither current smokers nor drinkers (Table 1).

TABLE 3 | The co-variates between MetS and periodontitis.

Co-variates	Categorization
Gender	Male
	Female
Age	<60 years old
	≥60 years old
Incomes	Low income: <600 USD/month
	Medium income: 600–1600 USD/month
	High income: >1600 USD/month
Education	Lower than high school
	High school—bachelor's degree
	Higher than bachelor's degree
Smoking	Current smoker: Someone who currently smoke.
	Former smoker: Someone who was able to quit smoking.
	Never smoker: Someone who has never smoked.
Alcohol consumption	Current drinker: Someone who currently drink alcohol.
	Former smoker: Someone who was able to quit drinking alcohol.
	Never smoker: Someone who has never drinking alcohol.
Exercise	None
	1–2 times/week
	≥3 times/week

Abbreviation: MetS, metabolic syndrome.

Periodontal assessments at baseline revealed that over 80% had moderate to severe periodontitis; furthermore, the extent of periodontitis expressed as mean percentage of sites of CAL ≥3 mm was 45%, while mean PD and CAL were 2.3 ± 0.6 and 2.7 ± 0.9 mm, respectively. One-quarter of the participants (25.3%) were diagnosed with MetS (Table 2).

The relationship between baseline periodontitis and increase in the number of MetS components over the 10-year period of 2003–2013 was examined through multivariate regression analysis, as presented in Tables 4–6. The analysis indicated that for every 1% increase in the prevalence of periodontitis sites was associated with a 0.2% heightened risk of acquiring further components of MetS (with $RR_{adjusted} = 1.002$) (Table 5).

TABLE 4 | Multivariate regression analysis comparing the association between MetS, severity of periodontal disease and other influencing factors as originally presented in 2003, and subsequent incidence and increased numbers of MetS components as noted in 2013.

	Multivariate regression					
	Incidence of MetS in 2013			Increase in number of MetS components in 2013		
Influencing factors in 2003	**$RR_{adjusted}$[a]**	**95% CI**		**$RR_{adjusted}$[a]**	**95% CI**	
Age group						
<45 years	1	—	—	1	—	—
45–60 years	**1.549***	1.153	2.080	**1.271***	1.146	1.411
>60 years	**2.897***	1.573	5.335	**1.719***	1.271	2.326
Gender						
Male	**1.358***	1.042	1.771	**1.309***	1.168	1.466
Female	1	—	—	1	—	—
Incomes						
<600 USD/month	**0.578***	0.365	0.914	**0.771***	0.646	0.921
600–1600 USD/month	0.881	0.697	1.112	0.939	0.855	1.032
>1600 USD/month	1	—	—	1	—	—
Education						
Lower than high school	**1.551***	1.138	2.114	1.082	0.946	1.238
High school—bachelor's degree	**1.445***	1.140	1.832	**1.135***	1.024	1.258
Higher than bachelor's degree	1	—	—	1	—	—
Smoking						
Never smoker	1	—	—	1	—	—
Former smoker	1.163	0.878	1.540	0.975	0.863	1.101
Current smoker	1.142	0.842	1.548	1.093	0.958	1.246
Alcohol consumption						
Never drinker	1	—	—	1	—	—
Former drinker	1.374	0.973	1.940	1.079	0.930	1.251
Current drinker	**1.317***	1.030	1.684	**1.108***	1.001	1.227
Exercise						
None	0.988	0.767	1.273	1.040	0.949	1.139
1–2 times/week	0.857	0.687	1.069	1.081	0.976	1.198
≥3 times/week	1	—	—	1	—	—
Severity of periodontal disease						
No/mild	1	—	—	1	—	—
Moderate	1.247	0.911	1.706	1.029	0.916	1.155
Severe	**1.432***	1.017	2.016	1.083	0.947	1.238

Note: Significant findings are indicated in bold.
Abbreviations: CI, confidence interval; MetS, metabolic syndrome; RR, relative risk.
[a]Adjusted for age, gender, income, education, smoking, alcohol consumption and exercise.
*p-value < 0.05.

Furthermore, the effect of periodontitis on the incidence of each MetS component was investigated by baseline periodontal data in 2003 and the incidence of each MetS component in 2013, as shown in Table 7. The results revealed that baseline periodontitis status influenced the risk of developing hyperglycaemia and hypertension. In particular, the risk of

TABLE 5 | Multivariate regression analysis comparing the association between MetS development, extent of periodontitis and other influencing factors as originally presented in 2003, and subsequent incidence and increased numbers of MetS components as noted in 2013.

	Multivariate regression					
	Incidence of MetS in 2013			Increase in number of MetS components in 2013		
Influencing factors in 2003	**$RR_{adjusted}$[a]**	**95% CI**		**$RR_{adjusted}$[a]**	**95% CI**	
Age group						
<45 years	1	—	—	1	—	—
45–60 years	**1.539***	1.145	2.068	**1.265***	1.140	1.405
>60 years	**2.763***	1.495	5.107	**1.677***	1.238	2.273
Gender						
Male	**1.358***	1.042	1.769	**1.314***	1.173	1.472
Female	1	—	—	1	—	—
Incomes						
<600 USD/month	**0.582***	0.368	0.920	**0.772***	0.647	0.921
600–1600 USD/month	0.886	0.702	1.118	0.942	0.858	1.035
>1600 USD/month	1	—	—	1	—	—
Education						
Lower than high school	**1.528***	1.120	2.084	1.070	0.935	1.225
High school—bachelor's degree	**1.451***	1.146	1.837	**1.132***	1.022	1.255
Higher than bachelor's degree	1	—	—	1	—	—
Smoking						
Never smoker	1	—	—	1	—	—
Former smoker	1.172	0.886	1.550	0.975	0.864	1.102
Current smoker	1.121	0.826	1.520	1.084	0.950	1.236
Alcohol consumption						
Never drinker	1	—	—	1	—	—
Former drinker	1.360	0.963	1.921	1.075	0.927	1.247
Current drinker	**1.311***	1.025	1.675	1.107	1.000	1.225
Exercise						
None	1.000	0.776	1.288	1.036	0.946	1.135
1–2 times/week	0.865	0.694	1.078	1.079	0.974	1.195
≥3 times/week	1	—	—	1	—	—
Extent (%site with CAL ≥3 mm)	**1.004***	1.001	1.008	**1.002***	1.000	1.003

Note: Significant findings are indicated in bold.
Abbreviations: CAL, clinical attachment loss; CI, confidence interval; MetS, metabolic syndrome; RR, relative risk.
[a]Adjusted for age, gender, income, education, smoking, alcohol consumption and exercise.
*p-value < 0.05.

developing hyperglycaemia over a decade was significantly elevated in individuals with severe periodontitis or those in higher quartile groups of mean PD, mean CAL or extent of periodontitis. Increased incidence of hypertension was significantly associated with the baseline level of mean CAL and the extent of periodontitis.

4 | Discussion

In this longitudinal study, we attempted to clarify the association between periodontitis and MetS using data derived from the 2003 and 2013 EGAT cohort study of Thailand (EGAT 2/2–2/4) (Charupinijkul et al. 2022; Vathesatogkit et al. 2012).

TABLE 6 | Multivariate regression analysis comparing the association between MetS development and baseline periodontal status presented in 2003, and subsequent incidence and increased numbers of MetS components as noted in 2013.

	Multivariate regression		
	Incidence of MetS in 2013		
Periodontal status in 2003	**$RR_{adjusted}$[a]**	**95% CI**	
Mean PD (mm)	1.048	0.885	1.240
Mean PD (quartile)			
Q1 (25th percentile)	1	—	—
Mean ± SD 1.67 ± 0.18 (1.047, 1.904[b])			
Q2 (50th percentile)	0.947	0.715	1.255
Mean ± SD 2.05 ± 0.08 (1.905, 2.198[b])			
Q3 (75th percentile)	1.045	0.791	1.380
Mean ± SD 2.39 ± 0.12 (2.200, 2.615[b])			
Q4 (above 75th percentile)	1.127	0.842	1.508
Mean ± SD 3.20 ± 0.57 (2.616, 6.460[b])			
Mean CAL (mm)	**1.119***	1.012	1.236
Mean CAL (quartile)			
Q1 (25th percentile)	1	—	—
Mean ± SD 1.83 ± 0.20 (1.065, 2.096[b])			
Q2 (50th percentile)	1.026	0.770	1.366
Mean ± SD 2.28 ± 0.11 (2.098, 2.476[b])			
Q3 (75th percentile)	1.207	0.912	1.596
Mean ± SD 2.71 ± 0.15 (2.477, 3.029[b])			
Q4 (above 75th percentile)	1.197	0.887	1.615
Mean ± SD 4.01 ± 1.07 (3.032, 8.733[b])			
Extent (%site with CAL ≥3 mm) (quartile)			
Q1 (25th percentile)	1	—	—
Mean ± SD 11.04 ± 5.90 (0.000, 20.238[b])			
Q2 (50th percentile)	1.017	0.766	1.349
Mean ± SD 30.45 ± 6.02 (20.312, 41.304[b])			
Q3 (75th percentile)	0.989	0.741	1.320
Mean ± SD 54.52 ± 8.19 (41.346, 68.518[b])			
Q4 (above 75th percentile)	**1.336***	1.006	1.776
Mean ± SD 86.40 ± 10.14 (68.750, 100.000[b])			
	Increase in number of MetS components in 2013		
Periodontal status in 2003	**$RR_{adjusted}$[a]**	**95% CI**	
Mean PD (mm)	1.020	0.948	1.097
Mean PD (quartile)			
Q1 (25th percentile)	1	—	—
Mean ± SD 1.67 ± 0.18 (1.047, 1.904[b])			

(Continues)

TABLE 6 | (Continued)

Periodontal status in 2003	Increase in number of MetS components in 2013		
	$RR_{adjusted}$[a]	95% CI	
Q2 (50th percentile)	0.970	0.872	1.079
Mean ± SD 2.05 ± 0.08 (1.905, 2.198[b])			
Q3 (75th percentile)	0.989	0.885	1.106
Mean ± SD 2.39 ± 0.12 (2.200, 2.615[b])			
Q4 (above 75th percentile)	1.018	0.900	1.153
Mean ± SD 3.20 ± 0.57 (2.616, 6.460[b])			
Mean CAL (mm)	1.047	1.000	1.096
Mean CAL (quartile)			
Q1 (25th percentile)	1	—	—
Mean ± SD 1.83 ± 0.20 (1.065, 2.096[b])			
Q2 (50th percentile)	1.006	0.903	1.120
Mean ± SD 2.28 ± 0.11 (2.098, 2.476[b])			
Q3 (75th percentile)	1.090	0.975	1.219
Mean ± SD 2.71 ± 0.15 (2.477, 3.029[b])			
Q4 (above 75th percentile)	1.041	0.918	1.180
Mean ± SD 4.01 ± 1.07 (3.032, 8.733[b])			
Extent (%site with CAL ≥3 mm) (quartile)			
Q1 (25th percentile)	1	—	—
Mean ± SD 11.04 ± 5.90 (0.000, 20.238[b])			
Q2 (50th percentile)	1.061	0.953	1.180
Mean ± SD 30.45 ± 6.02 (20.312, 41.304[b])			
Q3 (75th percentile)	0.991	0.884	1.110
Mean ± SD 54.52 ± 8.19 (41.346, 68.518[b])			
Q4 (above 75th percentile)	1.091	0.968	1.231
Mean ± SD 86.40 ± 10.14 (68.750, 100.000[b])			

Note: Significant findings are indicated in bold.
Abbreviations: CAL, clinical attachment loss; CI, confidence interval; MetS, metabolic syndrome; PD, pocket depth; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile; RR, relative risk; SD, standard deviation.
[a]Adjusted for age, gender, income, education, smoking, alcohol consumption and exercise.
[b]Minimum, maximum observed values for each quartile.
*p-value < 0.05.

Our data indicate that approximately one-quarter of the population (25.4%) had MetS, in concurrence with similar prevalence rates globally (D'Aiuto et al. 2008; Lamster and Pagan 2017; Saklayen 2018). Furthermore, Ranasinghe et al. (2017) conducted a comprehensive systematic review of cohorts from China, South Korea and Taiwan, noting that in most of these Asian countries, similar to Thailand, nearly one-fifth of the adult population (or even more) was affected by MetS with a secular increase in prevalence.

On the other hand, in terms of the prevalence of periodontitis, 80% of our cohort had moderate to severe disease, which is considerably higher than the 6.1% and 12.2% in Thai adults aged 35–44 years and 60–74 years, respectively, reported in the most recent available Thai National Oral Health Survey (Dental Health Division. Report on the eighth national oral health survey of Thailand 2018) and those of the broader global population studies conducted by Eke et al. (2018) and Marcenes et al. (2013). This discrepancy is likely due to differences in methodology, diagnostic criteria and age as well as the specific demographic profile of the EGAT cohort. The foregoing countrywide Thai survey, for instance, relied on the CPITN score, which is likely to underestimate the prevalence of severe periodontitis because of its exclusion of CAL measurements (Baelum et al. 1993).

Our findings revealed a significant correlation between the severity and extent of periodontitis, as well as the level of mean CAL and the incidence of MetS. Notably, our research stands out as the

TABLE 7 | Multivariate regression analysis comparing the association between incidence of each MetS component in 2013 and baseline periodontal status presented in 2003.

Periodontal status in 2003	Incidence of each MetS component in 2013									
	Obesity		Hypertriglyceridemia		Low HDL-C		Hypertension		Hyperglycaemia	
	$RR_{adjusted}$[a]	95% CI	$RR_{adjusted}$[a]	95% CI	$RR_{adjusted}$[a]	95% CI	$RR_{adjusted}$[a]	95% CI	$RR_{adjusted}$[a]	95% CI
Mean PD (mm)	1.077	0.925–1.253	0.971	0.860–1.097	1.004	0.893–1.130	1.104	0.996–1.224	1.075	0.952–1.214
Mean PD (Quartile)										
Q1 (25th percentile)	1	—	1	—	1	—	1	—	1	—
Q2 (50th percentile)	1.022	0.819–1.275	0.963	0.800–1.160	0.933	0.772–1.128	1.055	0.884–1.259	1.087	0.881–1.341
Q3 (75th percentile)	1.049	0.832–1.324	0.943	0.779–1.140	0.997	0.824–1.206	1.107	0.927–1.322	1.208	0.982–1.487
Q4 (above 75th percentile)	1.095	0.841–1.424	0.936	0.759–1.155	1.045	0.851–1.282	1.147	0.948–1.387	**1.263***	1.016–1.570
Mean CAL (mm)	1.089	0.992–1.196	0.997	0.924–1.077	1.018	0.946–1.095	**1.069***	1.002–1.141	1.073	0.994–1.157
Mean CAL (quartile)										
Q1 (25th percentile)	1	—	1	—	1	—	1	—	1	—
Q2 (50th percentile)	1.080	0.866–1.347	0.968	0.801–1.169	0.904	0.748–1.093	1.135	0.954–1.352	1.146	0.925–1.420
Q3 (75th percentile)	1.013	0.794–1.292	1.045	0.865–1.263	0.961	0.795–1.162	1.178	0.985–1.410	**1.438***	1.168–1.769
Q4 (above 75th percentile)	1.273	0.987–1.642	0.895	0.723–1.109	0.954	0.776–1.171	1.095	0.902–1.329	**1.303***	1.040–1.631
Severity of periodontitis										
No/mild	1	—	1	—	1	—	1	—	1	—
Moderate	0.964	0.772–1.204	1.056	0.866–1.289	1.059	0.859–1.305	1.100	0.907–1.333	1.049	0.837–1.315
Severe	1.043	0.802–1.356	0.989	0.788–1.242	1.151	0.914–1.449	1.136	0.915–1.410	**1.286***	1.009–1.639
Extent (%sites with CAL ≥3 mm)	1.002	0.999–1.005	1.000	0.998–1.003	1.001	0.999–1.004	**1.003***	1.001–1.006	1.002	0.999–1.004
Extent (%sites with CAL ≥3 mm) (quartile)										
Q1 (25th percentile)	1	—	1	—	1	—	1	—	1	—
Q2 (50th percentile)	1.087	0.872–1.355	0.998	0.828–1.203	1.083	0.898–1.307	1.091	0.915–1.302	1.139	0.925–1.403
Q3 (75th percentile)	1.016	0.797–1.295	0.907	0.746–1.103	0.970	0.795–1.183	1.109	0.925–1.329	**1.258***	1.023–1.547
Q4 (above 75th percentile)	1.165	0.907–1.496	1.012	0.826–1.240	1.136	0.928–1.391	1.170	0.968–1.415	1.184	0.950–1.474

Note: Significant findings are indicated in bold.

Abbreviations: CAL, clinical attachment loss; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; PD, pocket depth; RR, relative risk.

[a]Adjusted for age, gender, income, education, smoking, alcohol consumption and exercise.

*p-value < 0.05.

first to delineate the influence of periodontitis severity on MetS incidence, leveraging comprehensive oral periodontal data in accordance with the CDC/AAP periodontal case definition (Eke, Page, et al., 2012). We used both the level of mean CAL and PD as primary periodontal parameters to identify periodontal disease sites, aligning with the updated periodontitis case definition from the 2017 World Workshop (Tonetti, Greenwell, and Kornman 2018). Both the 2012 CDC/AAP criteria and the 2018 EFP/AAP periodontitis case definitions are considered gold standards. Ortigara et al. (2021) found high agreement between these two classifications. While a previous report (Saito et al. 2024) relied on the index teeth and Community Periodontal Index (CPI) to estimate periodontal status, our analysis went beyond by merely assessing periodontitis severity to its extent, contributing to a better understanding of the link between periodontitis and MetS.

We also evaluated the role of periodontitis in the progression of MetS, specifically examining the increase in the number of MetS components over the 10-year period. The findings from multivariate regression analysis suggested that with each percentage point increase in the extent of periodontitis, there is a 0.2% increase in the likelihood of developing additional MetS components. This association mirrors the findings of several studies that have identified a close link between periodontitis and MetS (D'Aiuto et al. 2008; Fukui et al. 2012; Han et al. 2010; Khader et al. 2008). A cross-sectional study by P. Li et al. (2009) and another by Alhabashneh et al. (2015) reported that individuals with MetS had a significantly higher extent of periodontitis. This was determined by the percentage of teeth with CAL ≥3 mm and the percentage of teeth with probing pocket depth (PPD) ≥3 mm, indicating a notable difference in the extent of periodontitis among those with MetS ($p < 0.005$). Regarding the development of each MetS component, our study found that hyperglycaemia and hypertension were the two MetS components most significantly affected by the existence of baseline periodontitis. This result is in concordance with the 2-year cohort study of S. I. Sakurai et al. (2019), which demonstrated a significant influence of periodontitis on these two systemic conditions.

Independent of periodontal health, the age of an individual emerged as a noteworthy factor impacting the development of MetS. The highest incidence of MetS we observed was in individuals over the age of 60, a finding that concurs well with previous studies from other regions that have noted a higher degree of MetS prevalence in the elderly (Boden et al. 1993; Hirode and Wong 2020; T. Sakurai et al. 2010; Yuenyongchaiwat, Pipatsitipong, and Sangprasert 2017). This increased susceptibility to MetS in older age groups can likely be attributed to age-related physiological changes such as enhanced insulin resistance, hormonal fluctuations and the increased accumulation of abdominal fat. These factors are well-known cofactors associated with the pathogenesis and development of MetS (Boden et al. 1993; T. Sakurai et al. 2010). Concerning lifestyle factors, previous studies have demonstrated a relationship between unhealthy lifestyles and MetS (Lin et al. 2019; Vajdi et al. 2023). Our findings indicate a significant association between current drinking habits and the development of MetS. This is in alignment with the results of a meta-analysis conducted in 2016 (Vancampfort et al. 2016), which found that more than one in five individuals with alcohol use disorder are affected by MetS. However, no effect between smoking and exercise habits on MetS was found in this study. This discrepancy may be due to the study design, which relied on self-reported data without precise delineation of activity intensity, duration or cessation (Liu et al. 2017; Martinez-Montoro et al. 2023; Shin, Oh, and Cho 2018; Tucker et al. 2016). As MetS has a multifactorial aetiology, the complex interplay between various genetic and environmental factors further modulates and obscures the association (Park et al. 2023).

A common linking thread between periodontal disease and MetS is increased levels of systemic inflammatory markers such as CRP, interleukin-1 beta (IL-1β) and tumour necrosis factor-alpha (TNF-α) (Loos et al. 2000). Some have, therefore, surmised this association to be a firm bidirectional link between periodontitis and MetS (Nibali et al. 2013), although it is still unclear whether these are causative or associative parameters between these entities. Intriguingly, non-surgical periodontal interventions have been shown to mitigate these inflammatory responses (Shimada et al. 2010). Torumtay et al. (2016) noted the effectiveness of these treatments in reducing both oxidative stress and inflammatory markers, thus benefitting patients with concurrent MetS and chronic periodontitis.

Despite the fact that numerous investigators have suggested a positive correlation between periodontitis and MetS, inconsistencies in the strength of this association still remain, which often arise from variations in study design, particularly the scarcity of longitudinal research tracking the progression of MetS. Our study, with a large cohort observed over 10 years, uniquely enabled the examination of both the changes in MetS components and the incidence of new MetS cases. A crucial strength of our approach is the comprehensive periodontal evaluation according to CDC/AAP guidelines for the epidemiological assessment of periodontal disease, which, as far as we are aware, has not been performed previously.

There are several limitations to our study. First, as the data were exclusively derived from employees from a single company, who were predominantly male with middle to high socio-economic status, it is difficult to extend the findings to the Thai population in general because this specific demography does not accurately reflect the population at large. Second, the retrospective nature of the study and the overall study design precluded exploration of the mechanisms underpinning the link between periodontitis and the onset of MetS. Thus, the temporality of MetS development over the observation period remains undetermined, highlighting a need for further sequentially adjusted longitudinal and intervention studies to deepen our understanding of this association. Third, the exclusion of individuals with severe tooth loss or those who are edentulous means that the relationship between periodontitis and MetS in these groups remains unclear. Finally, the lack of data on the oral health history of the cohort, especially regarding periodontal interventions over a decade, limits the control over confounding variables in the data analysis.

5 | Conclusion

This study in a Thai population highlights the potential effect of the severity and extent of periodontitis on the incidence and progression of MetS. The presence of periodontitis might elevate

the risk of developing hyperglycaemia and hypertension, which could lead to the onset of MetS. Therefore, maintaining a healthy periodontal status and effectively managing periodontitis could be one of the strategies in preventing the onset and advancement of MetS. Further longitudinal research, particularly interventional studies, is needed to confirm the benefits of periodontal treatment on MetS development.

Author Contributions

S.T. and B.I.N.A. conceptualized and designed the study, conducted data collection and analysis and wrote the manuscript. A.L., P.V., L.T. and W.W. participated in the survey and contributed to data analysis. L.S. reviewed and edited the text for language. All authors approved the final version for publication.

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Conflict of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.