ความสัมพันธ์ระหว่างโรคปริทันต์อักเสบและโรคความดันโลหิตสูงในคนไทยวัยผู้ใหญ่กลุ่มหนึ่ง

Association Between Periodontitis and Hypertension among a Group of Thai Adults

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บทคัดย่อ

เนื่องจากมีการศึกษาพบว่าโรคปริทันต์อักเสบอาจส่งผลเพิ่มความเสี่ยงต่อการเกิดโรคความดันโลหิตสูง แต่ยังขาดข้อมูลสนับสนุนจากการศึกษาทางระบาดวิทยาจากกลุ่มประชาการขนาดใหญ่โดยเฉพาะในประเทศแถบเอเชีย ดังนั้นงานวิจัยนี้จึงจัดทำขึ้นเพื่อศึกษาความสัมพันธ์ระหว่างโรคปริทันต์อักเสบและโรคความดันโลหิตสูงในกลุ่มพนักงานการไฟฟ้าฝ่ายผลิตแห่งประเทศไทย (EGAT) จำนวน 1,378 คน ช่วงอายุ 53-73 ปี ได้รับการสัมภาษณ์ ตรวจทางการแพทย์ ตรวจสภาวะปริทันต์และแบ่งปืน 3 กลุ่มตามระดับความรุนแรงของโรคปริทันต์ ส่วนการวินิจฉัยโรคความดันโลหิตสูงจะใช้เกณฑ์คือเมื่อมีค่าเฉลี่ยความดันโลหิตซีสโตลิคตั้งแต่ 140 มิลลิเมตรปรอทขึ้นไป หรือเมื่อมีค่าเฉลี่ยความดันโลหิตไดแอสโตลิตตั้งแต่ 90 มิลลิเมตรปรอทขึ้นไป หรือเมื่อได้รับยารักษาโรคความดันโลหิตสูง แล้วนำข้อมูลมาวิเคราะห์ความสัมพันธ์ระหว่างระดับความรุนแรงของโรคปริทันต์และโรคความดันโลหิตสูง ซึ่งผลการศึกษาพบว่าระดับความรุนแรงของโรคปริทันต์ที่เพิ่มขึ้นมีความสัมพันธ์กับการเพิ่มความเสี่ยงโรคความดันโลหิตสูง โดยมีค่า crude odds ratios สำหรับโรคปริทันต์อักเสบระดับปานกลางและระดับรุนแรงเป็น 1.60 (95% confidence interval (CI): 1.12-2.29, $P = 0.010$) และ 2.07 (95% CI: 1.43-3.00, $P = 0.001$) ตามลำดับ และภายหลังการควบคุมปัจจัยที่ส่งผลต่อโรคความดันโลหิตสูงซึ่งได้แก่ อายุ เพศ ระดับการศึกษา โรคเบาหวาน การสูบบุหรี่ การบริโภคแอลกอฮอล์ ความถี่การออกกำลังกาย โรคอ้วน ไตรกลีเซอไรด์ในเลือดสูงและไขมันในเลือดสูง พบว่าโรคปริทันต์อักเสบระดับรุนแรงมีความสัมพันธ์กับการเพิ่มความเสี่ยงโรคความดันโลหิตสูงอย่างมีนัยสำคัญทางสถิติโดยมีค่า odds ratio เป็น 1.55 (95% CI: 1.03-2.33, $P = 0.035$) ข้อสรุปจากการศึกษาประชากรไทยวัยผู้ใหญ่กลุ่มนี้พบว่าโรคปริทันต์อักเสบระดับรุนแรงสัมพันธ์กับการเพิ่มความเสี่ยงต่อโรคความดันโลหิตสูง อย่างไรก็ตามยังคงต้องการการสนับสนุน

คำสำคัญ: *โรคปริทันต์อักเสบ โรคความดันโลหิตสูง ความดันโลหิตสูง คนไทยวัยผู้ใหญ่ งานวิจัยระบาดวิทยา การศึกษาแบบตัดขวาง*

Abstract

Previous studies suggest that periodontitis may be associated with an increasing risk of hypertension. However, data from large epidemiological studies, particularly in Asian populations, are limited. The aim of this cross-sectional study was to examine the association between periodontitis and hypertension using data from a cohort study in a Thai population. The study population comprised 1,378 employees of the Electricity Generating Authority of Thailand (EGAT), aged 53 to 73 years old. All participants received medical and periodontal examinations. Periodontal probing depth and clinical attachment level were recorded and the participants were categorized into no/mild, moderate, or severe periodontitis groups according to the Center for Disease Control and Prevention and the American Academy of Periodontology case definition. Hypertension was determined as having systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or taking antihypertensive medication. The logistic regression was used to determine the association between periodontitis severity and hypertension. The results of univariate analysis showed that the risk of hypertension increased with increasing periodontitis severity with crude odds ratios of 1.60 (95% confidence interval (CI): 1.12-2.29; $P = 0.010$) and 2.07 (95% CI: 1.43-3.00; $P = 0.001$) for moderate and severe periodontitis, respectively. After adjusting confounding factors including age, gender, education level, diabetes mellitus, smoking status, alcohol consumption, frequency of exercise, obesity, hypertriglyceridemia, and hypercholesterolemia, the association between severe periodontitis and hypertension remained significant with an odds ratio of 1.55 (95% CI: 1.03-2.33; $P = 0.035$). In conclusion, severe periodontitis was associated with an increasing risk of hypertension in this group of Thai adults. Further prospective studies are needed to confirm our findings.

Keywords: *Periodontitis, hypertension, high blood pressure, Thai adults, epidemiological study, cross-sectional study*

1. Introduction

Hypertension is a major risk factor for cardiovascular disease (CVD), leading to premature death and disability (Chobanian et al., 2003). The prevalence of hypertension has been rising worldwide (Kearney et al., 2005). In Thailand, one out of four adults or around 10 million people have hypertension and almost half of these individuals are unaware of their conditions (WHO Thailand, 2017). Hypertension is a multifactorial disease (Oparil, Zaman, and Calhoun, 2003). Several dietary and lifestyle factors, as well as chronic inflammation, have been implicated as risk factors for hypertension (De Miguel et al., 2015).

Periodontitis is a disease of the tooth supporting tissues, caused by host immuno-inflammatory response to subgingival plaque (Kornman, 2008). The disease is characterized by chronic inflammation and destruction of the periodontal connective tissue and alveolar bone. It has been hypothesized that periodontitis may be associated with an increased risk for hypertension (Tonetti and Van Dyke, 2013). This may be partly attributed to the fact that periodontitis is associated with elevated levels of systemic inflammatory markers such as C-reactive proteins (CRP),

fibrinogen, and white blood cells (Tsioufis et al., 2011). These inflammatory markers are known to be related to endothelial dysfunction and dysregulation of blood pressure control (Amar et al., 2003). However, results from epidemiological studies of the association between periodontitis and hypertension remain inconclusive. The majority of studies supported a positive association (Iwashima et al., 2014, Rivas-Tumanyan et al., 2013) whereas others failed to observe the association (Nesse et al., 2010, Ollikianen et al., 2014). Moreover, there are limited data from large scale epidemiological studies, particularly in Asian populations (Choi et al., 2015, Kawabata et al., 2016). Most of these large scale studies also have methodological flaws such as inadequate adjustment for potential confounders (Choi et al., 2015) or the use of the community periodontal index (CPI) (Choi et al., 2015, Iwashima et al., 2014, Kawabata et al., 2016, Nesse et al., 2010), which has been shown to underestimate the prevalence of periodontitis (Nesse et al., 2010). To date, there have not been any epidemiological studies that examine the association between these two diseases in Thai population.

2. Objective

To examine the association between periodontitis and hypertension using data from a cohort study in a Thai population.

3. Materials and Methods

3.1 Study population

This cross-sectional study was conducted in 2002 among the employees and retired personnel of the Electricity Generating Authority of Thailand (EGAT). Individuals with complete data on all variables were included in the present investigation. The study was approved by the Ethics Review Committee of the Faculty of Medicine at Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. All participants signed an informed consent prior to the study.

3.2 Assessment of periodontal status

Periodontal examinations were carried out by four experienced periodontists and three postgraduate students from the Department of Periodontology, Faculty of Dentistry, Chulalongkorn University as previously described (Torrungruang et al., 2005). One maxillary quadrant and one contralateral mandibular quadrant were randomly selected. All teeth in these quadrants were examined except third molars and retained roots. Individuals who were at risk from bacterial endocarditis or hematogenous total joint infection, or were undergoing hemodialysis, and those with fewer than six teeth in the selected two quadrants were excluded from periodontal examinations.

The examinations included the number of missing teeth, probing depth (PD) and gingival recession (RE). PD and RE were measured using a PCP-UNC 15 probe on six sites per tooth (mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual and distolingual). Clinical attachment level (CAL) was calculated as the sum of PD and RE.

Calibration for periodontal measurements was carried out among seven examiners before the study. The weighted kappa coefficient (within ± 1 mm) between each pair of examiners ranged from 0.72-0.90 for PD and 0.69-0.79 for CAL. The weighted kappa coefficient (within ± 1 mm) within each examiner range from 0.85-0.96 for PD and 0.80-0.97 for CAL.

3.3 Assessment of hypertension

Mean blood pressure was calculated. Blood pressure recording was conducted twice after a 5-minute rest, using auscultatory method and seated measurement at brachial artery with a validated automatic. Participants were diagnosed as hypertension if a mean systolic blood pressure was ≥140 mmHg or a mean diastolic blood pressure was ≥90 mmHg or both or if they were currently taking prescribed antihypertensive medication (Vathesatogkit et al., 2012).

3.4 Assessment of potential confounders

Variables known to be associated with hypertension were assessed using questionnaire, interview, anthropometric measurements, and blood examinations. Age and educational attainment were self-reported. Smoking status, alcohol consumption, and physical activities were assessed by using questionnaire. Measures of weight, height, and waist circumference (wc) were made through the examination of the participants dressed in light clothing, but without shoes. Blood examinations of fasting blood sugar, triglyceride level, and total cholesterol level were collected using standard protocols (Sritara et al., 2003). Then all variables were stratified as followed: *Age* was dichotomized into two groups: <60 years and ≥60 years; *Education level* was stratified as ≤high school and >high school; *Diabetes mellitus* was diagnosed if an individual had fasting blood sugar ≥126 mg/dl or had been taking anti-diabetic drugs during the past 2 weeks (Expert committee on the diagnosis and classification of diabetes mellitus, 2003); *Smoking status* was classified as non-smokers, former smokers, and current smokers. Smokers were defined as persons who had smoked at least 100 cigarettes in their lifetime; *Alcohol consumption* was classified as non-drinkers, former drinkers, and current drinkers ('drinkers' was defined as persons who had consumed any types of alcoholic beverage at least 12 drinks in a one-year period); *Exercise* was dichotomized into two groups: 1-2 and ≥3 sessions/week (Vathesatogkit et al., 2012); *Body mass index (BMI)* was calculated from weight in kilograms divided by square height in meters and divided into two categories: <30 and ≥30 kg/m^2 (WHO, International Association for the Study of Obesity, and International Obesity Task Force, 2000); *WC* was measured at the level of umbilicus in centimeters and divided into two categories using cutoff point of ≤88 for female and ≤102 for male; *Hypertriglyceridemia* was diagnosed if an individual had triglyceride ≥150 mg/dl; and *Hypercholesterolemia* was diagnosed if an individual had total cholesterol ≥240 mg/dl or had been taking lipid-lowering drugs (NCEP III, 2002).

3.5 Data analyses

The participants were categorized into three groups: no/mild, moderate, and severe periodontitis, according to the Center for Disease Control and Prevention and the American Academy of Periodontology (CDC/AAP) case definition (Page and Eke, 2007). No/mild periodontitis (defined as having <2 interproximal sites with CAL ≥4 mm

and <2 interproximal sites with PD ≥5 mm), Moderate periodontitis (defined as having ≥2 interproximal sites with CAL ≥4 mm (not on the same tooth), or ≥2 interproximal sites with PD ≥5 mm (not on the same tooth)), and Severe periodontitis (defined as having ≥2 interproximal sites with CAL ≥6 mm (not on the same tooth), and ≥1 interproximal site with PD ≥5 mm).

SPSS software program (SPSS version 22.0; IBM Corp., Chicago, IL, USA) was used for statistical analysis. Statistical significance was determined at $\alpha = 0.05$. Pearson chi-square was used to test the association between hypertension and each categorical variable. The logistic regression model was used to investigate the degree of association between periodontal disease severity and hypertension, adjusting for potential confounders as described above. Wald statistic was used to determine statistical significance. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated for each independent variable.

4. Results

The study population comprised 1,378 individuals with a mean ± SD age of 59 ± 5 years (age range of between 53 and 73) and 77.10% were men. 661 participants (48.00%) were diagnosed with hypertension, and their mean SBP ± SD and mean DBP ± SD were 142.30 ± 15.65 and 91.16 + 9.20 mmHg, respectively. For participants with normal blood pressure, their mean SBP ± SD and mean DBP ± SD were 116.62 ± 10.55 and 76.00 ± 7.50 mmHg, respectively. The demographic and clinical characteristics of normotensive and hypertensive participants are presented in Table 1. The hypertensive participants had higher proportions of age ≥60 years, male sex, ≤high school education, diabetes mellitus, former smokers, current or occasional drinkers, BMI ≥30 kg/m^2, waist circumference >88 cm in female or >102 cm in male, triglyceride ≥150 mg/dl and severe periodontitis, compared to normotensive participants (P <0.005).

Table 1 Demographic and clinical characteristics of participants diagnosed with hypertension compared to those with normal blood pressure

Variables	Total N (%)	No hypertension (N = 717) N (%)	Hypertension (N = 661) N (%)
Age (years)*			
<60	791 (57.40)	447 (62.30)	344 (52.00)
≥60	587 (42.80)	270 (37.70)	317 (48.00)
Gender*			
Female	315 (22.90)	210 (29.30)	105 (15.90)
Male	1,063 (77.10)	507 (70.70)	556 (84.10)
Education level*			
≤High school	324 (23.50)	133 (18.50)	191 (28.90)
>High school	1,054 (76.50)	584 (81.50)	470 (71.10)

Variables	Total N (%)	No hypertension (N = 717) N (%)	Hypertension (N = 661) N (%)
Diabetes mellitus*			
No	1,160 (84.20)	632 (88.10)	528 (79.90)
Yes	218 (15.80)	85 (11.90)	133 (20.10)
Smoking status*			
Non-smoker	655 (47.53)	363 (50.60)	292 (44.20)
Former smoker	535 (38.82)	243 (33.90)	292 (44.20)
Current smoker	188 (13.65)	111 (15.50)	77 (11.60)
Alcohol consumption*			
Non-drinker	406 (29.46)	239 (33.30)	167 (25.30)
Former drinker	336 (24.38)	188 (26.26)	148 (22.40)
Current/occasional drinker†	636 (46.16)	290 (40.44)	346 (52.30)
Exercise (sessions/week)			
1-2	338 (24.50)	189 (26.40)	149 (22.50)
≥3	1,040 (75.50)	528 (73.60)	512 (77.50)
BMI (kg/m^2)*			
<30.0	1,302 (94.50)	699 (97.50)	603 (91.20)
≥30.0	76 (5.50)	18 (2.50)	58 (8.80)
WC (cm)*			
≤88 in female or ≤102 in male	1,204 (87.40)	645 (90.00)	559 (84.60)
>88 in female or >102 in male	174 (12.60)	72 (10.00)	102 (15.40)
Triglyceride (mg/dl)*			
<150	891 (64.70)	496 (69.20)	395 (36.90)
≥150	487 (35.30)	221 (30.80)	417 (63.10)
Hypercholesterolemia (Total cholesterol ≥240 mg/dl or taking medication)			
No	541 (39.90)	297 (41.40)	244 (36.90)
Yes	839 (60.70)	420 (58.60)	417 (63.10)
Periodontitis severity (Page and Eke, 2007)*			
No/mild	157 (11.40)	101 (14.10)	56 (8.50)
Moderate	740 (53.70)	392 (54.70)	348 (52.60)
Severe	481 (34.90)	224 (31.20)	257 (38.90)

* P <0.005., † Occasional drinker = less than once per month.

Moreover, the proportion of participants who had hypertension was assessed according to periodontitis severity (Figure 1). The no/mild periodontitis group had the highest proportion of normotensive individuals and the

lowest proportion of hypertensive individuals. In contrast, the severe periodontitis groups had the lowest proportion of normotensive individuals and the highest proportion of hypertensive individuals. The differences between groups were statistically significant (P <0.005).

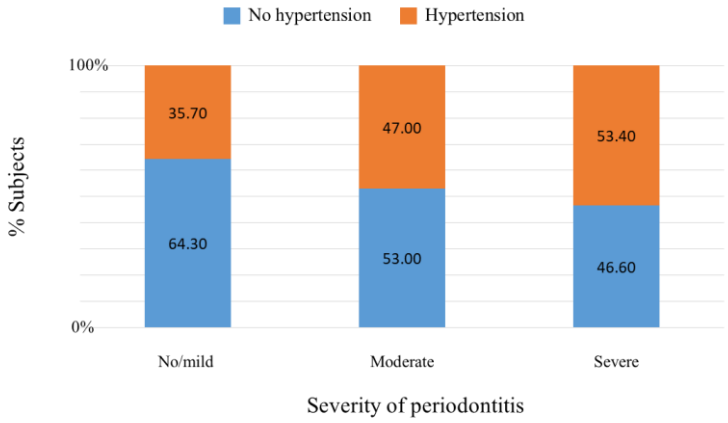

Figure 1 Proportion of subjects with diagnosis of hypertension according to the severity of periodontitis

Logistic regression analysis was used to assess the magnitude of associations between periodontitis severity and hypertension (Table 2). In univariable analysis, both moderate and severe periodontitis groups were associated with an increasing risk of hypertension, with odds ratios of 1.60 (95% CI; 1.12-2.29, P = 0.010) and 2.07 (95% CI; 1.43-3.00, P = 0.001), respectively. After adjustment for potential confounding factors, there was a significantly increasing risk of hypertension in the severe periodontitis group, with an odds ratio of 1.55 (95% CI; 1.03-2.33, P = 0.035). For the moderate periodontitis group, there was a trend for an increased risk of hypertension, with an odds ratio of 1.35 (95% CI; 0.92-1.98); however, the association did not reach statistical significance (P = 0.123).

Table 2 Logistic regression analysis of the association between periodontitis severity and hypertension

Variables	**Crude OR (95% CI)**	***P* value**	**Adjusted OR (95% CI)**	***P* value**
Moderate periodontitis	1.60 (1.12-2.29)	0.010	1.35 (0.92 - 1.98)	0.123
Severe periodontitis	2.07 (1.43-3.00)	0.001	1.55 (1.03 - 2.33)	0.035
Age ≥60 years	1.53 (1.23-1.89)	0.001	1.51 (1.20 - 1.90)	0.001
Male	2.19 (1.69-2.85)	0.001	2.75 (1.85 - 4.10)	0.001
≤High school	1.78 (1.39-2.30)	0.001	1.53 (1.17 - 1.20)	0.002
Diabetes mellitus	1.87 (1.39-2.52)	0.001	1.45 (1.06 - 1.98)	0.020
Smoking status				
Former smoker	1.49 (1.19-1.88)	0.001	0.86 (0.65 - 1.16)	0.339
Current smoker	0.86 (0.62-1.20)	0.378	0.52 (0.35 - 0.76)	0.030

Variables	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Alcohol consumption	1.13 (0.84-1.51)	0.424	0.78 (0.55 - 1.11)	0.169
Former drinker	1.71 (1.33-2.20)	0.001	1.15 (0.82 - 1.61)	0.412
Current/occasional drinker				
Exercise 1-2 sessions/week	0.81 (0.64-1.04)	0.100	0.88 (0.67 -1.14)	0.333
BMI ≥30 kg/m^2	3.74 (2.18-6.41)	0.001	2.59 (1.40-4.77)	0.002
WC >88 cm (F) or >102 cm (M)*	1.64 (1.18-2.26)	0.003	1.85 (1.22 -2.80)	0.004
Triglyceride ≥150 mg/dl	1.51 (1.21-1.89)	0.001	1.30 (1.03 - 1.66)	0.030
Hypercholesterolemia (Total cholesterol ≥240 mg/dl or taking medication)	1.21 (0.97-1.50)	0.087	1.26 (1.00 - 1.60)	0.051

* F = Female, M = Male.

5. Discussion

The results from the present study demonstrated, for the first time, that severe periodontitis was associated with an increasing risk of hypertension among this group of Thai adults. The association remained significant after controlling potential confounders including age, gender, educational level, diabetes mellitus, smoking status, alcohol consumption, frequency of exercise, obesity, hypertriglyceridemia, and hypercholesterolemia.

Epidemiological studies have reported the inconsistent results regarding the association between periodontitis and hypertension. Most studies supported positively between these two diseases (Iwashima et al., 2014, Rivas-Tumanyan et al., 2013) whereas the others did not (Nesse et al., 2010, Ollikainen et al., 2014). These may be due to demographic variables such as age, gender, and population size, or difference in methodology and research design among studies. In Asian region, limited large scale population was conducted for the association study (Choi et al., 2015, Kawabata et al., 2016) while the majority from western countries (Chrysanthakopoulos and Chrysanthakopoulos, 2016, Darnaud et al., 2015, Holmlund, Holm, and Lind, 2006, Rivas-Tumanyan et al., 2012, Tsakos et al., 2010). Moreover, there were differences in diagnostic criteria of periodontitis and hypertension among studies. Regarding a variety of periodontal criteria, the use of CPI (Choi et al., 2015, Kawabata et al., 2016), CDC/AAP case definition (Rivas-Tumanyan et al., 2013, Tsakos et al., 2010), a percentage of sites of PD and/or CAL (Chrysanthakopoulos and Chrysanthakopoulos, 2016, Holmlund, Holm, and Lind, 2006), or other periodontal indices (Darnaud et al., 2015) was observed. Regarding hypertension criteria, the use of self-reporting (Chrysanthakopoulos and Chrysanthakopoulos, 2016, Rivas-Tumanyan et al., 2012), blood pressure measurement (Kawabata et al., 2016), and/or current prescribed antihypertensive medication (Choi et al., 2015, Tsakos et al., 2010) were observed.

The results of this study revealed the significant association between severe periodontitis and hypertension which confirmed the previous study in Puerto Rico (Rivas-Tumanyan et al., 2013). It should be noted that both used

the same periodontal criteria (CDC/AAP), shared similar population characteristics (all adults and predominant males), and used similar confounding factors (age, sex, smoking, and alcohol consumption). Interestingly, their study comprised small-scale data, 128 participants, and they found high OR of 4.20 (95% CI; 1.28-13.80, P <0.05) as compared to this study which incorporated large-scale data. 1,378 participants with the OR of 1.55 (95% CI; 1.03-2.33, P = 0.035). Meanwhile, a much larger-scale study of the Third National Health and Nutrition Examination Survey (approximately 14,000 participants), which used the same periodontal diagnosis criteria, did not report a significant association between severe periodontitis and hypertension (OR = 1.2, 95% CI; 0.7-2.1) (Tsakos et al., 2010). They included many adjusting confounders such as age, sex, ethnicity, CRP, creatinine, Na^+/K^+ ratio, BMI, alcohol consumption, smoking, seven chronic conditions, education, and poverty-income ratio. Hence, the analysis of the association may be obscured by the number of their confounders.

In relation to strengths of this study, the sample size of Thai adults was large enough to allow meaningful analyses with good statistical power. Second, periodontal status was clinically evaluated through PD and CAL measurement, and the severity was precisely classified by CDC/AAP case definition. This classification defines the disease by determining the thresholds of PD and CAL and the number of affected sites which provide suitable estimates of the prevalence of periodontitis (Page and Eke, 2007). There are only a few studies which used these criteria for periodontal status (Rivas-Tumanyan et al., 2013, Tsakos et al., 2010). Third, regarding the diagnosis of hypertension, this study classified the participants by blood pressure measurement, and currently prescribed antihypertensive medication, which are required in studying hypertension prevalence (Ong et al., 2007). Several studies used these hypertension diagnosis criteria (Choi et al., 2015, Iwashima et al., 2014, Rivas-Tumanyan et al., 2013, Tsakos et al., 2010). The questionnaire or self-reporting method may have resulted in under-diagnosis of hypertension and underestimation of the magnitude of the association between periodontitis and hypertension (Martin-Cabezas et al., 2016). However, this study also has limitation. The cross-sectional design couldn't establish the clear direction of the association between periodontitis and hypertension. The prospective design is needed to confirm the true relationship between these two diseases.

6. Conclusion

Severe periodontitis was independently associated with an increasing risk of hypertension in this group of Thai adults. The findings, if confirmed in further prospective studies, suggest that regular periodontal check-up and maintaining healthy periodontal status may help reduce the risk of hypertension, which is connected to many serious cardiovascular conditions.

7. Acknowledgment

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