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Periodontitis Prevalence and Severity in Indonesians With Type 2 Diabetes

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Background: The prevalence of diabetes mellitus type 2 (DM2) in Indonesia is high and still rising. Periodontitis is associated with DM2. No study has investigated this association in Indonesia, nor has any study investigated this association using a variety of methods to operationalize periodontitis. Therefore this study compared prevalence and severity of periodontitis in DM2 patients to healthy controls, using different methods to operationalize periodontitis.

Methods: 78 DM2 and 76 healthy subjects underwent a full mouth periodontal screening assessing probing pocket depth, gingival recession, plaque index and bleeding on probing. Using these measurements, periodontitis prevalence and severity was operationalized in various ways. Differences in periodontitis prevalence and severity between DM2 and healthy subjects were analyzed using univariate analyses. In regression analyses, periodontitis prevalence and severity were predicted on the basis of DM2 presence, controlling for confounders and effect modification.

Results: Prevalence of periodontitis was significantly higher in DM2 compared to healthy subjects, showing odds ratios of 5.0 and 6.1. Likewise, periodontitis severity was significantly higher in DM2 subjects.

Conclusion: Indonesian DM2 subjects had more prevalent and more severe periodontitis than Indonesian healthy subjects, independent of confounding factors or the methods used to operationalize periodontitis.

KEYWORDS:

Periodontitis (MeSH), Periodontal Inflamed Surface Area, PISA, Diabetes Mellitus (MeSH)

Diabetes mellitus (DM) is a chronic disease characterized by dysregulation of carbohydrate, protein and lipid metabolism. An elevation of blood glucose level (hyperglycemia) is the primary feature of DM and results from either a defect in insulin secretion by pancreatic beta cells, a decrease in insulin sensitivity, or a combination of both. The most common form of DM is DM type 2 (DM2), which accounts for 85% of all

diabetes patients. [1] The estimated world wide prevalence of DM is 220.5 million, or 2.8 % of the world's population. DM currently is the twelfth leading cause of death in the world. The prevalence is estimated to rise up to 4.4%, putting DM in the top ten leading causes of death by 2030. [2, 3] With the increasing prevalence of DM, this already vast and world wide epidemic will increasingly pose serious problems to public health. These problems mostly arise from the complications associated with DM like myocardial infarction, cerebrovascular disease, retinopathy, nephropathy and neuropathy. [4]

Periodontitis is more prevalent and severe among patients with DM2 than among healthy controls. [5-7] Thus, DM2 may initiate or deteriorate periodontitis. However, the reverse could also be true, i.e. periodontitis may initiate or deteriorate DM2. The strongest support for this comes from studies showing that treatment of periodontitis improves glycaemic control in DM2 patients. [8-13] Thus, there is an association between DM2 and periodontitis that appears to be bilateral causal in nature (i.e. one causes or deteriorates the other and vice-versa).

The strength of associations between periodontitis and DM2 appears to differ geographically. Studies performed in different locations, i.e. performed among different ethnic groups, show different associations between periodontitis and DM2. [5, 14-17] These differences in the strength of associations may, apart from differences in study design and data analysis, be based on genetic, dietary, cultural and other differences between ethnic groups. [18] Therefore, findings among one ethnic population cannot automatically be generalized to another ethnic population.

South East Asia hosts approximately 10% of the world's current population. With 240 million inhabitants, Indonesia is the 4th most populous country in the world. The prevalence of DM in South East Asia is 5.3%. [19] In Indonesia, the prevalence of DM in 2008 was 5.7%, [20] putting Indonesia in the top ten of countries with the highest number of DM patients in the world. By the year 2030, the estimated number of patients with DM in Indonesia will be over 20 million (approximately 10% of the population). [2] With this high and rising prevalence of DM2 in Indonesia, periodontitis prevalence and severity may also rise. To the best of our knowledge, only three studies report on the association between periodontitis and DM2 in South East Asia; one in Thailand, [21] one is Singapore, [22] and one in Indonesia. [23] Unfortunately, in the latter study, the way in which periodontitis was measured and defined remains unclear. Neither did this study make a distinction between DM type 1 and DM type 2 patients, leaving many questions unanswered.

Another question that remains unanswered is the influence of using a particular method to operationalize periodontitis on the strength of an association between periodontitis and DM2. The use of different methods to operationalize periodontitis prevalence and severity may influence not only the strength of the associations between a given disease and periodontitis, but may even influence whether an association is observed at all. For example, in research linking periodontitis to preterm low birth weight, 13 different methods have been used to operationalize periodontitis. Depending on the method used, either an association [24, 25] or no association [26] between periodontitis and preterm low birth weight was observed. The same may be true for periodontitis and DM2.

Therefore, this study assessed prevalence and severity of periodontitis among DM2 patients in Indonesia, using multiple, commonly used methods to operationalize both periodontitis prevalence and severity.

SUBJECTS AND METHODS

DM2 patients were recruited at three different sites, namely 1) Internal Medicine Dept. of the Dr. Sardjito Hospital, 2) Prof. Soedomo Dental Hospital, Faculty of Dentistry, Gadjah Mada University and 3) Diabetes Center of Jogjakarta International Hospital, Indonesia. DM2 patients were diagnosed according to World Health Organization criteria: fasting blood glucose level ≥126 mg/dl and/or a postprandial blood glucose level ≥200 mg/dl. [27] Healthy controls were recruited in Prof. Soedomo Dental Hospital. Inclusion criteria for all subjects in this study were an age 18 years or over, and having ≥8 remaining teeth. This study was approved by the Ethical Committee for Research of the Medical Faculty of Gadjah Mada University, Yogjakarta, Indonesia and was conducted from July 2008 until February 2009.

To assess whether periodontitis prevalence and severity differed between DM2 patients and healthy controls, 78 DM2 patients and 76 healthy controls, who gave informed consent, underwent a full mouth periodontal examination. Full mouth periodontal probing pocket depth (PPD), gingival recession, plaque score and bleeding on probing (BOP) measurements were performed on all teeth, on six sites per tooth. All permanent fully erupted teeth were examined with a manual periodontal colour coded standard probe.‖ Measurements were made in millimetres and were rounded to the nearest whole millimetre. CAL was defined as the distance from the cemento enamel junction (CEJ) to the bottom of the pocket/sulcus, and calculated as the mathematical sum of the PPD and gingival recession measurements [28]. BOP was recorded as either present or absent within 30 seconds after probing at 6 sites per tooth. The number of missing teeth was also recorded. Plaque score was defined as being present or absent at 6 points on each tooth. [29]

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Periodontitis prevalence, extent and severity were operationalized using a variety of methods, all of which are currently used in literature studying the association between periodontitis and other diseases. All methods used to operationalize periodontitis prevalence and severity were calculated using conventional clinical measurements obtained during the full mouth periodontal examination. Periodontitis prevalence was operationalized by using two diagnostic threshold values; 1) having one site with PPD ≥4 mm and CAL ≥3 mm, [26] and 2) having one site with PPD ≥5 mm and CAL ≥2 mm. [30] The following methods to operationalize periodontitis extent and severity were calculated using a freely accessible online spreadsheet.¶ The number of sites with PPD ≥4, ≥5 and ≥6 mm, the numbers of sites with CAL ≥3, ≥4, ≥5 and ≥6 mm, mean PPD, mean CAL and the percentage of sites with BOP. [26]

Additionally, two recently introduced measures of periodontitis severity, the Periodontal Epithelial Surface Area (PESA) and the Periodontal Inflamed Surface Area (PISA) [31] were both calculated using another freely downloadable spreadsheet.¶ PESA reflects the surface area of *all* pocket epithelium in square millimetres, whereas PISA reflects the surface area of *bleeding* pocket epithelium in square millimetres. PESA and

¶ (www.parsprototo.info). Microsoft Excel 2003 spreadsheet for Windows

PISA are calculated using conventional CAL, gingival recession and BOP measurements. PISA quantifies the amount of inflamed periodontal tissue and it is suggested that PISA thereby quantifies the inflammatory burden posed by periodontitis.

Furthermore, all participants completed a validated general health assessment questionnaire, [32-34] to check for other medical conditions that might be a risk factor for periodontitis. The original questionnaire was translated from English into Indonesian, a reverse translation to English was made to check for potential differences. No substantial differences were found. Additionally, ethnicity[35], Body Mass Index (BMI)[36], dental plaque, age, gender, smoking (pack years), and Socio Economic Status (SES, operationalized using level of education) were recorded for each participant, since these are potential determinants of periodontitis. [37]

To assure that healthy controls were not undiagnosed diabetes patients, all participants underwent venepuncture to obtain a blood sample. Blood glucose and glycosilated (glycated) haemoglobin (HbA1c) were determined for both DM2 patient and healthy controls. Controls with a blood HbA1c level of ≥6.5% were excluded from the analysis, to exclude latent DM2 status.

STATISTICAL ANALYSIS

Differences in periodontitis prevalence, extent and severity between DM2 and healthy subjects were analyzed first using univariate analyses (i.e. the independent sample t-test or Chi-square test as appropriate). Likewise, differences in potential predictors of periodontitis (namely: age, gender, BMI, SES, smoking, plaque score, number of teeth, ethnicity and other medical conditions) between DM2 patients and healthy controls were tested for significance using univariate analyses. In case both periodontitis prevalence, extent and severity and any of the potential predictors of periodontitis differed significantly between DM2 patients and healthy controls, the predictors of periodontitis other than DM2 might act as confounders or effect modifiers.

Since periodontitis severity was operationalized as several interval variables (i.e. PISA, or number of sites with PPD ≥4mm), linear regression analyses (method: backward stepwise) were performed to predict periodontitis extent and severity on the basis of DM2 presence and the other potential predictors (age, gender, BMI, SES, smoking, plaque score, number of teeth, ethnicity and other medical conditions). To facilitate clinical interpretation of presented analyses, age was centered to it's mean (age - 53.86). Since periodontitis prevalence was operationalized as two dichotomous variables, logistic regression analyses were performed in a similar way. Odds ratios and 95% confidence intervals were calculated using these logistic regression analyses. Interaction between different predictors of periodontitis was explored. Statistics were calculated using SPSS 16.0.

RESULTS

Of the original 76 healthy controls, 11 subjects were excluded because of HbA1c levels >6.5%, leaving 65 "true" healthy controls and 78 DM2 patients (table 1). The prevalence of periodontitis in DM2 subjects was significantly higher than healthy controls, regardless of the definition used (table 2). The extend and severity of periodontitis was

also significantly higher in participants with DM2 when compared to controls, again independent of the method used to operationalize periodontitis severity (table 3).

Age and hypertension were the only potential predictors of periodontitis prevalence and severity that differed significantly between DM2 and healthy subjects in the univariate analysis (table 1). In the multiple linear regression analyses, controlling for age and hypertension as potential confounders, DM2 remained a significant predictor of all measures of periodontitis severity (table 4). Age was an additional predictor of periodontitis severity, together with DM2, whenever periodontitis severity was operationalized using CAL. Age did not modify the effect of DM2 on periodontitis severity. Hypertension was not a predictor of periodontitis prevalence or severity.

DISCUSSION

This study revealed that Indonesian DM2 subjects had significantly increased prevalence, extent and severity of periodontitis compared to healthy Indonesian subjects. Moreover, the increased prevalence, extent and severity of periodontitis among Indonesian DM2 subjects were independent of the methods used to operationalize periodontitis. Furthermore, the increased prevalence, extent and severity of periodontitis appeared independent of confounding factors (i.e.: age, gender, smoking, BMI, ethnicity, SES and other medical conditions).

Age was an additional predictor of all methods that used CAL to operationalize periodontitis severity. This could have been expected since CAL reflects the accumulation of damage sustained by the periodontium over time. In other words, with increasing age, CAL increases. Nevertheless, DM2 remained a significant predictor of every method used to operationalize periodontitis prevalence and severity.

Prior to the study we did not perform a formal sample size calculation although this study is the second on periodontitis and DM2 in Indonesia. From the first study on this topic it is not clear how periodontitis was measured and defined.[23] Also no distinction was made between DM type 1 and DM2 patients in that study. In a post-hoc power analysis it appeared that we had a power of .92 to find a difference in prevalence of periodontitis of 21%, between controls (n=65, prevalence=71%) and DM2 patients (n=78, prevalence=91%). A sample of 50 DM2 patients and 50 controls would have been enough to detect this difference (Power: 0.80).

A limitation of this study is that we did not use a population based sampling scheme to select DM2 patients. However, Indonesian DM2 patients regularly visit hospitals to make use of the lab facilities. Thus, selection of DM2 patients at two hospitals does not mean a subset of patients with more severe DM2 patients was selected. Rather, these DM2 patients may be thought to represent a sample of diagnosed and treated Indonesian DM2 patients. However, 'true' DM2 associated increased periodontitis risk may be underestimated, since a substantial portion of DM2 patients often goes undiagnosed. Likely, these patients have worse blood sugar control and consequently worse periodontal status. On the other hand, the DM2 patients that were recruited from a dental hospital may have visited this hospital for periodontitis, overestimating DM2 associated periodontitis prevalence in this subgroup. Likewise, since controls were all selected from the same dental hospital, the prevalence of periodontitis in controls may also have been

overestimated. Since the prevalence in both groups might be overestimated, the overall effect on calculated DM2 associated periodontitis risk may have been small. Finally, selection of healthy controls at a dental hospital may not be representative of the general Indonesian population without DM2. Thus, although some threats to the generalizability of our results remain, the increased DM2 associated periodontitis risk does appear to have sufficient generalizability and might sooner have been underestimated rather than overestimated.

The finding that DM2 subjects have an increased prevalence and severity of periodontitis is in line with other studies. [30, 38, 39] A major achievement of current study is that a large variety of methods to operationalize periodontitis prevalence and severity has been applied, and that the conclusions that could be drawn from the results were irrespective of the measures used. This indicates that this association is robust. As the prevalence of DM2 in Indonesia, and South East Asia, is already high and is predicted to rise further, the prevalence and severity of periodontitis may also rise. Due the vast number of people living in Indonesia, and South East Asia, and the proposed bilateral association between DM2 and periodontitis, this will increasingly pose serious problems to public health.

Two main mechanisms are thought to underlie the proposed bilateral association between DM2 and periodontitis. One underlying mechanism is that DM2 may alter local immune responses within periodontal tissue. DM2 may result in small vessel damage within the periodontium, resulting in poor nutrient delivery, decreased oxygen diffusion and decreased elimination of metabolic waste products. [40] Furthermore, hyperglycaemia alters collagen metabolism which predisposes to impaired wound healing. In general, hyperglycemia results in the formation of proteins known as Advanced Glycation End products (AGEs). AGEs may be associated with a state of enhanced oxidative stress, thereby accelerating tissue injury. AGEs also function as a chemotactic for monocytes, thereby magnifying the inflammatory response, delaying wound healing and tissue repair and inducing connective-tissue damage and bone resorption. Finally, hyperglycaemia and the imbalance in lipid metabolism impair neutrophil and monocyte functioning. [41, 42-44] All of these factors may contribute to DM2 predisposing to periodontitis.

The second underlying mechanism of the association between DM2 and periodontitis is that periodontitis may play a role in initiating, or exacerbating DM2. [7, 43, 45] Periodontitis poses an inflammatory burden consisting of increased serum levels of inflammatory mediators, like C-reactive protein and Interleukin-6. [46] This inflammatory burden in turn leads to deteriorating blood glucose control in DM2 patients. [43] The higher the amount of inflamed periodontal tissue, the higher the inflammatory burden, and the poorer blood glucose control in DM2 patients may be thought to be.

PISA quantifies the amount of inflamed periodontal tissue (representing it as the surface area of inflamed periodontal epithelium in mm^2), and it is suggested that PISA thereby quantifies the inflammatory burden posed by periodontitis. [31] It was shown that there is indeed a dose-relationship between PISA and HbA1c in DM2 patients in the Dutch Caribbean. [47] Likewise, the present study finding of a significantly higher PISA among DM2 subjects, may mean that periodontitis is a risk factor for poor glucose control. Treating periodontitis might improve blood glucose control, [8-13] and prevention

and treatment of periodontitis in DM2 patients might contribute to better general health in DM2 patients. [48, 49]

In conclusion, this study shows that periodontitis prevalence is significantly higher in a group of Indonesian DM2 patients compared to a group of healthy Indonesians. Furthermore, Indonesian DM2 subjects have more extended and more severe periodontitis than healthy Indonesian subjects. Given the already high and increasing prevalence of DM2 in Indonesia, DM2 patients should be screened for periodontitis and oral (preventive) health care should become part of the regular care provided to Indonesian DM2 patients. Given the proposed bilateral association between DM2 and periodontitis, such care may contribute to better oral and overall health.

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REFERENCES

1. Mealy B. Diabetes mellitus. In: Greenberg MS, Glick M, eds. *Burket's Oral Medicine Diagnosis and Treatment*, 10ed. New York: BC. Decker Inc; 2003:563-577.

2. Wild S, Roglic K, Green A, Sicree R, King H. Global prevalence of diabetes. Estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27:1047-1053.

3. WHO. The Global Burden of Disease 2004 Update. Available at: http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html. Accessed March 25, 2009.

4. Zimmet P. Preventing diabetic complications: Primary care perspective. *Diabetes Res Clin Pract* 2009; 84: 107-116.

5. Campus G, Salem A, Uzzau S, Baldoni E, Tonolo G. Diabetes and periodontal disease: a case-control study. *J Periodontol* 2005; 76: 418–425.

6. Jansson H, Lindholm E, Lindh C, Groop L, Bratthall G. Type 2 diabetes and risk for periodontal disease: a role for dental health awareness. *J Clin Periodontol* 2006; 33: 408-414.

7. Taylor GW, Borgnakke WS. Periodontal disease: associations with diabetes, glycemic control and complications. *Oral Dis* 2008;14:191-203.

8. Grossi SG. Treatment of periodontal disease and control of diabetes: an assessment of the evidence and need for future research. *Ann Periodontol* 2001; 6: 138-145.

9. Taylor GW. The effects of periodontal treatment on diabetes. *J Am Dent Assoc* 2003;134: 41S-48S.

10. Kiran M, Arpak N, Unsal E, Erdogan MF. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. *J Clin Periodontol* 2005; 32: 266-272.

11. Faria-Almeida R, Navarro A, Bascones A. Clinical and metabolic changes after conventional treatment of type 2 diabetic patients with chronic periodontitis. *J Periodontol* 2006; 77: 591-598.

12. Darre L, Vergnes JN, Gourdy P, Sixou M. Efficacy of periodontal treatment on glycaemic control in diabetic patients: A meta analysis of international studies. *Diabetes Metab* 2008; 34: 497-506.

13. O'Connell PAA, Taba Jr M, Nomizo A, et al. Effect of periodontal therapy on glycemic control and inflammatory markers. *J Periodontol 2008*; 79: 774-783.

14. Lu HK, Yang PC. Cross-sectional analysis of different variables of patients with non-insulin dependent diabetes and their periodontal status. *Int J Periodontics Restorative Dent* 2004; 24: 71–79.

15. Mansour AA, Abd-Al-Sada N. Periodontal disease among diabetics in Iraq. Med Gen Med 2005; 7(2) http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=16369228. accessed March 30, 2009.

16. Novak MJ, Potter RM, Blodgett J, Ebersole JL. Periodontal disease in Hispanic Americans with type 2 diabetes. *J Periodontol* 2008; 79: 629-636.

17. Wang TT, Chen TH, Wang PE,et al. A Population-based study on the association between type 2 diabetes and periodontal disease in 12.123 middle-aged Taiwanese (KCIS No.21). *J Clin Periodontol* 2009;36: 372-379.

18. Bhopal R, Rankin J. Concept and terminology in ethnicity, race and health: be aware of the ongoing debate. *Br Dent J* 1999; 186: 483-484.

19. Procopiou M, Philippe J. The metabolic syndrome and type 2 diabetes: Epidemiological figures and country specificities. *Cerebrovasc Dis* 2005; 20: 2-8.

20. Ministry of Health Republic of Indonesia. The prevalence of Diabetes mellitus in Indonesia increase up to 21.3 millons [in Indonesia] available at: www.depkes.go.id. Accessed November 30, 2009.

21. Torrungruang K, Tamsailom S, Rojanasomsith K, et al. Risk indicators of periodontal disease in older Thai adults. *J Periodontol* 2005; 76: 558-565.

22. Lim LP, Tay FBK, Sum CF, Thai AC. Relationship between markers of metabolic control and inflammation on severity of periodontal disease in patients with diabetes mellitus. *J Clin Periodontol* 2007; 34: 118-123.

23. Md Ayu Lely S, Indirawati T. The effect of controlled blood glucose on degree of tooth mobility of diabetes patients in Persahabatan hospital of Jakarta [in Indonesian]. Media Litbang kesehatan 2004; XIV, 38-43.

24. Scannapieco FA, Bush RB, Paju S. Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review. *Ann Periodontol* 2003;8: 70–78.

25. Khader YS, Ta'ani Q. Periodontal diseases and the risk of preterm birth and low birth weight: a meta-analysis. *J Periodontol* 2005; 76: 161–165.

26. Vettore MV, Leal M, Leao AT, Da Silva AM, Lamarca GA, Sheiham A. The Relationship between periodontitis and preterm low birth weight. *J Dent Res* 2008; 87: 73–78.

27. Alberti KGMM, Zimmet PZ. Definition, Diagnosis and classification of Diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional Report of a WHO consultation. *Diabet Med* 1998; 15:539-553.

28. Armitage GC. The complete periodontal examination. *Periodontol 2000* 2004; 34: 22-33.

29. Mercado FB, Marshall RI, Kletsov AC, Bartold PM. Relationship Between Rheumatoid Arthritis and Periodontitis. *J Periodontol* 2001;72:779-87

30. Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. *Ann Periodontol* 2001; 6: 91-98.

31. Nesse W, Abbas F, Van der Ploeg I, Spijkervet FKL, Dijkstra P U, Vissink A. Periodontal inflamed surface area: quantifying inflammatory burden. *J Clin Periodontol* 2008;35: 668-673.

32. De Jong KJM, Oosting J, Peters GJM., Abraham-Inpijn L. Detecting medical problems in dentistry: A survey of 4.087 patients in the Netherlands. *Eur J Med* 1992;1: 23-29.

33. De Jong KJM, Abraham-Inpjin L, Vincker F, Declerk D. The validity of medical risk-related history for dental patients in Belgium. *Int Dent J* 1997; 47: 16-20.

34. De Jong KJM, Abraham-Inpijn L. A risk-related patients-administered medical questionnaire for dental practice. *Int Dent J* 1994; 44: 471-479.

35. Borrell LN, Taylor GW, Borgnakke WS, et al. Factors Influencing the effect of race on established periodontitis prevalence. *J Public Health Dent* 2003; 63: 20-29.

36. Kumar S, Dagli RJ, Dhanni C, Duraiwamy P. Relationship of body mass index with periodontal health status of green marble in Kesariyaji, India. *Braz Oral Res* 2009;23:365-369.

37. Borrell LN, Papapanou PN. Analytical epidemiology of periodontitis. *J Clin Periodontol* 2005;32: 132-158.

38. Tsai C, Hayes C, Taylor GW. Glycemic control of type 2 diabetes and severe periodontal disease in the US adult population. *Community Dent Oral Epidemiol* 2002; 30: 182–192.

39. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A. Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. *J Diabetes Complication* 2006; 20: 59-68.

40. Furukawa T, Wakai K, Yamanouchi K, et al. Associations of periodontal damage and tooth loss with atherogenic factors among patients with type 2 diabetes mellitus. *Intern Med* 2007; 46: 1359-1364.

41. Ryan ME, Carnu O, Kamer A. The Influence of diabetes on the periodontal tissue. *J Am Dent Assoc* 2003; 134: 34S-40S.

42. Mealy BL, Oates TW. Diabetes and periodontal diseases. *J Periodontol* 2006; 77: 1289-1303.

43. Soell M, Hassan M, Miliauskaite A, Haikel Y, Selimovic D. The Oral cavity of elderly patients in diabetic. *Diabetes Metab* 2007; 33: S10-S18.

44. Janket S J, Jones JA, Meurman JH, Baird AE, Van Dyke TE. Oral infection, hyperglycemia, and endothelial dysfunction. *Oral Surg Oral Med Oral Pathol Oral Rad Endod* 2008;105: 173-179.

45. Saito T, Shimazaki Y, Kiyohara Y, et al. The severity of periodontal disease is associated with development of glucose intolerance in non-diabetics: The Hiyasama Study. *J Dental Res* 2004; 83: 485-490.

46. D'Aiuto F, Parkar M, Andreou G, et al. Periodontitis and systemic inflammation: Control of the local infection is associated with a reduction in serum inflammatory markers. *J Dent Res* 2004; 83: 156-160.

47. Nesse W, Linde A, Abbas F, et al. Dose-response relationship between periodontal inflamed surface area and HbA1c in type 2 diabetics. *J Clin Periodontol* 2009;36: 295-300.

48. Saremi A, Nelson RG, Tulloch-Reid M, et al. Periodontal disease and mortality in type 2 diabetes. *Diabetes Care* 2005; 28: 27-32.

49. Shultis WA, Weil EJ, Looker HC, et al. Effect of periodontitis on overt nephropathy and end-stage renal disease in type 2 diabetes. *Diabetes Care* 2007; 30: 306-311.

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Table 1. Characteristics of healthy subjects and DM2 and potential determinants of periodontitis severity

Patient Characteristics	Controls (n=65)	DM2 (n=78)	Difference (95%CI)	*p* value
Age: mean (SD) yr	50.5(10.6)	56.7(9.4)	6.2 (2.8 to 9.5)	<0.001‡
Gender: n (%)				0.180*
Man	22(34%)	35(45%)		
Woman	43(66%)	43(55%)		
Smoking: n (%)	10(15%)	14(18%)		0.683*
Java origin: n (%)	60(92%)	73(94%)		0.765*
Education: n (%)				0.762*
Low	17(26%)	18(23%)		
Middle	26(40%)	29(37%)		
High	22(34%)	31(40%)		
BMI (SD) (kg/m^2)	24.6(3.9)	25.1(3.8)		0.460
Number of tooth (SD) (n)	24.5(5.5)	22.9(6.1)		0.112
Plaque score (SD) (%)	92.5(9.2)	90.8(7.6)		0.211
Medical conditions: n (%)†				
1. Hypertension	12 (18%)	26 (33%)	15% (0.3% to 29%)	<0.05*‡
2. Gastritis	4 (6%)	10 (13%)		0.182*
3. Anemia	2 (3%)	0 (0%)		0.119*
4. Angina Pectoris	0 (0%)	3 (4%)		0.110*

*Results of Chi-square test, other results are the results of the independent samples t test,

†Only diseases with a prevalence of at least 1% (i.e. 2 patients) were analyzed

‡statistically significant difference ($p \leq 0.05$) between DM2 and controls

95%CI: 95% Confidence Interval

BMI: Body Mass Index

DM2: Diabetes Mellitus type 2

Education: (low: elementary & junior school, middle: high school, high: university) HbA1c: Glycosilated/Glycated Hemoglobin

n: number of participants

SD: Standard Deviation

yr: year

Table 2. Differences in periodontitis prevalence between healthy subjects and DM2.

Periodontitis prevalence	Controls n=65	DM2 n=78	Difference (95%CI)	OR (95%CI)	*p* value†
PPD4&CAL3 (yes)	46(71%)	72(92%)	21%(9% to 32%)	5.0 (1.8 to 13.3)	0.001*
PPD5&CAL2 (yes)	20(31%)	57(73%)	42%(26% to 55%)	6.1 (2.9 to 12.6)	<0.001*

* Result of Chi-square test

†statistically significant difference ($p \leq 0.05$) between DM2 and controls

OR: Odds Ratio's were calculated using binary logistic regression analyses controlling for confounders

95%CI: 95% Confidence Interval

DM2: Diabetes Mellitus type 2

PPD: Probing Pocket Depth

CAL: Clinical Attachment Loss

Periodontitis severity	Controls (n=65) Mean (SD)	DM2 (n=78) Mean (SD)	Difference (95%CI)	*p* value*
PESA (mm^2)	863.0(259.4) mm^2	1190.5(1161.5) mm^2	327.5(58.3 to 596.6) mm^2	0.018
PISA (mm^2)	154.1(192.1) mm^2	429.4(964.9) mm^2	275.3(52.9 to 497.6) mm^2	0.016
Number of sites with:				
CAL > 3 mm	35.8(23.1) sites	63.5(29.9) sites	27.6(18.8 to 36.4) sites	<0.001
CAL > 4 mm	12.3(15.1) sites	37.1(27.2) sites	24.8(17.7 to 31.9) sites	<0.001
CAL > 5 mm	5.9(10.2) sites	22.9(21.4) sites	16.9(11.5 to 22.4) sites	<0.001
CAL > 6 mm	3.1(7.3) sites	13.7(16.2) sites	10.6(6.6 to 14.7) sites	<0.001
PPD > 4 mm	4.5(7.9) sites	16.6(21.2) sites	12.1(6.9 to 17.3) sites	<0.001
PPD > 5 mm	1.4(3.7) sites	7.7(12.5) sites	6.3 (3.4 to 9.2) sites	<0.001
PPD > 6 mm	0.8(2.3) sites	4.5(9.3) sites	3.7(1.5 to 5.9) sites	0.001
BOP (%)	14.2(13.3) %	24.9(16.1) %	10.7(5.8 to 15.5) %	<0.001
CAL mean (mm)	2.2(0.9) mm	3.1(1.3) mm	0.9(0.5 to 1.3) mm	<0.001
PPD mean (mm)	1.8(0.4) mm	2.2(0.6) mm	0.4(0.2 to 0.5) mm	<0.001

PPD4&CAL3: participants with one site exhibiting both PPD 4 mm & CAL 3 mm,

PPD5&CAL2: participants with one site exhibiting both PPD 5 mm & CAL 2 mm

Table 3. Differences in periodontitis severity between DM2 and healthy subjects

*statistically significant difference ($p \leq 0.05$) between DM2 and controls

95%CI: 95% Confidence Interval

BOP: Bleeding On Probing

CAL: Clinical Attachment Loss

DM2: Diabetes Mellitus type 2

PESA: Periodontal Epithelial Surface Area

PISA: Periodontal Inflamed Surface Area

PPD: Probing Pocket Depth

SD: Standard Deviation

Table 4. DM2 and age as statistical predictors of periodontitis extent and severity: Results of multiple linear regression analyses with periodontitis operationalized according to commonly used definitions

Dependent variable Model predictors	β Unstandardized	β Standardized	p-value of β (†)	R^2	95% CI of β
PESA				0.03	
DM2	327.49	0.18	<0.05		36.65 to 618.33
Constant	863.04		<0.001		648.25 to 1077.84
PISA				0.04	
DM2	275.29	0.19	<0.05		34.69 to 515.89
Constant	154.06		0.089		-23.63 to 331.76
BOP%				0.11	
DM2	10.65	0.34	<0.001		5.71 to 15.60
Constant	14.23		<0.001		10.58 to 17.89
*PPD > 4 mm				0.12	
DM2	12.10	0.34	<0.001		6.60 to 17.60
Constant	4.92		<0.05		0.43 to 8.56
*PPD > 5 mm				0.10	
DM2	6.30	0.31	<0.001		3.13 to 9.47
Constant	1.35		0.254		-0.98 to 3.69
*PPD > 6 mm				0.07	
DM2	3.70	0.26	0.002		1.36 to 6.03
Constant	0.75		0.388		-0.97 to 2.47
PPD mean				0.11	
DM2	0.37	0.33	<0.001		0.19 to 0.54
Constant	1.83		<0.001		1.70 to 1.96
*CAL > 3 mm				0.24	
DM2	24.25	0.40	<0.001		14.99 to 33.49
Age centered	0.54	0.19	0.017		0.10 to 0.98
Constant	37.7		<0.001		31.0 to 44.4
*CAL > 4mm DM2	20.85	0.41	<0.001	0.29	13.31 to 28.40
Age centered	0.64	0.26	0.001		0.28 to 1.00
Constant	14.5		<0.001		9.0 to 19.9
*CAL > 5 mm				0.25	
DM2	14.12	0.37	<0.001		8.31 to 19.94
Age centered	0.46	0.25	0.002		0.18 to 0.74
Constant	7.5		0.001		3.26 to 11.68
*CAL > 6 mm				0.19	
DM2	8.82	0.32	<0.001		4.42 to 13.22
Age centered	0.29	0.22	0.008		0.08 to 0.50
Constant	4.03		0.013		0.85 to 7.22
*CAL mean				0.21	
DM2	0.71	0.29	<0.001		0.33 to 1.09
Age centered	0.03	0.27	0.001		0.01 to 0.05
Constant	2.27		<0.001		2.00 to 2.54

* = Number of sites with

† a *p*-value of ≤0.05 was considered statistically significant

p = probability, *β*: unstandardized coefficient

95%CI: 95% Confidence Interval

Independent variables:

Age centered = Age- Mean age

Constant and

DM2: Diabetes Mellitus type 2

Dependent variables (periodontitis severity measures) are underlined:

BOP: Bleeding On Probing

Number of sites with CAL: Clinical Attachment Loss ≥3, ≥4, ≥5 & ≥6 mm

CAL mean

PESA: Periodontal Epithelial Surface Area

PISA: Periodontal Inflamed Surface Area

Number of sites with PPD: Probing Pocket Depth ≥4, ≥5 & ≥6 mm

PPD mean