Assessment of lipid profile in Saudi type 2 diabetic and non-diabetic periodontal patients

Dalal H. Al-Otaibi, BDS, MSc, Nadir A. Babay, MSc, PhD, Syed S. Habib, MBBS, FCPS, Khalid Almas, MSc, FDSRCS.

ABSTRACT

الأهداف: تقييم درجة/شدة أمراض اللثة و الأنسجة حول السنية عند السكريين من النموذج الثاني و غير السكريين، و دراسة مستوى الشحوم عند المرضى المصابين بالتهاب الأنسجة حول السنية السكريين من النموذج الثاني و غير السكريين، مقارنتاً بالأشخاص الأصحاء فمويا وجسدياً.

الطريقة: أُجريت هذه الدراسة في كلية طب الأسنان – جامعة الملك سعود بالرياض – المملكة العربية السعودية، في الفترة مابين فبراير 2003م وحتى يونيو 2004م. شملت الدراسة 90 مريضا تم تقسيمهم إلى ثلاث مجموعات متساوية، تكونت كل مجموعة من 30 عنصرا مع مراعاة تطابق العمر والجنس، شملت المجموعة الأولى العناصر الأصحاء فمويا وجسدياً، وشملت المجموعة الثانية مرضى التهاب اللثة والأنسجة حول السنية الأصحاء جسديا، وشكلت عناصر المجموعة الثالثة المرضى المصابين بأمراض اللثة والأنسجة حول السنية وداء السكري من النموذج الثاني. تم تحديد المعايير التالية عند بداية الدراسة وهي: اللويحة الجرثومية – النزف التالي للسبر – أعماق الجيوب (PPD) – ومستوى الارتباط السريري (CAL). كما تم أيضاً تحديد مستويات السكر وخضاب الدم الجلوكوزي ونسبة الكوليسترول والبوتينات الشحمية منخفضة الكثافة (LDL) والشحوم الثلاثية والبوتينات الشحمية عالية الكثافة.

النتائج: أظهرت النتائج ارتفاع واضح في معدل المعايير حول السنية (عمق الجيوب PPD - والارتباط السريري CAL) عند المرضى المصابين بأمراض اللثة والأنسجة حول السنية في السكريين مقارنة مع غير السكريين. كما تبين أيضاً أن مستويات الكوليسترول والبروتينات الشحمية منخفضة الكثافة والشحوم الثلاثية كانت مرتفعة بدرجة ملحوظة لدى مرضى التهاب اللثة والأنسجة حول السنية مع المقارنة بالأشخاص الأصحاء فمويا و جسديا (p<0.05).

خاتمة: تشير نتائج هذه الدراسة إلى أن مرضى السكري من النموذج الثاني معرضين لخطر الإصابة بالتهاب اللثة والأنسجة حول السنية أكثر من غير المصابين بالسكري. كما تؤكد أيضا على وجود علاقة بين مستويات الشحوم في الدم والإصابة بالتهاب اللثة والأنسجة و حول السنية. يمكن اعتبار ذلك كعلاقة رابطة بين الإصابة المزمنة بأمراض اللثة و الأنسجة حول السنية و داء السكري من النموذج الثاني.

Objectives: To study the extent of periodontal disease in diabetic and non-diabetic periodontitis patients, and to investigate the relationship of dyslipidemia and periodontal disease, in diabetic and non-diabetic periodontitis patients.

Methods: This is a cross-sectional study at the Department of Preventive Dental Sciences (College of Dentistry) and Department of Physiology (College of Medicine), King Saud University, Riyadh, Kingdom of Saudi Arabia, from February 2003 to June 2004. A total of 90 patients was recruited, and divided into 3 equal groups of 30 subjects, with age and gender matched, and divided as follows: group 1 (healthy group): periodontally and systemically healthy subjects, group 2 (periodontitis group): chronic periodontitis patients with no systemic disease, group 3 (diabetic group): chronic periodontitis patients with type 2 diabetes mellitus. Plaque index, bleeding on probing, probing pocket depth (PPD), and clinical attachment level (CAL) were measured at the time of initial examination. The glycated hemoglobin, total cholesterol, low density lipoprotein (LDL), triglyceride, high density lipoprotein were also measured.

Results: Periodontal parameters (PPD and CAL) were of significantly higher value in the diabetic patients, when compared to the periodontitis patients (p<0.05). The total cholesterol, LDL, and triglyceride were also found to be significantly higher among the periodontitis patients than the healthy subjects (p<0.05).

Conclusion: This study indicated that type 2 diabetic patients had a higher risk to develop advanced periodontal disease than the non-diabetic subjects. It also highlighted the association of dyslipidemia in periodontitis patients.

Saudi Med J 2008; Vol. 29 (5): 723-727

From the Department of Preventive Dental Sciences, College of Dentistry (Al-Otaibi, Babay), King Saud University, and Department of Physiology (Habib), College of Medicine and King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia and Division of Periodontology (Almas), University of Connecticut, United States of America.

Received 8th September 2007. Accepted 24th February 2008.

Address correspondence and reprint request to: Dr. Dalal H. Al-Otaibi, College of Dentistry, King Saud University, PO Box 285506, Riyadh 11323, Kingdom of Saudi Arabia. Tel. +966 (1) 4784524 Ext. 388. E-mail: dalal_dent@hotmail.com

Periodontitis and diabetes are 2 of the most common chronic diseases in humans. Periodontitis may produce a number of alterations in systemic health.[1,2] The association between periodontitis and acute cerebral infarction/stroke, coronary heart disease, and diabetes has been widely reported in the literature.[3-8] The prevalence, severity, and extent of periodontal disease are higher in patients with diabetes mellitus than in non-diabetic controls.[9,10] The importance of the total cholesterol and, in particular, the low density lipoprotein (LDL) is well established in the development of atherosclerosis.[11] Systemic exposure to infectious challenges such as bacterial lipopolysaccharide (LPS), can result in the release of inflammatory cytokines such as interleukin1 β (IL-l β), and tumor necrosis factor alpha (TNFα) that will alter the fat metabolism, and promote hyperlipidemia.[12] Poorly controlled type 2 diabetics with hyperlipidemia have shown more severe gingival inflammation, and a trend for increased levels of IL1-β.[13] When dyslipidemia and diabetes mellitus are considered, a great interest has been directed towards the investigation of plasma lipids, and related compounds in healthy and diseased individuals, during the last 2-3 decades. This is due to the well-established close association between abnormal lipid levels and the development of coronary heart disease, one of the major killer diseases of recent times.[14] Several lipoprotein abnormalities were described in diabetic subjects.[15] In both type 1 and type 2 diabetes, hyperglycemia is often accompanied by hyperlipidemia.[15,16] There is evidence to suggest that even low level chronic exposure to gram-negative microorganisms, or their LPS can manifest a similar response.[17] In localized oral infection such as periodontitis, the potential exists for chronic low-level systemic exposure to periodontal microorganisms/LPS leading to generalized alterations in lipid metabolism. It has also been speculated that triglycerides may provide a unifying link between diabetes mellitus, adult periodontitis, and coronary heart disease through heightened responsiveness to cell agonists, such as bacterial LPS.[18] Higher levels of total cholesterol, LDL, and triglycerides among periodontally disease subjects were reported.[19] The assessment of periodontal health and lipid status, among diabetic and periodontitis patients in the Saudi population is lacking. Therefore, this study was conducted, first to evaluate, and compare the periodontal condition between the diabetic patients and non-diabetic subjects with periodontitis. Secondly, to study and compare the lipid profile of periodontitis patients, with and without diabetes mellitus, with periodontally and systemically healthy subjects.

Methods. This cross sectional study was carried out at the Department of Preventive Dental Sciences (College of Dentistry) and Department of Physiology (College of Medicine), King Saud University, Riyadh, Kingdom of Saudi Arabia from February 2003 to June 2004. The Dental College Ethics Review Board approved this study, and informed written consent was obtained from each participant. A total of 90 patients were recruited, and divided into 3 groups of 30 subjects each, age and gender matched, and divided as follows: group 1: periodontally and systemically healthy subjects (control group), group 2 included chronic periodontitis patients with no systemic disease (periodontitis group), group 3 had chronic periodontitis patients with type 2 diabetes mellitus (diabetic group). Patients included were Saudi nationals with an age range from 35-55 years old. The periodontitis subjects were systematically healthy with no relevant medical history. The attachment loss was ≥2 mm, in at least 3 different sites in the periodontitis. The second group included patients with type 2 diabetes mellitus with no complications. Presence of at least 20 teeth was also taken as inclusion criteria. The exclusion criteria was any acute infection orally or systemically, diabetic ketoacidosis and non ketotic hyperosmolar diabetes, renal or thyroid disease, familial hypercholesterolemias, ischemic heart disease or myocardial infarction, drug ingestion including steroids, oral contraceptive and hypolipidemic drugs, pregnancy, periodontal treatment during the past 6 months, and any antimicrobial medication during the past 4 weeks. History regarding the medical status, diabetes mellitus, and oral hygiene habit was taken. The following periodontal parameters were recorded in a full mouth examination, excluding the third molars. The plaque index (PI) was assessed according to the criteria of the PI.[20] The gingival bleeding index (GBI) was used to indicate the presence or absence of bleeding on probing (BOP) within 10 seconds.[21] The probing pocket depth (PPD) was obtained using a Michigan "0" periodontal probe with Williams markings, measured at 6 sites around each tooth: the mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual and distolingual. The clinical attachment levels (CAL) was assessed at 4 sites around each tooth: the mesiobuccal, midbuccal, midlingual, and distolingual. The number of missing teeth was also recorded.

Blood sample analysis. A 15 ml blood sample was taken after 12-14 hours of overnight fasting for all the subjects, from the antecubital vein directly into a disposable plastic syringe. The measurements of fasting blood glucose level, total cholesterol, triglycerides, LDL, and high-density lipoprotein (HDL) were made using an autoanalyzer (Dimension RXL Clinical Chemistry System, Dade Behring, USA). Glycated hemoglobin (HbA1c) was assessed.

Statistical analysis. Descriptive statistics, means, and standard deviation of the means (SD) were calculated. The significance of the difference was determined using

the analysis of variance, ANOVA test, and Tukey's multiple comparison analysis with a level of significance at $p<0.05$. The data was analyzed using the SPSS 10 (SPSS Inc. Chicago, IL, USA) software system.

Results. All the diabetic patients in the study group were either on an oral hypoglycemic agent or on diet. The glycemic control of the diabetic group was assessed by the estimation of HbA1c. Most of the diabetic patients were well controlled with HbA1c less than or equal to 9%, and only 4 were moderately controlled with HbA1c between 9-11%. The mean PI percentage was significantly higher in group 3 and group 2, when compared to group 1. The percentage of BOP followed the same pattern as the PI. It was significantly higher in group 3 and group 2, when compared to group 1. The mean PPD was significantly higher in group 3 when compared to group 2. Group 1 had significantly less mean of PPD when compared to both group 2 and group 3. The mean CAL was significantly higher in group 3 when compared to group 2. In group 1, the CAL was significantly less than both group 2 and group 3 (**Table 1**). The total cholesterol level was significantly higher in group 2 and group 3, when compared to group 1. The mean triglyceride was significantly higher in group 3 and in group 2, when compared to group 1. The LDL mean was elevated significantly in the group 2 and group 3, when compared to group 1. The HDL mean was significantly higher in group 1 when compared to group 2 and group 3. These differences were statistically significant at $p<0.05$ (**Table 2**).

Table 1 - Periodontal parameters in control group (group 1), periodontitis group (group 2), and diabetic group (group 3).

Parameters	Group 1	Group 2	Group 3
PI (%)	51.94±34.20*	80.67±20.97	85.29±16.15
BOP (%)	20.42±10.72*	46.38±17.90	55.82±21.34
PPD (mm)	0.39±0.31*	2.03±0.79†	2.57±0.89‡
CAL (mm)	1.35±0.30*	2.75±0.56†	3.21±0.92‡

Data is expressed as mean±SD, * - significant at $p<0.05$ as compared to the periodontitis and the diabetic groups, † - significant at $p<0.05$ as compared to the healthy and the diabetic groups, ‡ - significant at $p<0.05$ as compared to the periodontitis and the control groups, PI - plaque index, BOP - bleeding on probing, PPD - probing pocket depth, CAL - clinical attachment level

Table 2 - Fasting blood glucose and lipid profile in control group (group 1), periodontitis group (group 2), and diabetic group (group 3).

Analysis (mmol/l)	Group 1	Group 2	Group 3
FBG	4.97±0.53	5.26±1.36	9.11±2.99*
Total cholesterol	4.70±0.73*	5.19±0.70	5.18±0.76
Triglyceride	1.23±0.47*	1.59±0.74	1.83±0.96
LDL	2.97±0.79*	3.56±0.72	3.44±0.55
HDL	1.09±0.32*	0.95±0.26	1.01±0.31

Data is expressed as mean±SD, * - significant at $p<0.05$ as compared to the other 2 groups, FBG - fast blood glucose, LDL - low-density lipoprotein, HDL - high-density lipoprotein.

Discussion. This study was conducted in a hospital based population to assess the periodontal condition of diabetic and non-diabetic Saudi subjects. The subjects were randomly selected from patients attending the dental clinic in the College of Dentistry at King Saud University, or those treated at the diabetic center at King Abdulaziz University Hospital. The PI was higher among the diabetic group when compared to the periodontitis with the difference not statistically significant. It was reported that diabetic patients had lower score of soft deposit when compared to non-diabetic.[22] It is possible that tissue alternations, and host resistance contributed to the outcome of periodontitis in diabetes more than the amount of plaque deposit.

The periodontitis and the diabetic group had a high percentage of BOP when compared to the control group, with the difference between the periodontitis and the diabetic groups were not statistically significant. This is in agreement with Ervasti[23] who found significantly high gingival bleeding in poorly controlled diabetics. The increase of bleeding in poorly controlled diabetics is due to the inflammation or the vascular changes in the gingiva, explaining the differences in the result according to Ervasti. The relation of the control of diabetes to the development of vascular changes has been studied by Tchobroutsky[24] who observed less vascular changes in well-controlled diabetes. This could explain why in the present study, the difference between the periodontitis and the diabetic groups was not significantly different, since most of the diabetic patients were well controlled.

The diabetic group showed significantly higher PPD and CAL when compared to the periodontitis group. This is in agreement with Emrich[10] et al who showed that diabetes increased the risk of developing destructive periodontal disease 3 fold than non-diabetics.[10,25,26] The same pattern of diabetic patients with high PPD, and CAL when compared to non-diabetic subjects was also observed in this investigation. The progression of periodontal disease is episodic, and severe periodontitis takes several months to develop.[27] It is more appropriate to consider long term rather than short term control, for better assessment of the periodontal disease among the diabetic patients using HbA1c score, which indicated the level of metabolic control of the previous 3 months. The total cholesterol, LDL, and triglycerides

were significantly higher in the diabetic group when compared to the control group. This is in agreement with Howard et al,[15] Kim et al,[16] and Merrin and Elkeles,[28] who reported that hyperglycemia is often accompanied by hyperlipidemia. Arisaka et al,[29] and Horrobin et al,[30] also reported that hyperlipidemia in diabetics is usually comprised of marked elevations of LDL, and triglycerides. In the Saudi population, several studies were conducted where the prevalence of diabetes mellitus was reported to be high.[31] Saudi diabetic patients had a high prevalence of lipid abnormalities including a significantly high level of cholesterol, and triglycerides.[32,33] Even though the diabetic patients in the present study were well and moderately controlled, they have shown a high lipid value. Hyperlipidemia persist even in subjects with good glycemic control as reported by Gary.[34] The elevations in serum lipids were more important, and much destructive than the glycemic state.[30,35,36]

Chronic periodontitis patients had shown a high level of total cholesterol, LDL, and triglyceride when compared to the control group in the present study. This is in agreement with Cutler et al,[13] and Losche et al[19] who reported a higher value of total cholesterol, LDL, and triglyceride in the periodontitis patients. They also stated that decreased metabolic control in type 2 diabetics might influence the increased serum triglycerides, and periodontal health.[36]

Dyslipidemia can be considered as a possible link between chronic periodontitis and diabetes mellitus. Periodic screening and early therapy for dyslipidemia among diabetic and periodontitis patients, to avoid advance systemic complications are recommended. Finally, within the limitations of this study, further studies of large populations including enough variation with respect to both the level of metabolic control, and the presence and severity of either diabetes mellitus or periodontal disease should be investigated.

References

1. Lim J, Pérez L, Guarda E, Fajuri A, Marchant E, Martínez A, et al. Periodontal disease among patients with acute coronary syndrome. ***Rev Med Chil*** 2005; 133: 183-189.
2. Otomo-Corgel J, Merin RL. Periodontal disease and systemic health-what you and your patients need to know. ***J Calif Dent Assoc*** 2002; 30: 307-311.
3. Losche W. Periodontitis and cardiovascular disease: periodontal treatment lowers plasma cholesterol. ***South Med J*** 2007; 100: 663-664.
4. Pussinen PJ, Alfthan G, Rissanen H, Reunanen A, Asikainen S, Knekt P. Antibodies to periodontal pathogens and stroke risk. ***Stroke*** 2004; 35: 2020-2023.
5. Bazile A, Bissada NF, Nair R, Siegel BP. Periodontal assessment of patients undergoing angioplasty for treatment of coronary artery disease. ***J Periodontol*** 2002; 73: 631-636.
6. Nakib SA, Pankow JS, Beck JD, Offenbacher S, Evans GW, Desvarieux M, et al. Periodontitis and coronary artery calcification: the Atherosclerosis Risk in Communities (ARIC) study. ***J Periodontol*** 2004; 75: 505-510.
7. Pucher J, Stewart J. Periodontal disease and diabetes mellitus. ***Curr Diab Rep*** 2004; 4: 46-50.
8. Saito T, Shimazaki Y, Kiyohara Y, Kato I, Kubo M, Iida M, et al. The severity of periodontal disease is associated with the development of glucose intolerance in non-diabetics: the Hisayama study. ***J Dent Res*** 2004; 83: 485-490.
9. Loe H. Periodontal disease. The sixth complication of diabetes mellitus. ***Diabetes Care*** 1993; 16: 329-334.
10. Emrich LJ, Shlossman M, Genco RJ. Periodontal disease in non-insulin-dependent diabetes mellitus. ***J Periodontol*** 1991; 62: 123-131.
11. Scannapieco FA, Bush RB, Paju S. Associations between periodontal disease and risk for atherosclerosis, cardiovascular disease, and stroke. A systematic review. ***Ann Periodontol*** 2003; 8: 38-53.
12. Engebretson S, Chertog R, Nichols A, Hey-Hadavi J, Celenti R, Grbic J. Plasma levels of tumour necrosis factor-alpha in patients with chronic periodontitis and type 2 diabetes. ***J Clin Periodontol*** 2007; 34: 18-24.
13. Cutler CW, Machen RL, Jotwani R, Iacopino AM. Heightened gingival inflammation and attachment loss in type 2 diabetics with hyperlipidemia. ***J Periodontol*** 1999; 70: 1313-1321.
14. Pyorala K, Laakso M, Uusitupa M. Diabetes and atherosclerosis: an epidemiologic view. ***Diabetes Metab Rev*** 1987; 3: 463-524.
15. Howard BV, Savage PJ, Bennion LJ, Bennett PH. Lipoprotein composition in diabetes mellitus. ***Atherosclerosis*** 1978; 30: 153-162.
16. Kim DK, Escalante DA, Garber AJ. Prevention of atherosclerosis in diabetes: emphasis on treatment for the abnormal lipoprotein metabolism of diabetes. ***Clin Ther*** 1993; 15: 766-778.
17. Lopes-Virella MF. Interactions between bacterial lipopolysaccharides and serum lipoproteins and their possible role in coronary heart disease. ***Eur Heart J*** 1993; Suppl 14: 118-124.
18. Salvi GE, Yalda B, Collins JG, Jones BH, Smith FW, Arnold RR, et al. Inflammatory mediator response as a potential risk marker for periodontal diseases in insulin-dependent diabetes mellitus patients. ***J Periodontol*** 1997; 68: 127-135.
19. Losche W, Karapetow F, Pohl A, Pohl C, Kocher T. Plasma lipid and blood glucose levels in patients with destructive periodontal disease. ***J Clin Periodontol*** 2000; 27: 537-541.
20. O'Leary TJ, Drake RB, Naylor JE. The plaque control record. ***J Periodontol*** 1972; 43: 38.
21. Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. ***Int Dent J*** 1975; 25: 229-235.
22. Cohen DW, Friedman LA, Shapiro J, Kyle GC, Franklin S. Diabetes mellitus and periodontal disease: two-year longitudinal observations. I. ***J Periodontol*** 1970; 41: 709-712.
23. Ervasti T, Knuuttila M, Pohjamo L, Haukipuro K. Relation between control of diabetes and gingival bleeding. ***J Periodontol*** 1985; 56: 154-157.
24. Tchobroutsky G. Relation of diabetic control of development of microvascular complications. ***Diabetologia*** 1978: 15: 143-152.
25. Grossi SG, Zambon JJ, Ho AW, Koch G, Dunford RG, Machtei EE, et. al. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. ***J Periodontol*** 1994; 65: 260-267.
26. Mealey BL, Oates TW; American Academy of Periodontology. Diabetes mellitus and periodontal diseases. ***J Periodontol*** 2006; 77: 1289-1303.

27. Buckley LA, Crowley MJ. A longitudinal study of untreated periodontal disease. ***J Clin Periodontol*** 1984: 11: 523-530.
28. Merrin PK, Elkeles RS. Treatment of diabetes: the effect on serum lipids and lipoproteins. ***Postgrad Med J*** 1991; 67: 931-937.
29. Arisaka M, Arisaka O, Yamashiro Y. Fatty acid and prostaglandin metabolism in children with diabetes mellitus. II. The effect of evening primrose oil supplementation on serum fatty acid and plasma prostaglandin levels. ***Prostaglandins Leukot Essent Fatty Acids*** 1991; 43: 197-201.
30. Horrobin DF. The roles of essential fatty acids in the development of diabetic neuropathy and other complications of diabetes mellitus. ***Prostaglandins Leukot Essent Fatty Acids*** 1988; 31: 181-197.
31. Karim A, Ogbeide DO, Siddiqui S, Al-Khalifa IM. Prevalence of diabetes mellitus in a Saudi community. ***Saudi Med J*** 2000; 21: 438-442.
32. Al-Nuaim AR, Famuyiwa O, Greer W. Hyperlipidemia among Saudi diabetic patients - pattern and clinical characteristic. ***Ann Saudi Med*** 1995; 15: 240-243.
33. El Hazmi MA, Al Swailem AR, Warsy AS, Al Meshari AA, Sulaimani R, Al-Swailem, et al. Lipids and related Parameters in Saudi type II diabetes mellitus patients. ***Ann Saudi Med*** 1999; 19: 304-307.
34. Gary NE. Quality of health care and costs: standards, outcome, and regulation. ***Bull N Y Acad Med*** 1992; 68: 245-249.
35. Cameron NE, Cotter MA, Robertson S. Essential fatty acid diet supplementation. Effects on peripheral nerve and skeletal muscle function and capillarization in streptozocin-induced diabetic rats. ***Diabetes*** 1991; 40: 532-539.
36. Cutler CW, Shinedling EA, Nunn M, Jotwani R, Kim BO, Nares S, et al. Association between periodontitis and hyperlipidemia: cause or effect? ***J Periodontol*** 1999; 70: 1429-1434.

Corrections, retractions and "Expressions of Concern"

Excerpts from the Uniform Requirements for Manuscripts Submitted to Biomedical Journals updated November 2003. Available from www.icmje.org

The corrections should appear on a numbered page, be listed in the contents page, include the complete original citation and link to the original article and vice versa if online.

The retraction and expression of concern, appear on a numbered page in a prominent section of the print journal as well as in the online version, be listed in the contents page, and include in its heading the title of the original article. The text of the retraction should explain why the article is being retracted and include a full original citation reference to it.

Editors may ask the author's institution to assure them of the validity of earlier work published in their journals or to retract it. If this is not done editors may choose to publish an announcement expressing concern that the validity of previously published work is uncertain.