Journal of Oral Hygiene & Health
ISSN: 2332-0702
Chwalba Artur and Ewa Otto-Buczkowska, Oral Hyg Health 2014, 2:6
DOI: 10.4172/2332-0702.1000167
Review Article
Open Access

Oral Health Problems among Diabetic Patients – Part of Dental Professionals in Diagnostic and Therapy

Chwalba Artur and Ewa Otto-Buczkowska*

Medical Specialist Centre in Gliwice, Poland

***Corresponding author:** Ewa Otto-Buczkowska, Jasnogórska 26/21, 44-100 Gliwice, Poland, Tel: 48 32 231 01; E-mail: em.buczkowski@pro.onet.pl

Received date: Sep 18, 2014; **Accepted date:** Nov 14, 2014; **Published date:** Nov 18, 2014

Abstract

Diabetes mellitus is a metabolic disease characterized by hyperglycemia. This is the result of a deficiency in insulin secretion or an increased cellular resistance to the actions of insulin, leading to a variety of metabolic abnormalities. Persistent hyperglycemia has been associated with the incidence and progression in diabetes-related complications, including oral health problems such as oral mucosal diseases, dental caries, salivary dysfunction, oral infections, taste and other neurosensory disorders. Dentists play a major role as part of an allied health team in providing oral care to patients with diabetes. Screening for diabetes and prediabetes in the dental office may provide an important benefit to patients. Several studies have demonstrated the beneficial effect of periodontal treatment on metabolic control of diabetic patients.

The aim of this article is to present an overview of opinions contained in the contemporary literature and presentation of the results of clinical trials performed in oral health problems among diabetic patients.

Keywords: Diabetes mellitus; Mucosal diseases; Salivary dysfunction; Periodontal disease; Dental caries

Introduction

Sickness-changes within the oral cavity are to be considering both as the complication of the diabetes as well as the reason of the difficulty in the metabolic compensation of the illness [1-3]. Every chronic hyperglycaemia, aside from its reasons, leads to the activation of the process of not enzymatic glycation of proteins, poliolic route and the oxidative stress.

The chronic hyperglycaemia and related inflammation leads to the disturbances in the balance between the metaloproteinase system and their inhibitors (MMP/TIMP), what becomes a reason of the pathological reconstruction of the vascular wall, the proliferation of the endothelium and arteriogensis [4-6].

Inflammatory focus in the human body, including the oral cavity, can on one hand be the reason of disturbances of the metabolic control of the diabetes, from the second hand – can accelerate the development hyperglycaemia related vascular complications [7-13]. Many authors think that fundamental role in the occurrence of complications plays the insufficient degree of the metabolic compensation. Other authors pay attention that also chronic changes within the oral cavity can unfavourably influence on the compensation of the diabetes [14-16]. To finally evaluate described above interactions further studies are indicated [17].

This issue is also highlighted in the publication presented by Teeuw and co-authors [18]. On the basis of extensive literature analysis Spanish authors formulated the conclusion that peridontal disease control can improve DM type 2 patient's glycaemia control; on the other hand glycaemia control improvement can influence better peridontal diseases control [10]. Lately American authors presented the results of multicentre trials on the influence of inflammatory changes of the paradontium on the degree of the metabolic compensation of the diabetes [19,20].

At the evaluation of oral cavity changes in diabetic patients usually the attention is paid mainly to the type 1 diabetes. These are usually younger patients at who more easily is to set the relation between these changes and the diabetes. In the diabetes mellitus type 2, concerning usually older people with different sickness-changes related to the age, the arteriosclerosis etc, the settlement whether changes found within the oral cavity have a relationship with the diabetes or else with other morbid conditions is difficult [7,21,22].

However lately more and more researches are dedicated also to patients with the type 2 diabetes [23-25]. In case of this group of patients the meaning of the bad metabolic control as the risk factor for the development of sickness-changes within the oral cavity is particularly underlined [26-34].

Lithuanian authors who explored comparative trials confirmed that the course of paradontium morbid conditions at patients with the diabetes mellitus type 2 it is particularly heavy [35]. This type of the diabetes develops usually slowly and its diagnosis and the commencement of the treatment are usually very late. Still very often diagnosis of this type of the diabetes it comes only in the moment of the appearance of heavy vascular complications.

The necessity of tightening of the criteria for earlier diagnostics of glucose homeostasis disturbances before the appearance of the clinically overt diabetes is discussed. Such pointers are metabolic syndrome features. This issue is discussed in the publication describing cause-effect relationships of the metabolic syndrome with changes in the paradontium [36].

Also other authors dealt with the issue of the coexistence of peridontosis at patients with metabolic syndrome [37,38]. Lately large number of articles representing results of trials on mechanisms binding the obesity with illnesses of the paradontium appeared [39]. In

the context of this observations of Spanish authors who paid attention on the usefulness of the dentists' evaluation of the occurrence of paradental pockets of the depth ≥ 5 mms, and numbers of lacking teeth are very interesting. Authors determined that the presence 4 or more lacking teeth and pockets about the depth 5 or more the mm, signals the necessity of the diagnosis, among other things towards the glucose metabolism dysregulation [40].

Similar observations were made by American authors who underlined the meaning of the presence ≥ of 26% teeth with deep pockets or ≥ 4 lacking teeth detection during the dental investigation for the further detection of the pre-diabetic status [41,42]. The chronic hyperglycaemia and related inflammation leads to triggering the processes lying at complications of the diabetes grassroots, including changes within the oral cavity, where different sickness-processes can exist - one of them are inflammatory disorders of the mucous membrane [43,44].

Inflammatory disorders of the oral cavity mucous membrane are often one of first symptoms of the newly revealed diabetes, so always at their statement careful interview of the concerning occurrence of other diabetes symptoms is indicated. The parallel occurrence of changes on the mucous membrane and within external urogenital tract should engage the diagnosis towards the presence of the glycosuria [45]. The issue of the occurrence of illnesses of the oral cavity in patients with diabetes and mutual dependence among the degree of the metabolic compensation, and an occurrence of these changes it is not new. Already in the year 1973 results of Polish research carried out in the group juvenile patients was published [46].

In 50% cases inflammation of gums was observed. In 1985 Gusberti and co-authors presented the results of their research in the group 77 juvenile patients [47]. Later researches confirmed the significantly greater frequency of the occurrence of changes in the paradontium at juvenile patients with the diabetes into comparisons to the group of healthy population [48]. Orbaket and co-authors introduced results of their research in the group 100 children patients, whereof 50 were children with the type 1 diabetes [49]. Authors evaluated the large number of health status indicators within the oral cavity. There found statistically significant differences of indicators: PI (*plaque index*), GI (*gingival index*), CI (*calculus index*) and their increase in the group of children with the diabetes.

Researches aiming to fix the factors participating in the pathogenesis of inflammatory changes of the paradontium in the diabetes are conducted [50,51].

Periodontal Disease

Paradontium diseases, relatively often appearing in the diabetes, are connected not only with the presence of infectious (bacteria, viruses, fungus) factors, but also with the presence of diabetic changes in vessels as the as result of the chronic hyperglycaemia which leads to the disturbance of the blood supply and the vulnerability to infections [13,52]. Relationships of paradontium diseases with the diabetes have the large representation in the literature [12,53].

Results of research over the pathogenesis of inflammatory changes of the paradontium at children with the diabetes of the type 1 were presented by Swedish authors [50]. They evaluated both the clinical state of gums (the tendency to bleeding) and the saliva IgG level in the group of 48 children with the diabetes. Both these indicators were increased, especially in the group of children with the badly controlled diabetes. Gümüş et al. found the decreased level of the reduced glutathione in the group of patients with the type 1diabetes [54].

The reduced glutathione is an antioxidant involved into many cellular functions – its reduced level can be involved in the destruction of tissues through the oxidative stress vulnerability increase. The investigation carried out in Poland in the occurrence of paradontium illnesses in the group of juvenile patients with type 1 diabetes showed the presence of the higher PDI indicator (*periodontal disease index*) at these patients [55]. Authors think that the type 1 diabetes can be a risk factor for the development of periodontal diseases.

Afterwards also other authors presented results of their own investigations over the occurrence of paradontium inflammable status at juvenile diabetic patients, finding the greater vulnerability to inflammation occurrence comparatively with healthy juvenile population [56-59].

Lalla and co-authors in the group 182 juvenile diabetic patient research confirmed the significantly greater frequency of the occurrence paradontium changes in comparisons with the group of healthy juvenile population [60]. It was stated in consideration with increased risk of paradontium changes occurrence the specialized programmes for the prophylaxis and the treatment of diabetes juvenile patients are necessary [61]. Also the reports that the risk of the paradontium illness development during the pregnancy at diabetic women is significantly higher than in the control group [62]. Xiong et al. presented the relationship of the paradontium illness occurrence with the development of diabetes at women with gestational diabetes (GDM) [63]. Despite many research decisive factors about the occurrence of paradontium changes at patients with the diabetes, were still not fully identified [29,64-69].

Preferansow and co-authors used the Russel index for the paradontium condition at diabetic patients. It's value in the group of patients with the diabetes was 2,14 in comparison with 0,99 ascertained in the healthy group [70]. Authors found that a reason of paradontium changes in diabetes patients was improper metabolic control. Limas et al. also underlined the meaning of the insufficient diabetes metabolic compensation as the risk factor for the occurrence of the paradontium diseases; they also paid attention and explored in the group of adult diabetic patients some parameters indicative of the insufficient degree of the metabolic compensation [71].

Salivary Dysfunction

Patients with diabetes often complaint for the oral cavity dryness. This can be the result, among other reasons, of an autonomic neuropathy. The investigations are conducted to explain the mechanisms of these changes [72-76]. Zalewska et al. introduced the results of the saliva glands function evaluation at diabetes 1 juvenile patients [77]. They found the changes are more expressed at younger children in comparison with adolescents group.

Waszkiel et al. found differences in the PH value and buffer capacity of saliva at children with type 1 diabetes in comparison with the group of healthy children [78]. Arene et al. investigating the group of children with newly diagnosed diabetes and with the long lasting diabetes found the essential relationship of the diabetes compensation degree with the paradontium state, buffer capacity of saliva, and also with peroxidase activity [79].

Siudikiene et al. presented their own investigations results carried out in the group of 63 diabetic children [80]. Significantly lower degree

of the saliva flow, the higher IgA, proteins and glucose concentration in the saliva of diabetic children was disclosed, what can be a factor favouring to the cariogenesis.

Gümüş et al. signalled decrease of the reduced glutathione level, what, according to their opinion can play role in the destruction of paradontium tissues [54]. The influence of the diabetes on the activity of saliva glands was also confirmed by other authors [81-86] Also interesting observations of Polish authors concerning salivary glands function changes at patients with the gestational diabetes were presented [87].

Dental Caries

Results obtained by different authors concerning occurrences of the caries at patients with the diabetes they are differentiated [88]. Main factor of the cariogenesis is considered reduced salivary secretion and the reduction of its pH and the growth of the density of the saliva in comparison with healthy persons.

The intensity of the caries process can be tied with the glucose concentration growth in the saliva and in the fluid of gingival pockets at patients with the improperly controlled diabetes. Miralles et al. found the significant increase of caries occurrence frequency at type 1 diabetes patients [89]. According to the authors, the degrees of the metabolic compensation, the length of the duration of the illness and the presence of complications of the diabetes had influence on the cariogenesis of teeth.

Miko et al. made a survey in 259 groups of adolescents [90]. The teeth caries was evaluated according to DMFT index. In the investigated group this indicator was higher than in the control group ($p<0.001$). Tagelsir et al. pay attention that the diabetes can indeed increase the risk of caries occurrence, however worse state of teeth at diabetic children authors bind mainly with the insufficient dental care [91].

Conclusion

Large number of clinical research appeared lately; their authors paid attention on the occurrence of oral cavity changes which can suggest the diagnosis of the diabetes at patients still not diagnosed as diabetic [92,93]. The extensive discussion of this issue presented the group of American researchers [94]. Based on carried out analyses, the authors indicate the necessity of screening tests broad applications, also at dentists' offices. Other authors also confirm this opinion [95-98].

Albert and co-authors [99] presented the results of the conference dedicated to the discussion about the national diabetes educative programme to promote the cooperation between dentists and doctors of different specialities as well as pharmacists, for the purpose of the improvement of methods for the early diabetes diagnosis and treatment. Also other authors dedicate much attention for the necessity of such interdisciplinary actions [100]. In conclusion there is a need to remind that every chronic hyperglycaemia, independently from its reason, leads to the activation of not enzymatic protein glycation process, poliolic route and the oxidative stress, what can lie at the base of many pathological processes going on within the oral cavity [4,101]. Changes within the oral cavity are considering both as the complication of the diabetes as well as the reason of the difficulty in metabolic disease compensation. Apart from the aspirations to the maximum metabolic compensation, what are the basis of the prevention and the treatment of diabetes complications, it's very important to provide to the patients maximally effective education and the dental care.

References

1. Drzewoski J (2010) Oral diseases in diabetic patients - underestimated complication. Diabetology after Diploma 7: 28-29.
2. Graves DT, Liu R, Alikhani M, Al-Mashat H, Trackman PC (2006) Diabetes-enhanced inflammation and apoptosis--impact on periodontal pathology. J Dent Res 85: 15-21.
3. Koziolek M, Kiedrowicz M, Kiedrowicz B, Dembowska E, Syrenich A (2001) [Symptoms of endocrine diseases in dental patients] Dent. Med. Probl 2: 229–235
4. Otto-Buczkowska E, Machnica L (2010) Metabolic memory - the implications for diabetic complications. Endokrynol Pol 61: 700-703.
5. Yu S, Li H, Ma Y, Fu Y (2012) Matrix metalloproteinase-1 of gingival fibroblasts influenced by advanced glycation end products (AGEs) and their association with receptor for AGEs and nuclear factor-IºB in gingival connective tissue. J Periodontol 83: 119-126.
6. Zizzi A, Tirabassi G, Aspriello SD, Piemontese M, Rubini C, et al. (2013) Gingival advanced glycation end-products in diabetes mellitus-associated chronic periodontitis: an immunohistochemical study. J Periodontal Res 48: 293-301.
7. Kuo LC, Polson AM, Kang T (2008) Associations between periodontal diseases and systemic diseases: a review of the inter-relationships and interactions with diabetes, respiratory diseases, cardiovascular diseases and osteoporosis. Public Health 122: 417-433.
8. Lamster IB, Lalla E, Borgnakke WS, Taylor GW (2008) The relationship between oral health and diabetes mellitus. J Am Dent Assoc 139 Suppl: 19S-24S.
9. Löe H (1993) Periodontal disease. The sixth complication of diabetes mellitus. Diabetes Care 16: 329-334.
10. SakallioÄŸlu EE, LAtfioÄŸlu M, SakallioÄŸlu U, Diraman E, Keskiner I (2008) Fluid dynamics of gingiva in diabetic and systemically healthy periodontitis patients. Arch Oral Biol 53: 646-651.
11. Shultis WA, Weil EJ, Looker HC, Curtis JM, Shlossman M, et al. (2007) Effect of periodontitis on overt nephropathy and end-stage renal disease in type 2 diabetes. Diabetes Care 30: 306-311.
12. Taylor GW, Borgnakke WS (2008) Periodontal disease: associations with diabetes, glycemic control and complications. Oral Dis 14: 191-203.
13. Wawrzkiewicz M, Braczkowski R (2009) The impast of hyperglycaemia on the development of periodontitis. Diabet Dosw Klin 9: 8-11
14. Chapple IL, Genco R (2013) working group 2 of the joint EFP/AAP workshop. Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Periodontol 84: S106-112
15. Gurav AN (2012) Periodontal therapy -- an adjuvant for glycemic control. Diabetes Metab Syndr 6: 218-223.
16. Santacroce L, Carlaio RG, Bottalico L (2010) Does it make sense that diabetes is reciprocally associated with periodontal disease? Endocr Metab Immune Disord Drug Targets 10: 57-70.
17. Borgnakke WS, Ylöstalo PV, Taylor GW, Genco RJ (2013) Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence. J Clin Periodontol. 14: S135-152.
18. Teeuw WJ, Gerdes VE, Loos BG (2010) Effect of periodontal treatment on glycemic control of diabetic patients: a systematic review and meta-analysis. Diabetes Care 33: 421-427.
19. Bascones-Martinez A, Matesanz-Perez P, Escribano-Bermejo M, González-Moles MÁ, Bascones-Ilundain J, et al. (2011) Periodontal disease and diabetes-Review of the Literature. Med Oral Patol Oral Cir Bucal 16: e722-729.
20. DPTT study group, Engebretson S, Gelato M, Hyman L, Michalowicz BS (2013) Design features of the Diabetes and Periodontal Therapy Trial (DPTT): a multicenter randomized single-masked clinical trial testing the effect of nonsurgical periodontal therapy on glycosylated hemoglobin

(HbA1c) levels in subjects with type 2 diabetes and chronic periodontitis. Contemp Clin Trials. 36: 515-526.

21. Kowalski M, Brocka E, Barylski M, Kowalczyk E, Pawlicki L, et al. (2009) [Assessment of the periodontal state in subjects with metabolic syndrome]. Pol Merkur Lekarski. 26: 620-625.
22. Kowalski M, Brocka E, Barylski M, Kowalczyk E, Pawlicki L, et al. (2009) [Estimation of oxidation-reduction balance in subjects with metabolic syndrome together with or without periodontal diseases]. Pol Merkur Lekarski 26: 626-630.
23. Al-Khabbaz AK (2014) Type 2 diabetes mellitus and periodontal disease severity. Oral Health Prev Dent 12: 77-82.
24. Haseeb M, Khawaja KI, Ataullah K, Munir MB, Fatima A (2012) Periodontal disease in type 2 diabetes mellitus. J Coll Physicians Surg Pak 22: 514-518.
25. Lakschevitz F, Aboodi G, Tenenbaum H, Glogauer M (2011) Diabetes and periodontal diseases: interplay and links. Curr Diabetes Rev 7: 433-439.
26. Awartani F (2009) Evaluation of the relationship between type 2 diabetes and periodontal disease. Odontostomatol Trop 32: 33-39.
27. Awartani FA (2009) Evaluation of the relationship between type 2 diabetes and periodontal disease. Saudi Med J 30: 902-906.
28. Chen L, Wei B, Li J, Liu F, Xuan D, et al. (2010) Association of periodontal parameters with metabolic level and systemic inflammatory markers in patients with type 2 diabetes. J Periodontol 81: 364-371.
29. KardeÅŸler L, Buduneli N, Cetinkalp S, Kinane DF (2010) Adipokines and inflammatory mediators after initial periodontal treatment in patients with type 2 diabetes and chronic periodontitis. J Periodontol 81: 24-33.
30. Lin SJ, Tu YK, Tsai SC, Lai SM, Lu HK (2012) Non-surgical periodontal therapy with and without subgingival minocycline administration in patients with poorly controlled type II diabetes: a randomized controlled clinical trial. Clin Oral Investig. 16: 599-609.
31. Makiura N, Ojima M, Kou Y, Furuta N, Okahashi N, et al. (2008) Relationship of Porphyromonas gingivalis with glycemic level in patients with type 2 diabetes following periodontal treatment. Oral Microbiol Immunol 23: 348-351.
32. Steffens JP, Glaci Reinke SM, Angel Muñoz M, Santos FA, Luiz Pilatti G (2010) [Review on periodontal disease and metabolic control of diabetes mellitus]. Rev Med Chil 138: 1172-1178.
33. StojanoviÄ N, KruniÄ J, Cicmil S, VukotiÄ O (2010) [Oral health status in patients with diabetes mellitus type 2 in relation to metabolic control of the disease]. Srp Arh Celok Lek 138: 420-424.
34. Tanwir F, Tariq A (2012) Effect of glycemic conrol on periodontal status. J Coll Physicians Surg Pak 22: 371-374.
35. Pranckeviciene A, Siudikiene J, Ostrauskas R, Machiulskiene V (2014) Severity of periodontal disease in adult patients with diabetes mellitus in relation to the type of diabetes. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 158: 117-123.
36. Gurav AN (2014) The association of periodontitis and metabolic syndrome. Dent Res J (Isfahan) 11: 1-10.
37. Kwon YE, Ha JE, Paik DI, Jin BH, Bae KH (2011) The relationship between periodontitis and metabolic syndrome among a Korean nationally representative sample of adults. J Clin Periodontol 38: 781-786.
38. López NJ, Quintero A, Casanova PA, Ibieta CI, Baelum V, et al. (2012) Effects of periodontal therapy on systemic markers of inflammation in patients with metabolic syndrome: a controlled clinical trial. J Periodontol 83: 267-278.
39. Zhu M, Nikolajczyk BS (2014) Immune cells link obesity-associated type 2 diabetes and periodontitis. J Dent Res 93: 346-352.
40. Dye BA, Genco RJ (2012) Tooth loss, pocket depth, and HbA1c information collected in a dental care setting may improve the identification of undiagnosed diabetes. J Evid Based Dent Pract. 12: 12-14.
41. Lalla E, Kunzel C, Burkett S, Cheng B, Lamster IB (2011) Identification of unrecognized diabetes and pre-diabetes in a dental setting. J Dent Res 90: 855-860.
42. Lalla E, Cheng B, Kunzel C, Burkett S, Lamster IB (2013) Dental findings and identification of undiagnosed hyperglycemia. J Dent Res 92: 888-892.
43. Cristina de Lima D, Nakata GC, Balducci I, Almeida JD (2008) Oral manifestations of diabetes mellitus in complete denture wearers. J Prosthet Dent 99: 60-65.
44. Otto-Buczkowska E, Kaminska H (2011) [Oral Heath problems among diabetic patients]. Twój Prz Stomatol 18:66-7
45. Otto-Buczkowska E, Jarosz-Chobot P, Olak-Bialon B (2006) [Ketoacidosis in patients with diabetes mellitus – clinical signs, diagnosis and treatment.] Physician 10: 60-64.
46. Otto-Buczkowska E, Pisulska-Otremba A (1973) [Examination of the masticatory organ in diabetic children]. Wiad Lek 26: 5-8.
47. Gusberti FA, Syed SA, Bacon G, Grossman N, Loesche WJ (1983) Puberty gingivitis in insulin-dependent diabetic children. I. Cross-sectional observations. J Periodontol 54: 714-720.
48. Iughetti L, Marino R, Bertolani MF, Bernasconi S (1999) Oral health in children and adolescents with IDDM--a review. J Pediatr Endocrinol Metab. 12: 603-610.
49. Orbak R, Simsek S, Orbak Z, Kavrut F, Colak M (2008) The influence of type-1 diabetes mellitus on dentition and oral health in children and adolescents. Yonsei Med J 49: 357-365.
50. Javed F, Sundin U, Altamash M, Klinge B, Engström PE (2009) Self-perceived oral health and salivary proteins in children with type 1 diabetes. J Oral Rehabil 36: 39-44.
51. Taylor JJ, Preshaw PM, Lalla E (2013) A Review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. J Periodontol. 84: S113-34.
52. Genco RJ, Grossi SG, Ho A, Nishimura F, Murayama Y (2005) A proposed model linking inflammation to obesity, diabetes, and periodontal infections. J Periodontol 76: 2075-2084.
53. Silvestre FJ, Miralles L, Llambes F, Bautista D, Solá-Izquierdo E, et al. (2009) Type 1 diabetes mellitus and periodontal disease: relationship to different clinical variables. Med Oral Patol Oral Cir Bucal 14: E175-179.
54. GAmAÅŸ P, Buduneli N, Cetinkalp S, Hawkins SI, Renaud D, et al. (2009) Salivary antioxidants in patients with type 1 or 2 diabetes and inflammatory periodontal disease: a case-control study. J Periodontol 80: 1440-1446.
55. Luczaj-Cepowicz E, Marczuk-Kolada G, Waszkiel D (2006) Evaluation of periodontal status in young patients with insulin-dependent diabetes mellitus (type 1). Adv Med Sci 51 Suppl 1: 134-137.
56. Dakovic D, Pavlovic MD (2008) Periodontal disease in children and adolescents with type 1 diabetes in Serbia. J Periodontol 79: 987-992.
57. Lal S, Cheng B, Kaplan S, Softness B, Greenberg E, et al. (2007) Gingival bleeding in 6- to 13-year-old children with diabetes mellitus. Pediatr Dent 29: 426-430.
58. Saes Busato IM, Bittencourt MS, Machado MA, Grégio AM, Azevedo-Alanis LR (2010) Association between metabolic control and oral health in adolescents with type 1 diabetes mellitus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 109: e51-56.
59. Wang MX, Wang X, Zhang Z, Qin M (2013) [The salivary factors related to caries and periodontal disease in children and adolescents with diabetes mellitus]. Zhonghua Kou Qiang Yi Xue Za Zhi 48: 545-549.
60. Lalla E, Cheng B, Lal S, Tucker S, Greenberg E, et al. (2006) Periodontal changes in children and adolescents with diabetes: a case-control study. Diabetes Care 29: 295-299.
61. Lal S, Cheng B, Kaplan S, Softness B, Greenberg E, et al. (2008) Accelerated tooth eruption in children with diabetes mellitus. Pediatrics 121: e1139-1143.
62. Ruiz DR, Romito GA, Dib SA (2011) Periodontal disease in gestational and type 1 diabetes mellitus pregnant women. Oral Dis 17: 515-521.
63. Xiong X, Elkind-Hirsch KE, Xie Y, Delarosa R, Maney P, et al. (2013) Periodontal disease as a potential risk factor for the development of

diabetes in women with a prior history of gestational diabetes mellitus. J Public Health Dent 73: 41-49.

64. Akalin FA, IÅŸiksal E, BaltacioÄŸlu E, Renda N, Karabulut E (2008) Superoxide dismutase activity in gingiva in type-2 diabetes mellitus patients with chronic periodontitis. Arch Oral Biol 53: 44-52.
65. Amano A, Kawai S (2007) [Diabetes and oral osteoporosis]. Clin Calcium 17: 186-191.
66. Chen L, Wei B, Li J, Liu F, Xuan D, et al. (2010) Association of periodontal parameters with metabolic level and systemic inflammatory markers in patients with type 2 diabetes. J Periodontol 81: 364-371.
67. Nagata T (2009) [Relationhip between diabetes and periodontal disease]. Clin Calcium 19: 1291-1298.
68. Pan Z, Guzeldemir E, Toygar HU, Bal N, Bulut S (2010) Nitric oxide synthase in gingival tissues of patients with chronic periodontitis and with and without diabetes. J Periodontol 81: 109-120.
69. SakallioÄŸlu EE, LAtfioaylu M, SakallioÄŸlu U, Diraman E, Keskiner I (2008) Fluid dynamics of gingiva in diabetic and systemically healthy periodontitis patients. Arch Oral Biol 53: 646-651.
70. Preferansow E, Goa, ebiewska M, Kulikowska-Bielaczyc E, GArska M (2006) The assessment of periodontium in patients with uncontrolled diabetes. Adv Med Sci 51 Suppl 1: 170-172.
71. Lim LP, Tay FB, Sum CF, Thai AC (2007) Relationship between markers of metabolic control and inflammation on severity of periodontal disease in patients with diabetes mellitus. J Clin Periodontol 34: 118-123.
72. Izumi M, Watanabe M, Sawaki K, Yamaguchi H, Kawaguchi M (2008) Expression of BMP7 is associated with resistance to diabetic stress: comparison among mouse salivary glands. Eur J Pharmacol 596: 1-5.
73. Mednieks MI, Szczepanski A, Clark B, Hand AR (2009) Protein expression in salivary glands of rats with streptozotocin diabetes. Int J Exp Pathol 90: 412-422.
74. Perrotti V, Piattelli A, Piccirilli M, Bianchi G, Di Giulio C, et al. (2007) Vascular endothelial growth factor expression (VEGF) in salivary glands of diabetic rats. Int J Immunopathol Pharmacol 20: 55-60.
75. Sabino-Silva R, Freitas HS, Lamers ML, Okamoto MM, Santos MF, et al. (2009) Na+-glucose cotransporter SGLT1 protein in salivary glands: potential involvement in the diabetes-induced decrease in salivary flow. J Membr Biol 228: 63-69.
76. Sabino-Silva R, Alves-Wagner AB, Burgi K, Okamoto MM, Alves AS, et al. (2010) SGLT1 protein expression in plasma membrane of acinar cells correlates with the sympathetic outflow to salivary glands in diabetic and hypertensive rats. Am J Physiol Endocrinol Metab 299: E1028-1037.
77. Zalewska A, Knaa M, Kuamiuk A, Waszkiewicz N, Niczyporuk M, et al. (2013) Salivary innate defense system in type 1 diabetes mellitus in children with mixed and permanent dentition. Acta Odontol Scand 71: 1493-1500.
78. Waszkiel D, Kuzmiuk A, Zalewska A, Luczaj-Cepowicz E, Zalewska-Szajda B (2009) Assessment of pH and Buffet capacity of silva In children and adolescents with type 1 diabetes mellitus. Czas Stomatol 62: 192-196.
79. Aren G, Sepet E, Ozdemir D, DinA§A§aÄŸ N, Gavener B, et al. (2003) Periodontal health, salivary status, and metabolic control in children with type 1 diabetes mellitus. J Periodontol 74: 1789-1795.
80. Siudikiene J, Machiulskiene V, Nyvad B, Tenovuo J, Nedzelskiene I (2008) Dental caries increments and related factors in children with type 1 diabetes mellitus. Caries Res 42: 354-362.
81. Alves C, Menezes R, BrandAo M (2012) Salivary flow and dental caries in Brazilian youth with type 1 diabetes mellitus. Indian J Dent Res 23: 758-762.
82. Dakovic D, Colic M, Cakic S, Mileusnic I, Hajdukovic Z, et al. (2013) Salivary interleukin-8 levels in children suffering from type 1 diabetes mellitus. J Clin Pediatr Dent 37: 377-380.
83. Moreira AR, Passos IA, Sampaio FC, Soares MS, Oliveira RJ (2009) Flow rate, pH and calcium concentration of saliva of children and adolescents with type 1 diabetes mellitus. Braz J Med Biol Res 42: 707-711.
84. Rai K, Hegde AM, Kamath A, Shetty S (2011) Dental caries and salivary alterations in Type I Diabetes. J Clin Pediatr Dent 36: 181-184.
85. Zalewska-Szajda B, Dariusz Szajda S, Waszkiewicz N, Chojnowska S, GoÅ›cik E, et al. (2013) Activity of N-acetyl-I-D-hexosaminidase in the saliva of children with type 1 diabetes. Postepy Hig Med Dosw (Online) 67: 996-999.
86. Zalewska A, KnaÅ M, Niczyporuk M, Razak HH, Waszkiewicz N, et al. (2013) Salivary lysosomal exoglycosidases profiles in patients with insulin-dependent and noninsulin-dependent diabetes mellitus. Adv Clin Exp Med 22: 659-666.
87. Zalewska A, KnaA M, GumiÄ Åny G, Niczyporuk M, Waszkiel D, et al. (2013) Salivary exoglycosidases in gestational diabetes . Postepy Hig Med Dosw (Online) 67: 315-320.
88. El-Tekeya M, El Tantawi M, Fetouh H, Mowafy E, Abo Khedr N (2012) Caries risk indicators in children with type 1 diabetes mellitus in relation to metabolic control. Pediatr Dent 34: 510-516.
89. Miralles L, Silvestre FJ, Hernández-Mijares A, Bautista D, Llambes F, et al. (2006) Dental caries in type 1 diabetics: influence of systemic factors of the disease upon the development of dental caries. Med Oral Patol Oral Cir Bucal 11: E256-260.
90. Miko S, Ambrus SJ, Sahafian S, Dinya E, Tamas G, et al. (2010) Dental caries and adolescents with type 1 diabetes. Br Dent J 208: E12.
91. Tagelsir A, Cauwels R, van Aken S, Vanobbergen J, Martens LC (2011) Dental caries and dental care level (restorative index) in children with diabetes mellitus type 1. Int J Paediatr Dent 21: 13-22.
92. Forbes K, Thomson WM, Kunzel C, Lalla E, Lamster IB (2008) Management of patients with diabetes by general dentists in New Zealand. J Periodontol 79: 1401-1408.
93. Lamster IB, Kunzel C, Lalla E (2012) Diabetes mellitus and oral health care: time for the next step. J Am Dent Assoc 143: 208-210.
94. Barasch A, Safford MM, Qvist V, Palmore R, Gesko D, et al. (2012) Dental Practice-Based Research Network Collaborative Group. Random blood glucose testing in dental practice: a community-based feasibility study from The Dental Practice-Based Research Network. J Am Dent Assoc143: 262-269.
95. AlGhamdi AS, Merdad K, Sonbul H, Bukhari SM, Elias WY (2013) Dental clinics as potent sources for screening undiagnosed diabetes and prediabetes. Am J Med Sci 345: 331-334.
96. Genco RJ, Schifferle RE, Dunford RG, Falkner KL, Hsu WC, et al. (2014) Screening for diabetes mellitus in dental practices: a field trial. J Am Dent Assoc 145: 57-64.
97. Lalla E, Lamster IB (2012) Assessment and management of patients with diabetes mellitus in the dental office. Dent Clin North Am 56: 819-829.
98. Mohamed K, Yates J, Roberts A (2014) Diabetes mellitus: considerations for the dental practitioner. Dent Update 41: 144-146, 149-50, 153-4.
99. Albert DA, Ward A, Allweiss P, Graves DT, Knowler WC, et al. (2012) Diabetes and oral disease: implications for health professionals. Ann N Y Acad Sci 1255: 1-15.
100. Bissett SM, Stone KM, Rapley T, Preshaw PM (2013) An exploratory qualitative interview study about collaboration between medicine and dentistry in relation to diabetes management. BMJ Open 3.
101. Ceriello A (2012) The emerging challenge in diabetes: the "metabolic memory". Vascul Pharmacol 57: 133-138.