

# Diabetes mellitus and periodontal disease

Teodor Salmen<sup>1,2</sup>, Bianca Margareta Mihai<sup>3</sup>, Ruxandra Andreea Iarca<sup>4</sup>, Bianca Adriana Stan<sup>5</sup>,  
Vlad Dima<sup>3</sup>, Roxana Elena Bohiltea<sup>6</sup>

<sup>1</sup> Doctoral School, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

<sup>2</sup> "N.C. Paulescu" National Institute for Diabetes Mellitus, Nutrition and Metabolic Disorders, Bucharest, Romania

<sup>3</sup> Filantropia Clinical Hospital, Bucharest, Romania

<sup>4</sup> Periodontology Department, "Titu Maiorescu" University, Bucharest, Romania

<sup>5</sup> Doctoral School of Dentistry, "Titu Maiorescu" University, Bucharest, Romania

<sup>6</sup> Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

## ABSTRACT

Diabetes mellitus (DM) is a chronic non-transmittable disease and, alongside periodontal disease, another chronic disease, but with infectious and inflammatory etiology, that have increasing prevalence. The link between the two comorbidities is bidirectional, with common aspects such the inflammatory state, altered immune response and healing process. This link is alimented, also, by oxidative stress, an element that can initiate proinflammatory pathways in both pathologies. Moreover, periodontal disease favors the development of DM complications by a multifactorial mechanism centered on hyperglycemia, that leads to damage of the endothelial vascular cells, characteristic for microvascular complications, while the periodontal bacteria and their waste products, and inflammatory cytokines lead to an increase in systemic inflammation and damage of the vascular walls that aggravates the atherogenic process. The increase of novel cases of type 2 DM or gestational DM in patients with periodontitis has no sufficient data. Dental caries is favored by DM and not by periodontal disease. So, DM is a well-known risk factor for periodontal disease and, on the other hand, periodontitis influences the metabolic control and favors the development of DM complications, but with a link between these conditions that is not fully understood. Other comorbidities, such as missing teeth, depression, osteoporosis are, also, positively associated to higher risk of development for periodontal disease. Patients with DM should be regularly screened for periodontal disease and referred to therapy if necessary, while the patients with periodontal disease should be screened for the presence of DM.

**Keywords:** diabetes mellitus, periodontal disease, inflammation, oxidative stress, microvascular and macrovascular complications

## INTRODUCTION

Diabetes mellitus (DM) is a chronic non-transmittable disease, characterized by defects in insulin production and/or action with alteration in glucose metabolism, with an increasing worldwide prevalence, that represents a serious problem through the systemic consequence that it generates on its own or in association with its comorbidities; while periodontitis, a chronic infectious inflammatory condition, leads to a progressive destruction of the periodontal ligaments and alveolar bones and to teeth loss (1-3).

The American Diabetes Association evaluated periodontitis as a complication of DM in 2008, but, recently, it was included in the list of DM comorbidities, respectively a simultaneously preexisting independent condition, or a related medical condition (4).

Comorbidity characterization requires the differentiation between joint risk and causal association, so, shortly, periodontitis represents an oral microbiome shift from symbiotic to dysbiotic type, simultaneously with a chronic inflammation of the tooth attachment apparatus tissue, while DM is trig-

gered by underexpression or tolerance to insulin expression. So, inflammation is the common aspect and, in DM it is impaired both at the immune response and also at healing process level, while in periodontitis it has an imbalance compared to immune response secondary to the dysbiotic flora (5).

The advanced glycation products and their receptor axis modifications produced in DM maintain, directly, a proinflammatory status, inclusive in the periodontal tissue, leading to a more intense catabolic status, augmentation of proinflammatory cytokines and impairment of RANKL/osteoprotegerin ratio. Indirect modifications, such as hyperglycemia in poorly controlled DM, leads to a dysbiotic periodontal microbiome, with further elevation of toll-like receptors levels and to host response, augmentating the previously inflammatory status (6,7).

### **BIDIRECTIONAL LINK BETWEEN DM AND PERIODONTITIS**

DM is a risk factor for periodontitis, but the relationship is bidirectional, because, periodontitis is not only an early sign of DM, but, also, a risk factor for several disease, including DM and cardiovascular disease (CVD) (atherosclerotic plaque instability, endothelial dysfunction and dyslipidemia) and others (2). Another argument is that periodontal treatment has effects in reducing glycated hemoglobin in DM. On the other hand, if we approach the problem from DM to periodontitis, there is not a fully understatement, a plausible explanation being represented by a proinflammatory response, in patients with DM, that leads to periodontitis susceptibility and progression in patients with diabetes, alongside with locally activated inflammatory mediators that may impair insulin signaling and aggravate the DM. DM increases the risk of periodontitis, by a presumably increase of salivary glucose levels, favoring bacterial growth in the gingival biofilm, but the literature data on this topic are few (8).

Liccardo et al. described another explanation for this link by oxidative stress, an element that can initiate proinflammatory pathways of both pathologies, such as in patients with DM and periodontitis, that presents higher levels of oxidative stress plasma biomarkers that may be the ones that activate the systemic proinflammatory pathways (9).

### **THE ASSOCIATION OF PERIODONTAL DISEASE AND DM COMPLICATIONS**

The mechanisms that predispose the patients with periodontitis to a higher risk for DM complications as compared to periodontal healthy patients seems to be multifactorial, but with a main element represented by hyperglycemia. A prolonged expo-

sure of the cells to high glucose levels leads to intracellular hyperglycemia, fact with important consequences in endothelial vascular cells, that normally have low glucose transport rates, because they are exposed to increased production of reactive oxygen species and altered gene expression by the hyperglycemic damage and they, consecutively, develop pathological changes characteristic for microvascular complications. On the other hand, periodontal bacteria and their waste products, alongside with the locally produced inflammatory cytokines by the inflamed periodontal tissues, lead to an increase in systemic inflammation and to a continuous exposure of the vascular walls to cytokines and bacteria aggravating the atherogenic process (10).

### **PERIODONTAL DISEASE AND NEW CASES OF DM**

Recent data from literature are reporting that periodontitis may be involved in the incidence of new cases of type 2 DM and even of gestational diabetes and, moreover, that the healthy subjects with periodontitis manifest moderate hyperglycemia compared with those with little or no periodontitis. These data about the link between periodontal disease and glycemic control and DM incidence in healthy individuals require further research to assess the extent of occurrence and involved mechanisms (11,12).

### **DENTAL CARIES, PERIODONTAL DISEASE AND DM**

From the triad of dental caries, periodontal disease and DM, patients with DM are susceptible to develop new or even recurrent dental caries due to alteration of the salivary secretion, characteristics of cleansing and buffering, but also due to an increase in the salivary quantity of carbohydrates, oral yeasts or streptococci and lactobacilli (13,14). Moreover, patients with DM are, also, predisposed to periodontal disease and, secondary, to tooth loss (15).

### **MANAGEMENT OF CASES WITH DM AND PERIODONTAL DISEASE**

The implications for clinical practice and public health derived from the studies that analyzed the link between DM and periodontal disease include several main points. The first one is in regard to clinicians, that should take into consideration the “2-way street” or the disease connection, respectively, a patient with DM and/or with poor glycemic control will develop a more severe periodontal if both DM and periodontitis are present, so the patients should be familiarized of this link and be instructed to enroll in oral health education programs and, also, teach that a proper control of their periodontal disease could lead to beneficial effects on their gly-

chemic control and complications of DM, in order to benefit from a better quality of life. The second aspect is regarding the diabetologists and physicians who should actively search sign and symptoms for the presence of periodontitis in patients with DM, such as halitosis, bleeding gums, gum soreness, drifting dentition and tooth mobility and to instruct the patients to address to an oral health practitioner. The third aspect is regarding the oral care providers, who should regularly perform a periodontal examination in each case of novel case of diagnostic of DM and to recommend to this patient to adhere to a regularly annual periodontal evaluation such as the recommendation for the patients of any age with DM, because, periodontitis treatment should not be delayed and oral rehabilitation is mandatory in order to restore the masticatory function (11).

The literature data show a positive and bidirectional association between DM and periodontal disease, thus, underlining the importance for regular screening in patients with periodontitis regarding the presence of DM and vice versa (12). Also, the link between DM and periodontal disease should include an important emphasize that should be put on the fact that not all the reported data confirmed the association between DM and periodontal disease and further analysis is needed, in order to be

able to conclude if there is a real link between these two highly prevalent disorders (9).

From the DM complications point of view, the evidence from observational studies and trials had demonstrated an association between higher levels of HbA1c levels and periodontal disease, so, patients with DM should be regularly screened for periodontal disease and referred to therapy if necessary, in order to limit the extent of development of DM complications (10).

## CONCLUSIONS

DM is a well-known risk factor for periodontal disease, while, on the other hand, periodontitis influences the metabolic control and favors the development of DM complications, but the link between these highly prevalent conditions is not fully understood.

Patients with DM are at an increased likelihood to develop periodontal disease. Other comorbidities, such as missing teeth, depression, osteoporosis are, also, positively associated to higher risk of development for periodontal disease. On the other hand, having a high educational level is associated with a lower risk of periodontal disease.

*Conflict of interest:* none declared  
*Financial support:* none declared

## REFERENCES

- Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract.* 2014 Feb;103(2):137-49.
- de Miguel-Infante A, Martínez-Huedo MA, Mora-Zamorano E, Hernández-Barrera V, Jiménez-Trujillo I, de Burgos-Lunar C, Cardenas Valladolid J, Jiménez-García R, Lopez-de-Andrés A. Periodontal disease in adults with diabetes, prevalence and risk factors. Results of an observational study. *Int J Clin Pract.* 2018 Nov 16:e13294.
- Tatakis DN, Kumar PS. Etiology and pathogenesis of periodontal diseases. *Dent Clin North Am.* 2005 Jul;49(3):491-516.
- American Diabetes Association. 3. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018 Jan;41(Suppl 1):S28-S37.
- Polak D, Sanui T, Nishimura F, Shapira L. Diabetes as a risk factor for periodontal disease-plausible mechanisms. *Periodontol 2000.* 2020 Jun;83(1):46-58.
- Vlassara H, Uribarri J. Advanced glycation end products (AGE) and diabetes: cause, effect, or both? *Curr Diab Rep.* 2014 Jan;14(1):453.
- Veloso CA, Fernandes JS, Volpe CM, Fagundes-Netto FS, Reis JS, Chaves MM, Nogueira-Machado JA. TLR4 and RAGE: similar routes leading to inflammation in type 2 diabetic patients. *Diabetes Metab.* 2011 Sep;37(4):336-42.
- Lalla E, Papapanou PN. Diabetes mellitus and periodontitis: a tale of two common interrelated diseases. *Nat Rev Endocrinol.* 2011 Jun 28;7(12):738-48.
- Liccardo D, Cannavo A, Spagnuolo G, Ferrara N, Cittadini A, Rengo C, Rengo G. Periodontal Disease: A Risk Factor for Diabetes and Cardiovascular Disease. *Int J Mol Sci.* 2019 Mar 20;20(6):1414.
- Nguyen ATM, Akhter R, Garde S, Scott C, Twigg SM, Colagiuri S, Ajwani S, Eberhard J. The association of periodontal disease with the complications of diabetes mellitus. A systematic review. *Diabetes Res Clin Pract.* 2020 Jul;165:108244.
- Genco RJ, Graziani F, Hasturk H. Effects of periodontal disease on glycemic control, complications, and incidence of diabetes mellitus. *Periodontol 2000.* 2020 Jun;83(1):59-65.
- Stöhr J, Barbaresko J, Neuenschwander M, Schlesinger S. Bidirectional association between periodontal disease and diabetes mellitus: a systematic review and meta-analysis of cohort studies. *Sci Rep.* 2021 Jul 1;11(1):13686.
- Rohani B. Oral manifestations in patients with diabetes mellitus. *World J Diabetes.* 2019 Sep 15;10(9):485-489.
- Genco RJ, Borgnakke WS. Diabetes as a potential risk for periodontitis: association studies. *Periodontol 2000.* 2020 Jun;83(1):40-45.
- Sadeghi R, Taleghani F, Mohammadi S, Zohri Z. The Effect of Diabetes Mellitus Type I on Periodontal and Dental Status. *J Clin Diagn Res.* 2017 Jul;11(7):ZC14-ZC17.