

## REVIEW



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## The assessment of two-way relationship between periodontal diseases and diabetes mellitus.

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### Abstract

Periodontal disease and diabetes mellitus have been said to have a two-way relationship, with diabetes leading to oral disease and periodontitis exacerbating hyperglycemia. The universal biologic mechanisms and demographic and behavioral risk drivers, underlying these associations in both directions, are also described.

Both the diseases are chronic and they are affecting large population worldwide. Periodontitis is also recognized as the sixth major complication of diabetes, while diabetes mellitus is a metabolic disorder which has an impact on the global health and plays a crucial role in the pathogenesis of periodontitis.

The aim of this article is to illustrate a systematic and comprehensive analysis of the literature, on the mutual relationship between diabetes mellitus and periodontal diseases, trying to identify if the prevalence of periodontitis is higher in diabetics or if the incidence of diabetes is greater in patients with periodontal disease. Moreover, our intention is to increase the level of awareness of diabetologists and dentists about the interaction between this two pathologies.

Oral and periodontal health should be promoted as integral components of diabetes management. Dental professionals can detect unrecognized potential dysglycemia and refer for medical examination. Furthermore, the control of periodontal disease may enhance glycemic control which contributes to a better control of periodontal disease.

**Keywords:** periodontal disease, diabetes mellitus, two-way relationship.

### Introduction

The oral cavity hosts an environment rich in bacteria, generating the mouth microbiome, which in pathogenic conditions can lead to alterations in oral soft and hard tissues, changes that can reflect specific systemic disease. If so far, the traditional pattern was to focus only on the oral cavity, recently there has been a change. Until now, diseases in the oral cavity were diagnosed and treated as loco-regional conditions, but the current trend is to find correlations between the pathogenesis of the oral cavity with systemic diseases and microflora elsewhere in the body, a different approach called systemic connection [1].

Periodontal disease is a group of chronic, inflammatory and microbial-induced conditions, normally manifesting in two major types, gingivitis and chronic periodontitis. Both types of periodontal disease have a bacterial etiology with gram-negative anaerobes predominating as periodontal pathogens [2, 3].

Gingivitis is an inflammation of the gums induced by biofilm or bacterial plaque, which is reversible, but can progress to individuals susceptible to chronic periodontitis. Gingivitis is treated clinically after the interruption of the mechanical action of the biofilm, usually through efficient and regular oral hygiene [2, 3].

Chronic periodontitis occurs in vulnerable people with prolonged accumulation of supra and subgingival bacterial plaque. The chronic presence of plaque results from the enrichment and maturation of the biofilm, causing continuous, uninterrupted inflammation, and, therefore, a permanent damage. Chronic periodontitis is characterized by the irreversible loss of the supporting structures of the tooth, including the fibers of the connective tissue at the gingival level, the periodontal ligament and the alveolar bone. This local, irreversible destruction of the marginal periodontium tissues, in severe cases, can lead to tooth loss [2, 3].

From an etiological, pathological, clinical and therapeutic point of view, diabetes mellitus is a heterogeneous syndrome. Diabetes mellitus is characterized by chronic hyperglycemia caused by decreased insulin secretion or insulin resistance of various tissues, especially muscle, fat and liver. As a result of hyperglycemia, insulin deficiency and hyperinsulinemia, a secondary manifestation of insulin resistance, there are also changes in protein, lipid and hydroelectrolytic metabolism. These changes, ultimately, lead to a complex disorder of the body's energy metabolism. Hyperglycemia and other associated abnormalities produce severe acute and chronic complications, altering the quality and reducing the duration of the patient's life [4].

In the oral cavity, periodontal disease is the most important complication of diabetes. However, a number of other lesions and oral disorders have been detected in patients with diabetes [5].

Given the linkage between the periodontal disease and diabetes mellitus, two entities which interact continuously, we intended to review the existing literature, asking the subsequent question: Is there any association between diabetes mellitus and the prevalence of periodontal disease or is the incidence of diabetes mellitus greater in patients with periodontitis?

Such interdisciplinary, patient centered care, could contribute to improved health, wellbeing and quality of live in people worldwide.

## Material and methods

We performed a bibliographic search on PubMed database, reviewing the interrelationship between diabetes and periodontal diseases.

The literature search was made using the following keywords: diabetes mellitus, glycated hemoglobin or metabolic control and periodontal disease, periodontitis or gingivitis.

Our attention was turned to the studies that follow the interaction between this diseases.

The inclusion criteria were articles or books, written in English and Romanian, containing the keywords mentioned. We included in our review researches performed on human subjects. We have excluded the papers that were published in other languages, than English or Romanian. The articles were selected and analyzed by a single reviewer.

We researched ninety seven documents from the examined topic.

The researched items were published from 1967 to 2016. Duplicates were eliminated, and the remaining articles, with potential abstracts and titles, were filtered, based on the inclusion and exclusion criteria. Of the total papers found, based on our search strategy, we chose thirty seven, which met the inclusion criteria. In our study were included thirty two articles and five books.

The articles have been divided as follows: thirteen were reviews of literature, two were comparative studies, one cross sectional study, a case control study and the other fifteen did not belong to a certain category.

Articles presenting various classifications for diabetes and periodontitis used over the years, varying clinical and radiographic criteria used to assess periodontal disease prevalence, extent and severity, evolving standards for the degree of glycemic control and changing methods for assessing complications associated with diabetes were included in our research.

## Results

Repercussions of diabetes mellitus on the periodontium.

Several studies have thoroughly investigated the influence of diabetes on oral wellness. In this context, the levels of glycemia have been shown to be peculiar, and cannot be overlooked [6, 7].

It was found that individuals with diabetes present local irritation such as increased gingival bleeding, enlarged gingiva, increased probing depths, considerable loss of attachment, more tooth loss caused by

increased tooth mobility and tendency towards greater alveolar bone loss [8].

Prolonged exposure to hyperglycemic condition results in decreased fibroblast proliferation, decreased collagen synthesis, enhanced collagen glycosylation and cross linkage resulting in defective collagen metabolism. Normal collagen is, therefore, replaced by highly polymerized and cross linked collagen. Increased collagenase activity results in excess removal of gingival collagen fibers. Vascular basement membrane thickening and alteration, narrowing of the lumina of the capillaries and precapillary arterioles and vascular degeneration of the gingiva leading to reduced oxygen consumption and oxidation of glucose. These angiopathies contribute to hampered delivery of nutrients to the surrounding tissues and inadequacy elimination of waste products necessary for maintenance of gingival tissues.

All the above referred mechanisms, contribute to aggressive removal of connective tissue and severe periodontal destruction [9].

The impact of periodontal diseases on diabetes mellitus.

As diabetes can cause alterations of the periodontal structures, the conditions of the supporting tissues of the tooth can also be unfavorable in the control of the glycemic level in the patients with diabetes.

The first testimony that confirms this theory emerges from the exploration started on people who belonged to the indigenous population of the Gila River in New Mexico. At the beginning of the study, it was found that severe periodontitis is associated with poor blood sugar control, with glycosylated hemoglobin of over 9.0%, being an unfavorable circumstance, even suggesting that severe periodontitis is a factor that destroys diabetes management [10].

The major characteristic of periodontitis is chronic inflammation of the periodontal tissues, inflammation that can contribute to insulin resistance or irregular blood sugar levels [11]. Chronic inflammation is considered to

link impaired oral health to poor blood sugar control [12].

Gram-negative microorganisms, which cause chronic periodontal infections, may increase insulin resistance. Some of these, such as *Prevotella intermedia*, *Porphyromonas gingivalis* or *Tannerella forsythensis*, increase levels of C-reactive protein (CRP), fibrinogen and interleukin 6 (IL-6) [13].

Additionally, systemic bacteremia can have an individual contribution in worsening the inflammation. It is well known that diabetes and insulin resistance, atherosclerosis and obesity are bounded by a prevalent agent, which is chronic inflammation. In this context, insulin sensitivity can be improved by blocking tumor necrosis factor (TNF- $\alpha$ ). This factor is interrelated with the production of interleukin 6 (IL-6) and C-reactive protein (CRP) [14]. It has been suggested that tumor necrosis factor (TNF- $\alpha$ ) may be responsible for the interconnection between diabetes and periodontal disease. Increasing the level of tumor necrosis factor (TNF- $\alpha$ ), plays an important role in stimulating fibroblasts, synthesizing degrading enzymes of osteoclasts and cellular matrix, resulting in active bone resorption [15, 16].

Recent evidence suggests, that chronic infections like periodontitis, may induce a chronic state of insulin resistance, which would then lead to poor glycemic control and contribute to the cycle of hyperglycemia, non-enzymatic irreversible glycosylation, AGEs of protein binding with further accumulation [17].

## Discussion

From the total of articles researched in this review, eighteen were related to the impact of diabetes mellitus on the periodontium, while nineteen of them studied the implication of periodontal disease on diabetes mellitus.

The relationship between diabetes and periodontal diseases has been the subject of many articles. Underlying the two-way relation between these diseases and act accordingly, could improve their screening and

management, with important benefits for the patients.

Countless epidemiological studies bring diabetes to the fore, as the major risk factor for periodontitis, the risk of developing periodontal disease, being even greater the weaker the metabolic control. Patients with poor blood glucose control will therefore have an extremely high risk of suffering from gingival and periodontal disease, and complications can lead to massive bone resorption at the alveolar ridges. This category of patients are also exposed to micro and macrovascular complications [18, 19].

The study of the prevalence of diabetes and the multitude of clinical cases existing in oral pathology, led to the conclusion that diabetes has the greatest impact on the oral cavity, being the most important systemic condition identified in the personal pathological history of patients presenting to the dental office [5]. Research conducted by Ervasti and colleagues has shown that in patients with poor diabetes control, gingival bleeding is more pronounced, compared to subjects in the control group, which included patients without diabetes or diabetic patients with good blood sugar control [20]. In the non-insulin dependent patient, gingival hypertrophy was detected, an oral pathology that was not present in those without diabetes. Untreated gingivitis can advance to periodontitis, which also has been detected in patients with poor blood sugar control [21].

Indian researchers have identified in patients with HbA1c > 8, increased depth of pocket probing depths and loss of gingival attachment, accompanied by abundant bacterial plaque and increased gingival inflammation, compared to patients with HbA1c ≤ 7 or HbA1c = 7-8 [22]. Following the two-year study, these researchers concluded that the risk of alveolar bone resorption is eleven times higher in patients with poor glycemic control, compared to subjects in the control group [23].

In young patients diagnosed with various forms of periodontitis, higher values of

glycated hemoglobin have been reported [24, 25]. Poor glycemic control, over two to five years, substantially increases the depth of periodontal probing and loss of gingival attachment, in diabetic patients, compared to patients with good metabolic control [26].

At the same time, a case-control study, recently elaborated, showed that children with diabetes lose gingival attachment remarkably widely, compared to young patients without diabetes [27]. Furthermore, research on epidemiological problems, has reflected a higher prevalence and harshness in the loss of gingival attachment and bone degeneration in diabetic adults [28, 29]. To determine the risk of osteolysis, the researchers conducted a two-year study, concluding that this risk is four times higher in patients with non-insulin dependent diabetes, than in patients without diabetes [30].

A longitudinal study, conducted over two years, showed that deep marginal periodontitis encountered in diabetic patients, deteriorates up to six times, the control of blood sugar [23]. After analyzing 25 reviews, it was concluded that a timely established treatment, in a proper way, helps to reduce glycemic (HbA1c) levels, by up to 0.9% [31].

Other systematic investigations, conducted during 2010, by analyzing data from articles in Cochrane databases, supported the same idea that is maintaining blood sugar under control, after the treatment of diseases of the superficial or deep marginal periodontium [32]. However, in order to maintain good clinical results and steady glycemic values, in laboratory investigations, requires a sustained periodontal treatment, performed periodically, at intervals of at least six months [33].

It is rational to suppose that poor glycemic control forecast a shortfall in periodontal disease management, especially that the impact of poor glycemic control is well known in severe periodontitis. At the same time, periodontal disease, can be triggered, as a consequence or complication of diabetes [34].

A number of researchers have focused on investigating non-oral complications of

diabetes, showing that cardiovascular complications, retinopathy and diabetic neuropathy, or proteinuria, have been more severe, when combined with periodontal disease [35].

Because periodontal disease is not accompanied by pain, at least in its infancy, most people do not realize that they suffer from periodontal disease, until the disease affects the supporting structures of the tooth and the destruction is marked. In order to maintain oral health in diabetic patients, early treatment of infections located in the superficial or deep periodontium is mandatory.

The treatment of periodontal disease will have a positive effect in maintaining glycemic control and limiting diabetic complications [36]. Most diabetologists support the existence of a close link between oral and systemic health, considering that an interdisciplinary, dental treatment, would have a positive impact for these patients [37].

## Conclusions

According to published reviews, it is obvious that there is an association between diabetes and periodontal disease. Patients with diabetes have a higher risk of developing periodontal lesions, specifically when there is no glycemic control. This category of patients will come to the dental office in dire need of periodontal treatment. All diabetic patients should benefit from routine consultations and preventive dental treatment, through professional hygiene of the oral cavity, in order to maintain oral health, in the general context of a healthy lifestyle.

The treatment of gingival and periodontal diseases, as well as their prevention, should be seen as an indispensable part in the management of diabetes mellitus. For this reason, the prevention of periodontitis in patients at risk of developing diabetes is required. Diabetic patients with poor metabolic control should be consulted more often, precisely if periodontal disease is already present. It is shown that the management of blood glucose levels and keeping them under

control, has its benefits for periodontal tissues, while the treatment of periodontal pathology improves the metabolism of diabetic patients.

Therefore, the clinical correlations between these two conditions should be further investigated, through various clinical and laboratory studies. Now is the time to be aware of this two-way relationship, between diabetes and periodontal disease, to be conscious of it and to treat it with the utmost importance, as a local condition in the oral cavity can influence the general condition of the body, and vice versa.

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