# Periodontitis una enfermedad multifactorial: Diabetes Mellitus

Periodontitis a multifactorial disease: Diabetes Mellitus

Periodontite uma doença multifatorial: Diabetes Mellitus

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## Resumen

La periodontitis es una enfermedad multifactorial, en la cual la placa bacteriana es el factor iniciador, influyendo a la vez factores locales como sistémicos. La diabetes es una enfermedad sistémica debida a una disminución de la secreción de la hormona insulina o a una deficiencia de su acción.

Objetivo: el propósito de este trabajo es explicar algunos conceptos básicos que ayuden a la compresión de la asociación bidireccional de la enfermedad periodontal con Diabetes Mellitus,

con base en los hallazgos científicos encontrados. Con el objetivo de conocer, tratar y cuidar la salud de un paciente diabético.

Metodología: se realizo una búsqueda bibliográfica en base de datos (pubmed, periodontology 2000, medline, scielo, elsevier, intramed, j periodontol, etc.) nacionales e internacionales, utilizando palabras claves.

Resultados: se escogieron 55 artículos para el estudio, destacando el objetivo de este trabajo que es la relación entre Diabetes Mellitus y enfermedad periodontal y viceversa.

Discusión/Conclusión: la asociación entre Diabetes Mellitus y periodontitis se ha reportado en numerosos estudios, al igual que en estudios en animales sugieren que la presencia de una condición tiende aumentar el riesgo y la severidad de la otra.

Palabras clave: Diabetes Mellitus, periodontitis, hiperlipidemia.

## Abstract

Periodontitis is a multifactorial disease, in which plaque is the initiator factor, influencing both local and systemic factors. Diabetes is a systemic disease due to a decrease in the secretion of the hormone insulin or a deficiency of its action.

Objective: The purpose of this paper is to explain some basic concepts that help to understand the bi-directional association of periodontal disease with Diabetes Mellitus, based on the scientific findings. In order to know, treat and care for the health of a diabetic patient.

Methodology: a bibliographic search was carried out in national and international databases (pubmed, periodontology 2000, medline, scielo, elsevier, intramed, j periodontol, etc.) using key words.

Results: 55 articles were chosen for the study, highlighting the objective of this work is the relationship between Diabetes Mellitus and periodontal disease.

Conclusion: The association between Diabetes Mellitus and periodontitis has been reported in numerous studies, as in animal studies suggest that the presence of one condition tends to increase the risk and severity of the other.

Key words: Diabetes Mellitus, periodontitis, hyperlipidemia.

#### Resumo

A periodontite é uma doença multifatorial em que a placa é o fator inicial que influencia fatores locais e sistêmicos. A diabetes é uma doença sistémica devido a uma diminuição da secreção da insulina ou da hormona a uma deficiência de acção.

Objetivo: O objetivo deste artigo é explicar alguns conceitos básicos que o ajudarão a compreensão da associação bidirecional da doença periodontal com Diabetes Mellitus, com base em descobertas científicas. A fim de compreender, tratar e cuidar da saúde de um paciente diabético.

Métodos: Um banco de dados de pesquisa literatura (PubMed, periodontia 2000, o Medline, Scielo, Elsevier, Intramed, j Periodontol, etc.) nacional e internacional, foi realizada utilizando palavras-chave.

Resultados: 55 artigos foram seleccionados para o estudo, com destaque para o objectivo deste trabalho é a relação entre a diabetes mellitus e doença periodontal e vice-versa.

Discussão / Conclusão: A associação entre diabetes mellitus e periodontite foi avaliado em diversos estudos, como os estudos em animais sugerem que a presença de uma condição, tende a aumentar o risco e gravidade da outra.

Palavras-chave: Diabetes Mellitus, periodontite, hiperlipidemia.

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# Introduction

Periodontitis is a multifactorial disease, characterized by chronic inflammation caused by bacterial microorganisms in a biofilm, causing progressive destruction of the dental support apparatus: loss of the periodontal ligament, bone destruction, periodontal pocket formation, gingival recessions and tooth loss.

Gingivitis and periodontitis are diseases that are initiated by a bacterial challenge with the reversible inflammation of gingivitis progressing to destructive periodontitis, driven by a complex unbalanced host response to the bacterial challenge. This response may be influenced by a number of risk factors that will affect susceptibility to disease development, rate of disease progression and even response to treatment.

(Miguel, P., Niño, A., Batista, K. 2016) Periodontitis is undoubtedly the most significant of these diseases, as it causes dental loss.

Periodontal diseases are believed to be the most common chronic inflammatory conditions in the world with an overall prevalence of periodontitis in the US. UU., Estimated in the range of 47% in adults aged 30 years or more. The World Health Organization (WHO) Oral Health Fact Sheet reports severe periodontal disease, which can result in tooth loss, in 15-20% of middle-aged adults (35-44).

Nowadays and after numerous epidemiological studies, the concept of the existence of certain risk factors that are to modulate the susceptibility or resistance of the host to suffer periodontal disease is accepted, therefore, in its development will be intervened several causes considering said Pathology of multifactorial etiology.

(Ghiotto G. et al. 2012) al igual que (Xiaodong, Z, Wenyi, Z., Xiaoli, L., Wu, Z., Yiming, L., 2015) Report that Diabetes Mellitus (DM) is undoubtedly a group of metabolic disorders characterized by hyperglycemia caused by defects in insulin secretion, insulin action, or both. There are two main types of diabetes: type 1 diabetes and the most common type 2 diabetes.

Data from epidemiological studies, as well as all animal studies suggest that the presence of one condition tends to increase the risk and severity of the other. It is widely accepted that

Diabetes Mellitus is a risk factor for increasing the prevalence and severity of periodontitis. (Tan, W., Tay, F., Lim, L, 2006).

Diabetes Mellitus is a risk factor for periodontitis; in turn, the metabolic control of diabetics is hampered by the presence of periodontal infection, increasing the risk of chronic complications and possibly diabetes mortality (Jiménez, T., Licea , M., 2013).

# Periodontal disease: multifactorial

Periodontitis is a multifactorial disease, caused by the prolonged presence of a subgingival biofilm, creating a chronic inflammation in the periodontal tissues causing destruction of them. In the progression of periodontal disease, a variety of causes and risk factors influence: social and behavioral factors, psychological factors, genetic factors, plaque microbial composition, dental factors, endocrine factors, systemic diseases, genetic diseases, hygiene problems, And sociodemographic, although only some of them have scientific evidence showing a causal relationship with periodontitis.

## Periodontitis and the relationship with Diabetes Mellitus

The association between diabetes mellitus and periodontitis has been reported in numerous studies. It is generally accepted that the interrelationship between Diabetes Mellitus and periodontitis is a two-way relationship. Data from epidemiological studies, as well as all animal studies suggest that the presence of one condition tends to increase the risk and severity of the other. It is widely accepted that Diabetes Mellitus is a risk factor for increasing the prevalence and severity of periodontitis. Conversely, periodontitis is an important factor in increasing the risk of complications of diabetes in patients with diabetes. (Jimenez, 2013, Herrera, SEPA, Dominguez 1993).

Although the epidemiological association between periodontitis and diabetes is relatively clear, the biological mechanisms of the association are still inconclusive. Subjects with DM, especially with a poorly controlled glycemic state, have a more severe and generalized periodontitis. Efforts to determine the mechanisms that give a higher incidence of periodontitis in DM focused on the differences in the subgingival microbiota. One report suggests that hyperglycemia is associated with an altered subgingival microbiota (Piyamas, A. et al. 2013).

(Xiaodong, Z, et al. 2015) He reads a series of studies. Epidemiological studies generally suggest an increased risk of periodontitis among people with Diabetes Mellitus. Nelson et al. (1990) found in their study that Arizona Pima Indians have a very high prevalence of Type 2 Diabetes Mellitus. In a subgroup of this population aged 15-54, the prevalence by age and sex adjusted for disease Periodontal disease was 60% in diabetic patients, while the rate was 36% in those of non-diabetic individuals. Similarly, in a study among African-Americans Gullah in South Carolina, 70.6% of diabetic patients had moderate periodontitis, which was much higher than the 10.6% prevalence among African Americans without diabetes (Fernandes et al. . At the international level, a study (Weinspach et al., 2013) in the German population reported that type 2 diabetic patients had a significantly higher periodontal detection rate than non-diabetic controls (3.52 vs 3.26, p <0.01) 0.8. A study (Al-Khabbaz et al., 2013) of cases and controls revealed that periodontal disease was more evident in children (4-14 years) with Type 1 Diabetes Mellitus in Kuwait than those who did not have diabetes. Plaque index, gingival index and catheter bleeding were significantly higher in patients with diabetes compared to non-diabetic control subjects.

#### Mellitus diabetes

The World Health Organization WHO (1999) says that diabetes mellitus is a metabolic disorder that has several causes; Is characterized by chronic hyperglycemia and metabolic disorders of carbohydrates, fats and proteins as a result of abnormalities of the secretion or effect of insulin. Over time, the disease can cause damage, dysfunction and insufficiency of various organs.

The two major forms of type 1 and type 2 diabetes mellitus, share clinical manifestations, but are characterized by having a different causality. Type 1 diabetes occurs when BETA cells in the pancreas are destroyed and an insufficient amount of insulin is produced. In most cases, type 1 diabetes is the result of an autoimmune inflammation, with destruction and apoptosis of the cells. Approximately 90% of patients with diabetes have type 2. The development of type 2 diabetes is directly related to the increase in the amount of visceral adipose tissue. Adipose tissue is considered an active hormone-regulating organism, which releases metabolically active molecules that can inhibit the body's ability to respond to insulin, which is called insulin resistance (Graves, D., Liu, R., Oates , T., 2008).

According to Roglic (quoted in Robles 2015). Type 2 Diabetes Mellitus (DM2) is a growing public health problem around the world. Since 2008, diabetes has been ranked as the seventh leading cause of death in the United States, with estimated annual direct costs of \$ 245,000,000,000. The International Diabetes Federation (Roglic, Unwin, 2010) reports that 4.6 million people between the ages of 20 and 79 died from diabetes in 2011, representing 8.2% of global mortality. What with respect to the calculations for the year 2010 represents an increase of 13.3%; Antecedents that increase the importance of early research, diagnosis and timely referral. In Latin America, there are 15 million people with Diabetes Mellitus and this figure is expected to reach 20 million in 10 years.

Today, approximately 20.4 million American adults have diabetes, with one-third of undiagnosed cases. In a study conducted in 2013 by DPTT (Design Features of the Diabetes and Periodontal Therapy Trial), the objective was to determine the effect of non-surgical periodontal therapy on Glycated Hemoglobin (HbA1c) in individuals with T2DM and chronic periodontitis compared With no treatment. We hypothesized that participants who received therapy would experience a 0.6% reduction in HbA1c compared to untreated controls. The DPTT was a multicenter, single-blind, randomized, controlled clinical phase III trial. Participants with moderately-controlled and moderate diabetes to advanced periodontitis were randomized to receive immediate or delayed periodontal treatment. Participants were assessed at baseline and at 3 and 6 months after randomization for multiple measures of diabetes and periodontitis control. The outcome of the primary study was the change in HbA1c from baseline to 6 months after the visit. This result, demonstrated to control the state of diabetes and in turn is associated periodontal disease with the risk of complications related to DM. Secondary outcomes included: HbA1c change from baseline to 3-month visit, change in clinical measures of chronic periodontitis (gingival index, catheter bleeding, depth of catheterization, loss of clinical insertion) at 3 and 6 months or Depth of catheterization, loss of clinical insertion and bleeding in catheterization. They are standard clinical measures used to evaluate the periodontal status of the individual (Nunn ME 2004). The exact mechanisms by which periodontal disease and its treatment may affect glycemic control in patients with type 2 diabetes have not been fully elucidated. A popular hypothesis involves inflammatory pathways common to the pathogenesis of periodontitis and insulin resistance. Specifically, Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-alpha), which are present in inflamed periodontal tissues, are known to adversely affect insulin signaling and action. Both IL-6 and TNF-alpha can enter the systemic circulation in patients with periodontitis, where over time they may alter insulin sensitivity in the target organs. Therefore, it is biologically plausible that a periodontitis can exacerbate glycemia in patients with T2DM and that treatment, by reducing levels of circulating cytokines, may improve glycemic control (Goldberg, 2007; Martins, 2009).

# Diabetes Mellitus and hyperlipidemia

Hyperlipidemia is a group of disorders characterized by an excess of lipids in the bloodstream. Patients with hyperlipidemia often exhibit elevations of Low Density Lipoproteins (LDL), triglycerides (TRG) and omega-6 free fatty acids. The elevation of omega-6 polyunsaturated fatty acids, in turn contributes to the formation of LDL / TRG. Hyperglycemia is often accompanied by hyperlipidemia in type 1 and type 2 diabetes. A number of studies have reported increased total cholesterol, TRG, LDL, and decreased HDL in diabetic patients (Xiaodong, Z, et al. 2015).

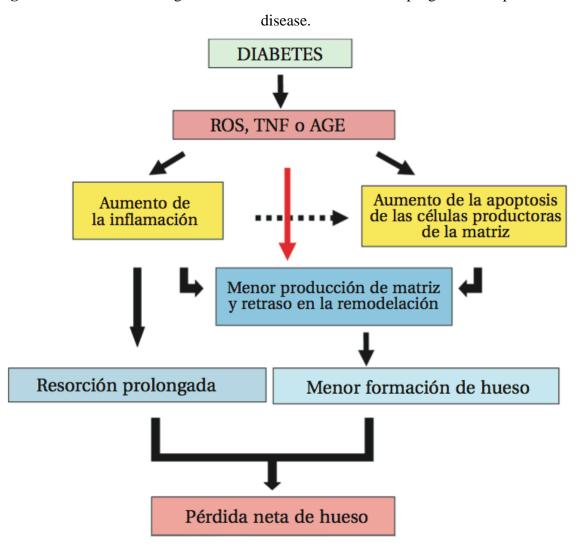
## **Diabetes and inflammation**

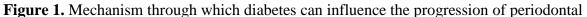
(Graves et. al 2008) Both type 1 and type 2 diabetes are associated with elevated systemic inflammatory markers. An increased serum concentration of Tumor Necrosis Factor (TNF-alpha) and Interleukin 6 (IL-6) has been demonstrated in diabetes. DM alters the inflammatory response to oral pathogens. For example, human gingival crevicular fluid in patients with type 1 diabetes and periodontal disease has a high concentration of Prostaglandin E2 (PGE2) and IL1-BETA compared to gingival crevicular fluid in non-diabetic patients with a similar degree of disease Periodontal disease. In addition, isolated monocytes from periodontal patients with type 1 diabetes produce significantly higher amounts of TNF-alpha, IL1-BETA, and PGE2 in response to lipopolysaccharide (LPS) compared to non-diabetic patients.14 The Biological Functions of Cytokines Are related to periodontiis, diabetes and lipid metabolism. Several authors agree that: 1) Cytokines are associated with insulin resistance and the risk of diabetes. 2) High levels of pro-inflammatory cytokines in periodontal tissues are associated with the risk of periodontitis because of their destructive tissue effects. 3) Cytokines exert effects on lipid metabolism by affecting the production of other cytokines, resulting in elevated levels of free

fatty acid, LDL and TRG. The effects of serum lipid elevation are due to increased hepatic TRG production and / or decreased clearance of TRG.

## Diabetes: wound healing

(Torres, 2007; Graves, 2008) It has been adequately documented that wound healing is delayed or incomplete in diabetics, which has also been demonstrated in animal models with diabetes. Several cellular mechanisms have been proposed, such as reduction or dysfunction of Polymorphonuclear Leukocytes (PMN) and macrophages, maintenance of cytokine expression and inflammatory cell infiltrate, reduction in the production of growth factors, Cell proliferation and extracellular matrix synthesis, as well as increased production of proteolytic enzymes (Figure 1).





Source: (Graves et. al 2008).

Synthesis, maturation and collagen homeostasis appear to be affected by glucose levels. In addition to finding decreased collagen production in association with diabetes, researchers have also found increased collagenase activity in gingival tissue in animals (Kumar M., Mishra L., Mohanty R., Nayak R., ). In some studies it was shown that the glycosylation of the preexisting collagen in the wound margins decreases its solubility altering its remodeling and in addition on the other hand the greater collagenase activity existing in the diabetic degrades the new synthesized collagen delaying and making it difficult to heal the wound. (Torres et al 2007).

Mealey & Ocampo (2008) Stated that the potential impact of elevation of systemic proinflammatory mediators in patients with diabetes is high. Systemic inflammation is significantly elevated in the presence of obesity, insulin resistance, hyperglycemia, and diabetes.

(Graves et al., 2008) An investigation by He H. and Liu R. in 2004 was carried out in diabetic and normal mice to know the healing response after tissue destruction induced by Porphyromonas Gingivalis. An inflammatory reaction was triggered as Porphyromonas Gingivalis was inoculated dead in the scalp of the mice, the results were shown that Diabetes Mellitus modifies the response to the bacteria increasing the number of fibroblasts positive for activated caspase 3, as well as the number Of apoptosis of the fibroblasts at the time of maximum healing. Therefore, the increase in apoptosis of these cells coincided with the reduction in the number of fibroblasts and with the decrease in the matrix producing capacity, therefore a greater delay in remodeling and restructuring, causing prolonged resorption, less bone formation, Both obtaining net loss of bone.

The increase in the apoptosis of these cells coincided with the reduction in the number of fibroblasts (Al-Mashat, H., Kandru, S., Liu, R., Behl, Y., Desta, T. & Graves, And with a decrease in matrix production capacity. Diabetes also led to a global induction of proapoptotic genes during the repair process. Of a total of 276 apoptotic genes examined, 71 genes increased twice or more, so that 63 of them were proapoptotic and 8 were antiapoptotic. This points to another mechanism by which diabetes can interfere with the ability to repair tissue damage by potentiating the death of matrix-producing cells.

#### How to identify a diabetic patient

Dentists are often not aware of the details of the situation and management of DM in their patient, and doctors do not usually evaluate the periodontal condition of their patients. That is why it is important to follow these steps that will help give an early diagnosis:

• It is important that the operator performs a detailed and profound anamnesis.

• Be direct with the patient in questions involving DM if it is suspected. What type of diabetes do you have? Since when does it suffer? Are you taking medication? Last date of clinical study? HbA1c values you manage? How many more in your family?

• Observe the patient from the moment he enters the office if he comes trembling, agitated, anxious, perspiration or tachycardia.

- Watch your limbs for scaling or dry or bruised skin.
- Weigh and measure the patient, and assess their physical condition.
- Perform a thorough oral review. It can be observed a series of changes in the mouth in the influence of the DM on the periodontium such as: gingival enlargement, sessile or pediculated gingival polyps, polypoid gingival proliferations, abscess formation, periodontitis and loss of dental bone support, increased insertion loss, Dental mobility, spontaneous hemorrhage to the sounding. Within the secondary alterations, it is possible to observe buccal alterations such as: a higher index of caries, queilosis, desiccation and cracking of the mucous membranes, buccal and lingual burning, lower salivary flow and alterations of the buccal flora, predominance of Candida Albicans, hemolytic streptococci and Staphylococci.

Perform laboratory tests for diagnosis:

Porcentaje	Estado	
4 - 6 %	Normal	
< 7 %	Control adecuado de DM	
7 - 8 %	Control moderado de DM	
> 8 %	Mejorar el control de DM	

Table 1. Glycosylated hemoglobin test (HbA1c).	Table 1.	Glycosylated	hemoglobin	test (HbA1c).
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Criteria of the American Diabetes Association for the diagnosis of Diabetes Mellitus, impaired glucose tolerance (ATG) and impaired fasting glucose (AGA).

1. Symptoms of diabetes plus random plasma glucose (no fasting)  $\geq 200 \text{ mg} / \text{dl}$ . Random glucose can be obtained at any time of the day since the last meal.

- 2. Fasting plasma glucose  $\geq$  126 mg / dl. The normal fasting is 70-100 mg / dl.
- Two-hour postprandial glucose ≥ 200 mg / dl during an oral glucose tolerance test. The normal is <140mg / dl.</li>

# Mouth and periodontal manifestations of the disease

#### Uncontrolled diabetics:

- 1. Dry mouth.
- 2. Diffuse erythema of the mucosa.
- 3. Saburral and red tongue, with marginal indentations.
- 4. Tendency to formation of periodontal abscesses.
- 5. "Diabetic periodontoclasia" and "diabetic stomatitis".
- 6. Enlarged gypsum.
- 7. Sessile or pedicled gingival polyps.
- 8. Sensitive, swollen, gingival papillae that bleeds deeply.
- 9. Polypoid gingival proliferations and loosening of teeth.

10. Increased frequency of periodontal disease with alveolar destruction, both vertical and horizontal.

11. Diabetics have less resistance to infections, although it is unclear whether they have a higher real frequency of infection, or if once contracted, infections thrive. This susceptibility to infections would prove to be a combination of microangiopathy, metabolic acidosis and ineffective phagocytosis of macrophages.

12. Alterations in the flora of the oral cavity with greater prevalence of Candida Albicans, Hemolytic Streptococcus and Staphylococcus.

13. Altered rash patterns.

- 14. Increased tooth sensitivity to percussion.
- 15. Increased incidence of enamel hypoplasia.
- 16. Increased incidence of caries (Torres 2007; Artuña).

#### Periodontal treatment in diabetics

Although some studies failed to observe the relationship between glycemic control and periodontitis, most studies generally support that good glycemic control decreases the severity of periodontitis, whereas poor glycemic control increases The risk of periodontitis (Bustamante 2013).

#### Do diabetic patients respond well to periodontal treatment?

Numerous studies of subjects with DM2 and periodontitis have shown improvement in metabolic control (decrease in 0.9-1% of glycosylated hemoglobin [HbA1c]) after being subjected to conventional periodontal treatment, with or without antibiotics, probably due to the decrease of IL-6, TNF-alpha, polymerase chain reaction (PCR), leptin and increased levels of adiponectin (Bustamante 2013). Recent studies have shown that intensive non-surgical periodontal treatment (6 hours of root and root polishing with an ultrasonic instrument) produces a significant increase in the systemic inflammatory response in subjects with periodontitis and general good health (Pavez et. al 2011).

• As part of their initial evaluation, patients with type 1, type 2 and gestational diabetes (GDM) should receive a full oral examination that includes a thorough periodontal examination (Zerón, A 2013).

- The patient should be asked to have a Glycated Hemoglobin (HbA1c) test.
- The patient should carry his glucose meter at each visit.

- Always bring your medicine to hand.
- If a surgical procedure is performed, approval of the treating physician will be required.
- Ask the patient to go with food intake whenever he or she visits.
- Perform prophylaxis to reduce bacterial load.
- Techniques of brushing and oral care.
- Use of chlorhexidine 0.12%
- Work by sextants to reduce working time.

• Perform non-surgical Phase I, scraping and smoothing, eliminating bacterial load and infectious foci (extraction of root remains) (Pavez et al. 2011).

• Azithromycin 500 mg every 24 hours for three days (Pavez et al. 2011). Low dose tetracyclines and chemically modified tetracyclines have been shown to significantly decrease collagenase production and collagen degradation. Such as: doxycycline, minocycline and tetracycline hydrochloride these have potential benefits in inhibiting the onset and progression of periodontitis, although it has not been reported on its use in diabetic patients.

- Reassessment of Glycosylated Hemoglobin after treatment.
- Revaluation for flap debridement surgery if the treatment requires it.
- Periodontal screening is recommended annually.

## Justification

There is a range of documented studies, where systemic diseases such as Diabetes Mellitus have a close relationship with oral health, modifying the host's response to periodontal microorganisms and exacerbating periodontal disease. It is for this reason that we believe justified to carry out this study based on the scientific knowledge obtained from the selection of data collected, in order to know, understand and analyze the systemic and oral problems that relate periodontal disease to Diabetes Mellitus.

# Objectives

• Identify the bidirectional relationship between periodontal disease and Diabetes Mellitus.

• Know the two types of illnesses in an individualized way, to later accurately identify how one disease exacerbates the other and vice versa.

- Identify whether Diabetes Mellitus is a risk factor for periodontal disease.
- Identify whether periodontal disease is a risk factor for developing Diabetes Mellitus.

• To know the stages and problems present in the healing of the wound, in a patient with diabetes and periodontitis.

• To identify the different oral and systemic manifestations of a patient with periodontal problems and with Diabetes Mellitus.

• To give more information about the care options and guidelines that must be had in treating these patients to provide them with medical-dental care with sufficient scientific support and better clinical results.

## Methodology

For the accomplishment of this bibliographical revision, a deep search was carried out in national and international database (pubmed, periodontology 2000, journal of periodontology, medline, scielo, elsevier, intramed, j periodontol, google academic). Data were obtained from the library of the Faculty of Dentistry Mexicali, both physical and digital. Using key words like: Diabetes Mellitus, periodontitis, hyperlipidemia.

We obtained 58 articles, of which 18 were discarded, based on the inclusion and exclusion criteria: 25 are bibliographic review, 3 are the result of experiments applied to the control group, 1 meta-analysis, 1 clinical case-control study, 1 cross-sectional study, 1 observational descriptive study, 1 clinical trial, multicenter, blinded, randomized, controlled, 1 epidemiological study, 2 research work, 2 data obtained from internet pages and 2 consensus reviews (Sociedad Española de Periodoncia [ SEPA], American Academy of Periodontology [AAP], European Federation of Periodontics [EFP]). Where articles with a different language

to English or Spanish were excluded, articles that were repeated in another database, articles that did not mention the relationship of both diseases, articles greater than ten years.

Among the inclusion criteria was the reference of articles no longer than 10 years (2006-2016), free and paid access, English and Spanish language, human and animal studies, that the text spoke of the diabetes-periodontitis relationship.

#### Results

The results show that if there is a bidirectional relationship between Periodontitis and Diabetes Mellitus, in which one disease helps to exacerbate the other, most authors agree on the information collected, although more research is needed on how the treatment of Periodontal disease positively helps to level the metabolic control of diabetes.

Diabetes Mellitus is considered a metabolic disorder that must be detected according to the diagnostic criteria proposed by the American Diabetes Association; It is also important that patients with the disease have adequate control of their blood glucose.

(Ghiotto G. et al. 2012) Studies have shown a bi-directional relationship between diabetes mellitus and periodontal disease, so the medical and dental professionals should know these relationships for the adequate diagnosis and treatment of patients.

(Martins N. et al 2007) This meta-analysis of 57 peer-reviewed studies leads to the conclusion that type 2 DM is a risk factor for periodontitis. The overall difference for CAL 1.0 mm (95% CI: 0.15 to 1.84, P < 0.021) was significant. In addition, longitudinal studies revealed significantly more progression of periodontal disease among type 2 diabetics compared to non-diabetics. However, evidence of an association between type 1 DM and periodontitis is insufficient.

(Kumar M. et al 2014) Periodontal diseases and Diabetes Mellitus are closely associated and are highly prevalent chronic diseases with many similarities in pathobiology. Diabetes clearly increases the risk of periodontal diseases, and biologically plausible mechanisms have been demonstrated in abundance. Less clear is the impact of periodontal diseases on the glycemic control of diabetes and the mechanisms through which this occurs. More research is needed to clarify this aspect of the relationship between periodontal diseases and diabetes. (Fajardo M. et al 2016) Diabetes Mellitus is a risk factor for the development of periodontal disease, but the latter may have negative effects on glycemia values. More severe forms of periodontal disease have been associated with elevated levels of advanced glycosylation products. Therefore, poor metabolic control maintained in diabetic subjects contributes to the development and progression of periodontal disease.

(Ross et al., 2010) Recent studies have shown that glucose increased the secretion of LPSstimulated TNF-alpha, IL1-BETA and IL-6 from human U937 macrophages by 6, 4 and 27fold, respectively. Obviously, the increase in IL-6 secretion stimulated by LPS with high glucose is much higher than that of TNF-alpha and IL1-BETA secretion, suggesting an important role of IL-6 in associated periodontal disease To diabetes.

The relationships described in this article linking diet, obesity, diabetes and periodontitis suggests that all health professionals work together to better address the overall health of the world's population, requiring a multidisciplinary approach for prevention, early diagnosis and Optimal care.

The most important oral disease associated with diabetes is the increased prevalence and severity of periodontitis. Persistent poor glycemic control has been associated with the incidence and progression of gingivitis, periodontitis, and loss of alveolar bone.

(*Ryan M. et al 2016*) An extensive review of the literature reveals that there is worldwide evidence that diabetes adversely affects periodontal health.

(Bascones-Martines A. et al 2014) This clearly established that glycemic control improves the periodontal status and control of periodontal infection improves glycaemia in diabetic patients, the clinical implication of this event has yet to be investigated. However, the possibility that both diseases may be sharing some common pathogenic aspects should always be kept in mind to ensure the early diagnosis of both.

(Oana A. et al 2013) Periodontal inflammation leads to an increase in circulating cytokines, inflammatory mediators and the autoimmune response to infection. The severity of periodontal destruction has been shown to be related to the effects of glycemic control, and other factors are also involved. In diabetic patients with periodontal disease, IL1-BETA, IL-6 and TNF

gradually increase with the evolution of Diabetes Mellitus, as well as periodontal bone lesions. A significant correlation between metabolic control and the severity and extent of periodontal lesions has also been reported.

(Vásquez E & López M. 2014) Demonstrates in a clinical case of a patient with poorly controlled type 1 diabetes and generalized aggressive periodontitis, as good glycemic control helps to improve periodontal treatment. Final laboratory tests revealed a glycemic control of 140 mg / dL, compared to baseline values of 220 mg / dL. Periodontal treatment did not present any complications and the metabolic control of their diabetes gave rise to a significant improvement in the periodontal condition.

Observational studies provided consistent evidence of a higher prevalence, severity, extent, or progression of at least one manifestation of periodontal disease in 13/17 reports reviewed (Taylor GW & Borgnakke WS 2008).

The objective of this non-systematic review was to explore and clarify the interrelationships and interactions between periodontal diseases and four common systemic diseases, namely diabetes, respiratory diseases, cardiovascular diseases and osteoporosis.

(Lan-Chen Kuo et al. 2008) Prolonged exposure to hyperglycemia is the main factor responsible for diabetic complications. Periodontal diseases are well established as a complication of diabetes, suggesting that patients with diabetes are more likely to develop periodontal diseases.

(Corbi et al., 2004) To our knowledge, this is the first study to investigate the association between DNA damage through the CBMN test and physical examination, biochemical measurements (metabolic control and pro-lipoprotein), and periodontal clinical parameters In patients who have or do not, 2 diabetes, dyslipidemia and Parkinson's disease. The results presented here indicate an association between type 2 diabetes and DNA damage, with respect to frequency of binucleate cells with micronuclei (MCF), MNF and nucleoplasmic bridges.

(Galvis M. et al. 2012) There is a bi-directional relationship between diabetes mellitus and periodontal disease, as current studies show how poor glycemic control helps to exacerbate periodontal disease, as well as good treatment of this Glycemic control of diabetes. This

relationship has tried to be explained through various theories, whether immunological, microbiological or ethiopathological. Everything indicates that the protagonists of this bidirectional relationship are the AGE, because they participate in the immunological process of both diseases.

## Conclusions

• Periodontal disease is a multifactorial disease and one of the most important risk factors is Diabetes Mellitus.

• It is important that the dentist and other health professionals have a thorough knowledge of diabetes, because of its wide prevalence, obesity is clearly associated with an increased risk of developing diabetes, as the prevalence and incidence of diabetes increase. Diabetes, so do the costs, both financial and morbidity and mortality.

• Patients with diabetes should know that the risk of periodontal disease increases with poorly controlled diabetes. They should also know that if they suffer from periodontal disease, their blood glucose control may be more difficult to manage and they will be at increased risk for complications from diabetes.

• The doctor and dentist must always be related and work as a team to provide the necessary care to the patient with DM and avoid a hypoglycemic shock or a serious infectious spread.

#### Bibliography

- Al-Khabbaz, A., Al-Shammari, K., Hasan, A., Abdul-Rasoul, M., Periodontal health of children with type 1 diabetes mellitus in Kuwait: a case-control study. Med Princ Pract 2013;22(2):144-9.
- Al-Mashat, H., Kandru, S., Liu, R., Behl, Y., Desta, T. & Graves DT. Diabetes enhances mRNA levels of proapoptotic genes and caspase activity, which contribute to impaired healing. Diabetes 2006: 55: 487–495.
- Artuña, V., Manifestaciones orales de la diabetes. URL, http://www.clinidabet.com/es/info/diabetes/02educacion/07educando/01.htm.
- Bascones-Martínez A., Muñoz-Corcuera M., Bascones-Ilundain J. Diabetes y periodontitis: una relación bidireccional, Med Clin (Barc). 2014 http://dx.doi.org/10.1016/j.medcli.2014.07.019
- Bustamante, G., Diabetes y enfermedad periodontal, Rev, act. Clin. Mod.v.31 la paz mayo 2013.
- Corbi S., Bastos A., Orrico S., Secolin R., Dos Santos R., Takahashi C., Scarel-caminaga R., Elevated micronucleus frequency in patients with type 2 diabetes, dyslipidemia and periodontitis, mutagenesis advances Access published september 18,2014, pp. 1-7, doi: 10.1093/mutage/geu043
- Díaz, R., Villegas, F., Diabetes e infección periodontal. Intramed, Revista nacional de odontología año 2 vol. VII, 2010.
- Domínguez, V., Calatrava, L., Ortega, P., Astasio, P., Pérez, L., de pereda, A. & García, J. Enfermedad periodontal en diabéticos juveniles y no diabéticos, Rev. San hig púb 1993, vol 67 no.6
- Fajardo M, Rodríguez O, Hernández M, Mora N. Diabetes mellitus y enfermedad periodontal: aspectos fisiopatológicos actuales de su relación. Rev. Scielo, Medisan Vol.20 No.6 Santiago de Cuba jun 2016.

- Fernandes, J., Wiegand, R., Salinas, C., Grossi, S., Sanders, J., Lopes-Virella, M., et al. Periodontal disease status in Gullah African americans with type 2 diabetes living in south Carolina. J Periodontol 2009;80:1062-8.
- Galvis M., Montoya Y., Saldarriaga A., diabetes y enfermedad periodontal: hacia un modelo clínico bidireccional, revista nacional de odontología, volumen 8, No 14, enero-julio 2012.
- Ghiotto G, López R, Tineo M, Villareal L, Alarcón M, Diabetes mellitus y enfermedad periodontal. Revisión bibliográfica de la situación actual. Rev. estomatol Heradiana. 2012, 22 (3)183-8.
- Graves, D., Liu, R., Oates, T., Inflamación y apoptosis potenciadas por la diabetes: impacto sobre la salud periodontal, Periodontology 2000 (Ed Esp), Vol. 20, 2008, 80-86.
- Goldberg, M., Han, Y., Yan, C., Shaw, M., Garner, W., TNF alpha supresses alpha-smooth muscle actin expression un human dermal fibroblastos, an implication for anormal wound healing. J invest dermatol, 2007,127: 2645-2655.
- Herrera D., Rodríguez-Casanovas H., Herrera J., Informe SEPA/ FUNDACIÓN SED, diabetes y enfermedades periodontales.
- Jiménez, T., Licea, M., Relación entre diabetes mellitus y enfermedad periodontal, revista Peruana de epidemiologia vol 17, núm. 3, diciembre 2013, pp 1-7. Recuperado de http://www.redalyc.org/articulo.oa?id=203129459002
- Kumar M., Mishra L., Mohanty R., Nayak R., Diabetesand gum disease: the diabolic duo, Diabetes & metabolic síndrome: Clinical research & reviews. elsevier 8 (2014) 255-258. Doi: http://dx.doi.org/10.1016/j.dsx.2014.09.022
- Kuo L., Polson A., Kang T., Associations between periodontal diseases and systemic diseases: a review of the inter-relationships and interactions with diabetes, respiratory diseases, cardiovascular diseases and osteoporosis, elsevier public health 2008, 122, 417-433 doi:10.1016/j.puhe.2007.07.004

- Martins, N., Vianna, M., Sansone, C., Sheiham, A., The relationship between diabetes mellitus and destructive periodontal disease: Meta-analysis, Oral health prev dent 2009; 7:107-127.
- Mealy, B., Ocampo, G., Diabetes mellitus y enfermedad periodontal. Periodontology 2000. 2008: 18(1);86-104.
- Miguel, P., Niño, A., Batista, K., Diabetes mellitus y enfermedad periodontal. Rev. Scielo, ccm vol.20 no.2 holguín abr-jun 2016.
- Nunn ME, interpretación de la etiología de la periodontitis: resumen de los factores de riesgo periodontales, periodontology 2000 (Ed Esp), Vol. 7, 2004, 11-23.
- Organización Mundial de la Salud OMS (1999). http://www.who.int/diabetes/actiononline/basics/es/
- Pavez, V., Araya, A., Baksai, N., Respuesta al tratamiento periodontal de diabéticos tipo 2 con mal control metabólico y obesos intolerantes a la glucosa, con periodontitis severa, Rev. Clin. Periodoncia Implantol. Rehabil. Oral Vol. 4(2); 50-53, 2011.
- Piyamas, A., Piyawan, A., Suwimol, T., Quantification of key periodontal pathogens in insulindependent type 2 diabetic and non-diabetic patients with generalized chronic periodontitis, Anaerobe 22 (2013) 64e68. Recuperado de http://www.elsevier.com/locate/anaerobe
- Robles, S., Rosas, C., Herrera, L., Rivas, N., Diabetes y periodontitis, conocimiento en profundidad de la salud de Valdivia 2013. Revista dental de Chile 2015, 106(1)4-8.
- Roglic, G., Unwin, N., Mortality attributable to diabetes: estimates for the year 2010. Diabetes Res Clin Pract. 2010 Jan;87(1):15-9.
- Ross J.H., Hardy D.C., Schuyler C.A., Slate E.H. Mize T.W., Huang Y. Expression of periodontal interleukin-6 protein is increased across patients with neither periodontal disease nor diabetes, patients with periodontal disease alone and patients with both diseases. J periodont Res 2010; 45:688-694.

- Ryan M., Raja V., Diet, obesity, diabetes, and periodontitis: a syndemic approach to management. Curr Oral Health Rep (2016) 3:14-27, Doi: 10.1007/s40496-016-0075-1
- Smith, P., Retamal, I., Cáceres, M., Romero, A., Silva, D., Arancibia, R. & Martínez, C., Diabetes y su impacto en el territorio periodontal. Rev clin, periodoncia Implanton. Rehabil oral Vol.5 (2) 90-92,2012.
- Tan, W., Tay, F., Lim, L., Diabetes as a risk factor for periodontal disease: current status and future considerations. Ann Acad Med Singap 2006;35; 571-81
- Taylor GW., Borgnakke WS., Periodontal disease: associations with diabetes, glycemic control and complications, oral diseases 2008, 14, 191-203. Doi: 10.1111/j.1601-0825.2008.01442.x
- The DPTT study group, S. Engebretson, M. Gelato, L. Hyman, B.S. Michalowicz, E. Schoenfeld, 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, Contemporary Clinical Trials 36 (2013) 515–526. Recuperado de http://www.elsevier.com/locate/conclintrial.
- Torres, M., Díaz, M., la diabetes mellitus y su vinculación en la etiología y patología de la enfermedad periodontal. Gaceta medica espirituana 2007, 9 (2).
- Vásquez E., López M., Tratamiento multidiciplinario en una paciente con periodontitis agresiva generalizada y diabetes mellitus tipo 1, revista odontológica mexicana, vol.18, núm. 1, enero-marzo 2014, pp32-37
- Velea O., Kralev C., Onisei D., Onisei D., Nica L., Velea I., European Scientific Journal march 2013 edition vol.9, N0.9 ISSN: 1857-7881
- Weinspach, K., Staufenbiel, I., Memenga-Nicksch, S., Ernst, S., Geurtsen, W., Gunay, H. Level of information about the relationship between diabetes mellitus and periodontitis results from a nationwide diabetes information program. Eur J Med Res 2013;18:6. http://dx.doi.org/10.1186/2047-783x-18-6.

- World Health Organization. Oral Health Fact Sheet. n. 318, April 2012. Public health solutions for oral diseases are most effective when they are integrated with those for other chronic diseases and with national public health programmes. The WHO Global Oral Health Programme aligns its work with the strategy of chronic disease prevention and health promotion. Emphasis is put on developing global policies in oral health promotion and oral disease prevention.
- Xiaodong, Z., Wenyi, Z., Xiaoli, L., Wu, Z., Yiming, L., Interrelationship between diabetes and periodontitis: Role of hyperlipidemia, archives of oral biology 60 (2015) 667–674. Recuperado de http://www.elsevier.com/locate/aob
- Zerón, A., Consenso Enfermedades Periodontales y Enfermedades Sistémicas, medigrafic, revista Mexicana de periodontología, Vol. III, 2013, Núm. 3. Pp. 99-108. Recuperado de www.medigraphic.com/periodontologia