Relationship between type 2 diabetes and periodontitis
La relación entre la diabetes tipo 2 y la periodontitis

Bruno A. Rodríguez-Ramírez [a], Pamela M. Rodríguez-Ramírez [b]

Abstract:

Diabetes is an endocrine disease characterized by high blood glucose levels mainly classified as diabetes type 1 (DM1) and type 2 (DM2). Periodontitis is an infectious disease that progressively progresses to the destruction of the supporting tissues of the tooth resulting in the loss of dental organs. Both conditions are considered chronic and are different entities that share a bidirectional relationship, with periodontitis being named the sixth complication of diabetes. Worldwide, the independent prevalence is very high and has become a public health problem. Studies have revealed their interaction leading to propose a multidisciplinary treatment in patients with diabetes and periodontitis, since in both situations there are exacerbated inflammatory processes becoming a very powerful combination for dental loss if both or one of them is not controlled and does not receive treatment. More severe periodontitis has been observed in subjects who do not have controlled levels of glycosylated hemoglobin (hAb1c) and this increases in subjects who do not receive periodontal treatment; therefore, the objective of the present literature review is to provide information on the association and risk factors of these conditions and to give guidelines for the creation and development of protocols in the management and multidisciplinary care.

Keywords:

Diabetes, periodontitis, Diabetes mellitus type2, DM2

Resumen:

La diabetes es una enfermedad endocrina caracterizada por altos niveles de glucosa en sangre clasificada en principio como diabetes tipo 1 (DM1) y tipo 2 (DM2). La periodontitis es una enfermedad infecciosa que avanza progresivamente hasta la destrucción de los tejidos de soporte del diente teniendo como resultado la perdida de órganos dentarios. Ambas condiciones son consideradas como crónicas y son entidades diferentes que comparten una relación bidireccional, siendo así la periodontitis nombrada la sexta complicación de la diabetes. A nivel mundial la prevalencia de manera independiente es muy alta convirtiéndose en un problema de salud pública. Estudios han revelado su interacción llevando a proponer un tratamiento multidisciplinario en pacientes con diabetes y periodontitis, ya que en ambas situaciones existen procesos inflamatorios exacerbados convirtiéndose en una combinación muy poderosa para la pérdida dental si ambas o una de ellas no es controlada y no recibe tratamiento. Se ha observado periodontitis más grave en sujetos que no tienen niveles controlados de hemoglobina glicosilada (hAb1c) y ésta se ve aumentada en sujetos que no reciben tratamiento periodontal, por lo tanto, el objetivo de la presente revisión literaria es brindar información sobre la asociación y factores de riesgo de estos padecimientos para y dar pauta a la creación y desarrollo de protocolos en el manejo y atención multidisciplinaria.

Palabras Clave:

Diabetes, periodontitis, diabetes mellitus tipo 2, DM2

INTRODUCTION

Type 2 diabetes mellitus (DM2) and periodontitis are chronic non-communicable diseases that are individually associated with mortality and constitute a public health problem because they affect thousands of people worldwide, although they are unique and different entities, both have a bidirectional relationship since subjects diagnosed with uncontrolled DM2 are associated with more severe stages of periodontitis and in people with this oral condition the levels of glycosylated hemoglobin (hbA1c) are increased compared to subjects who do not present periodontitis or who have a controlled oral treatment for this condition.

Bruno Alberto Rodríguez Ramírez [a], Pamela Marianna Rodríguez Ramírez [b]

[a] Corresponding author, Private practice, https://orcid.org/0000-0002-1565-2779, Email: vrunorod@live.fr

[b] Co-author, Private practice, https://orcid.org/0009-0002-8993-5947, Email: pamelarodz00@gmail.com

Subjects with uncontrolled DM2 are more susceptible to periodontitis and are an impediment to adequate treatment response. Therefore, according to H. Löe, periodontitis has been considered since 1976 as the sixth complication of diabetes.[1–3]

PERIODONTIUM

The periodontium is constituted by two types of tissues; the soft tissues that includes gum and periodontal ligament and the hard or mineralized tissue such as the root cementum and the alveolar bone. It is a complex support system whose main function is to fix the dental organs to the alveolar bone and cover them to give them protection with the masticatory mucosa of the oral cavity. The literature described by Jan Lindhe calls it the "attachment apparatus" or "supporting tissue of the teeth" and it is a biologically developing system that throughout the life of a human being undergoes changes in form and function that are realized by the oral environment of the host (Figure 1).[4,5]
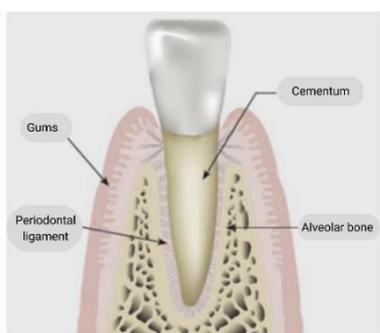

Figure 1. Structure components of the periodontium.[5]

PERIODONTITIS

Periodontitis is a chronic non-communicable disease that is initiated by the accumulation of biofilm above and below the gum level (gingival margin), the human cavity is home to a bacterial community with about 700 species of which the human being is a carrier of between 50 to 200 of them which contribute positively to oral health by physically and chemically restricting the entry of foreign bacteria through saliva and mucus to be ingested and destroyed in the stomach by its extremely low pH [6]; but when there is a dysbiosis between the oral microbiome and the host, an inflammatory process develops together with progressive destruction of the supporting tissues of the tooth. It is characterized by clinically visible loss of the gingival attachment, mainly horizontal bone loss, less than 15% (stage I), 15% to 30% (stage II) in the coronal third and extending to the middle or apical third of the root (stage III and IV) observable radiographically in addition to the pathological migration in the direction of the tooth root of the area where the gum is attached to the tooth (junctional epithelium).[2,7,8]

Oral health is an important pillar in the prevention or appearance of this condition since tooth brushing mechanically removes the biofilm preventing the accumulation of bacteria on the tooth surface and gingiva, but it is not the only focus of attention since periodontitis is multifactorial.[9]

ETIOLOGY

In periodontitis, a group of factors that influence the immune response stands out, such as factors in the structure and anatomy of the tissue, but can be altered by environmental factors or behavior of the individual, it is considered that excessive occlusal forces are related to the progression of existing periodontitis, On the other hand, the periodontal ligament adapts to these loads causing resorption of the alveolar ridge which causes dental mobility thus leading to determine that the loss of periodontal tissue is a cause of certain systemic and multifactorial disorders that give us important data at the time of diagnosis.

Not forget that the mouth has the second most diverse microbial community in the organism, located in soft tissues such as the oral mucosa and hard tissues such as the surface of the teeth, and there must be a balance in the oral microbiome to maintain a symbiosis (state of health). When this health condition is broken the main symptoms are loss of periodontal tissue attachment leading to the formation of periodontal pockets and reduction of the alveolar bone level.[10-12]

Several studies cultured gram-negative bacteria and detected the three most prevalent subgingival bacteria in patients with periodontitis; Porphyromona gingivalis, Treponema denticola and Tannerella forsythia, which they called the "Red Complex".[6]

EPIDEMIOLOGY

The World Health Organization (WHO) considers periodontitis to be one of the most prevalent oral diseases, which in its most severe form has a worldwide prevalence of 19% in people over 15 years of age, representing more than 1 billion cases.[13]

Studies carried out by the Epidemiological Surveillance System for Oral Pathologies (SIVEPAB) in Mexico report that in 2020, with a figure of 48,263 of the total population, 44% of the population had a healthy periodontium; registering an increase in the prevalence of periodontitis in older adults as age advances, obtaining a 2. 5% in the first group (20 to 34 years) to 19.8% in the second group analyzed (80 and over), but the numbers are reduced to four out of ten in ages 50 years and older. In 2011, Medina Solís, et al. reported that the prevalence in the state of Hidalgo was 80% (Figure 2).[14,15]
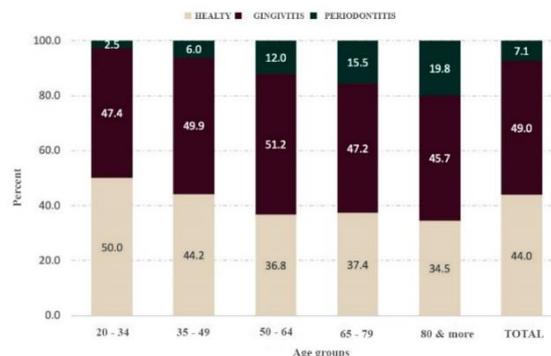

Figure 2. SIVEPAB Distribution of periodontal status in adult population by age group.[14]

CLASSIFICATION OF PERIODONTITIS

A structured classification is for the diagnosis and treatment of the disease according to the characteristics, the most previously used in periodontitis is from the year 1999 and was used for more than 2 decades; since then, systems have been managed to try to classify it with a greater sensitivity at the time of diagnosis and treatment, but in each proposed classification there was a complication.

During the 2 decades that this classification was in use, physicians, researchers, epidemiologists, among other specialists in the area expressed the difficulty in differentiating between cases of chronic and aggressive periodontitis, but it was thanks to scientific advances and a more detailed understanding of periodontal disease that led to the proposal of a new classification at the 2017 World Workshop that encompasses health, gingivitis and periodontitis, was published in 2018.[8,16,17]

The current classification is based on the use of stages and grades for diagnosis, the staging used in oncology, considers the observable clinical presentation communicating the current severity and extent of the disease and has been adapted to periodontitis, having as goals to classify by stages the severity and complexity and by grades the progress and severity of the disease and four stages and three grades have been determined where diabetes is considered as a risk factor in the progression of periodontitis (Tables 1 and 2).[8,17]

DIABETES

Diabetes mellitus (DM) is a serious and complex chronic disease that requires periodic medical attention that occurs when the body cannot adequately use the insulin produced or the pancreas does not produce enough insulin and comprises a group of heterogeneous disorders that share the increased concentration of glucose in the blood (hyperglycemia) and disorders in the metabolism of carbohydrates, proteins and fats producing symptoms such as neuropathy, retinopathy and visual disturbances, nephropathy, polyuria and polydipsia as well as fatigue, weight loss, ketoacidosis or syndrome, protein and fat producing symptoms such as neuropathy, retinopathy and visual disturbances, nephropathy, polyuria and polydipsia as well as fatigue, weight loss, ketoacidosis or hyperosmolar non-ketoacid syndrome having as risk a coma state and where the individual is more susceptible to infections caused by the combination of metabolic acidosis, microangiopathy due to an ineffective response in macrophage phagocytosis. Diabetes affects healing at the systemic level due to glycation end products in hyperglycemic patients. The American Diabetes Association determines that values ≥6.5% (48 mmol/mol) fasting plasma glucose suggest a diagnosis of diabetes provided they have been confirmed by another test or be persistent to the same test at least twice. Individuals with diabetes are at increased risk for periodontitis with greater severity if it is not controlled and there are different oral manifestations such as dry mouth (xerostomia), diffuse erythema of the mucosa, a red, flavored tongue, there is a greater tendency for periodontal abscess formation, gum inflammation, gingival papillae that bleed larger due to inflammatory tendency, higher incidence of

caries, alterations in the oral microbiota, polypoid gingival proliferations as well as tooth mobility.[18-23]

ETIOLOGY

Genetics plays an important role in an individual's susceptibility to type 2 Diabetes Mellitus (DM2). Hyperglycemia develops when the glucose production increases favoring the insulin resistance decreasing glucose uptake in adipose tissue and muscles; reduced insulin release is due to β-cell dysfunction in the pancreas, but an unhealthy diet and a sedentary lifestyle favor the development of DM. Many cases could be prevented by maintaining a healthy weight, engaging in frequent physical activity, consuming healthy foods, avoiding tobacco smoking and alcohol consumption, among other lifestyle changes.[24]

Table 1. Current classification of periodontitis by stages of severity adapted by Tonetti et al.[8]

Stages	Interdental CAL at site of greatest loss	Radiographic bone loss	Tooth loss
I	1-2mm	Coronal third (<15%)	No tooth loss
II	3-4mm	Coronal third (15% - 30%)	
III	≤5mm	Extending to middle or apical third of the root	≤ 4
IV			≥5

Table 2. Current classification of periodontitis by grade of progression adapted by Tonetti et al.[8]

Grade	A (slow)	B (moderate)	C (fast)
		Rate of progression	
Direct evidence	No loss evidence Bone/CAL	Loss <2mm	Loss ≥2mm
Indirect evidence (phenotype)	Heavy biofilm deposits with low levels of destruction	Destruction commensurate with biofilm deposits	Tissue destruction is greater than film deposition.
Smoking	Non-smoker	<10 cigarretes/ day	≥10 cigarretes/ day
Diabetes	Normoglycemic /non diagnosis of diabetes	HbA1c < 7	HbA1c >7

EPIDEMIOLOGY

The International Diabetes Federation (FDA) in 2021 estimated that the worldwide prevalence in individuals between 20 and 79 years was 537 million mainly in DM2 having an exponential increase in the last 20 years, this translates to 1 in 10 adults in this age range that in the same year caused 6.7 deaths worldwide, estimated to increase to 643 million by 2030. According to the FDA it is estimated that 45.8% of cases in adults are not diagnosed, this makes us question that they do not have a treatment and that complications may be greater than in

individuals who do and life expectancy is reduced by 8 years. The National Institute of Statistics and Geography mentions that in 2018 the prevalence in Mexico was 10.32% and in Hidalgo it was 12.83% in population older than 20 years old increasing the percentage at a national level in adults aged 60 to 69 years up to 25.8%.[19,24-26]

DIABETES CLASIFICATION

As mentioned above, the use and validation of a classification is important to determine which treatment for each type of condition, and diabetes is classified as follows:[27]

1.- DM1: Also called insulin-dependent, it is a problem caused by immunological factors due to β-cell destruction leading to insulin deficiency resulting in hyperglycemia. It is thought to be the combination of genetic predisposition and environmental triggers such as enterovirus infection. Characteristic symptoms are polyuria (increased urine volume) and polydipsia (increased thirst) and about one third may present with diabetic ketoacidosis.[19,20,27]

2.- DM2: Characterized by the progressive loss of insulin secretion from the β-cells, causing insulin resistance, also known as non-insulin-dependent and represents 90% of cases diagnosed after 40 years of age, although the diagnosis is increasingly made at younger ages, due to lifestyle, type of diet and lack of exercise, which is why it is associated with obesity.[20]

3.- Gestational diabetes: Another type of diabetes that develops during the second or third trimester of pregnancy, but if it occurs before the 20th week it is likely that the diabetes was manifested before conception.[19,27]

4.- Specific types of diabetes: These are due to other causes not mentioned above, such as monogenic diabetes syndromes, neonatal diabetes, juvenile diabetes at the onset of maturity, diseases of the pancreas such as cystic fibrosis or pancreatitis, diabetes induced by chemicals or drugs such as glucocorticoids in the treatment of HIV/AIDS or after organ transplantation.[27]

THE BIDIRECTIONAL RELATIONSHIP OF PERIODONTITIS AND DIABETES MELLITUS

The risk of developing periodontitis increases in subjects with diabetes, resulting in tooth loss and being the most common cause of tooth extraction. There are microvascular complications of diabetes that are associated with severe periodontitis. Studies relating periodontitis to diabetes show that the risk of periodontitis increases when glycosylated hemoglobin levels are not controlled. Biofilm bacteria under the gum (subgingival) aid in the destruction of hard and soft tissues of the periodontium. There is increased inflammation that is associated with both conditions due to elevated levels of inflammatory cytokines such as interleukin-1 and interleukin-6, tumor necrosis factor alpha (TNF- α) secreted mainly by mast cells, basophils, macrophages, phagocytic and endothelial cells accompanied by an increase in neutrophils. Th17 cells (t helper cells) secrete IL-17 inducing the expression of the nuclear receptor kappa B ligand/osteoprotegerin of osteoblasts leading to activation of osteoclasts causing bone resorption, oxidative stress as well as acute phase inflammatory markers such as C-

reactive protein and in subjects with uncontrolled diabetes are affected by a local proinflammatory environment in the gingiva influencing tissue degrading enzymes by increasing metalloproteinases and their inhibitors. This demonstrates an important role in periodontal destruction (Figure 3).[2,18.28,29]

Figure 3. **Relationship between diabetes and periodontitis. IL-1 (interleucine-1) IL-6 (interleucine-6), TNF- α (tumor necrosis factor-alpha).[18]**
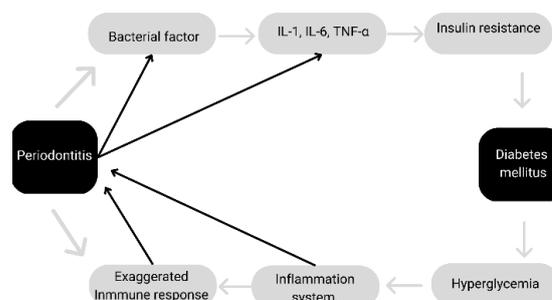
SUBGINGIVAL INFECTION AND DESTRUCTION OF PERIODONTAL TISSUES

Infection below the gum (subgingival) is a feature in advanced stages of periodontitis that begins when bacterial colonies attach to the host's tooth surfaces. This triggers several events, including bacterial growth and biofilm formation as well as the entry of the pathogen into the cells interfering with the immune defense. Regarding the destruction and degradation of periodontal tissues there are two important pathways; the first is through the interactions of osteoblasts and stroma that occur for bone formation or resorption in bone remodeling processes and the second pathway is through inflammatory cytokines that are produced locally in response to periodontal bacteria and together with the products of these bacteria there are higher serum concentrations of proinflammatory biomarkers and together they are responsible for tissue degradation and bone loss. [30,31]

Oxidative stress in periodontal tissues increases with hyperglycemia, studies indicate that the use of antioxidant micronutrients is favorable for reducing inflammation and thus bone loss enhanced by diabetes.[32]

TREATMENT FOR DM2 AND PERIODONTITIS

Studies carried out in the United States, Japan and Taiwan show that patients with periodontitis are more likely to develop prediabetes and diabetes, giving great importance to periodontal treatment since it is very effective and does not imply any risk in subjects with diabetes, resulting in a reduction of hbA1c levels from 0.27 to 0.48% after 3 months.[2]

The treatment of DM2 includes several aspects, from the appropriate therapy described by the physician, a balanced diet high in fiber, trying to consume vegetables, legumes, fruits mainly, avoiding the intake of refined carbohydrates and reducing saturated fats, all this with advice from the nutritionist,

moderate physical activity at least 30 minutes a day 5 times a week.[19]

A 12-month study of patients diagnosed with DM2 who underwent intensive periodontal treatment, subgingival scaling of all dental organs and surgical periodontal therapy concluded that the periodontal intervention is similar to that obtained by adding a second drug for the control of diabetes and reducing HbA1c levels.[33]

RECOMMENDATIONS FOR PHYSICIANS, DENTISTS AND OTHER HEALTH CARE PROFESSIONALS IN RELATION WITH DIABETES

There are a couple of recommendations addressed to health care personnel who are in contact with subjects with diabetes since this condition is a risk factor for developing periodontitis and not receiving periodontal therapy has a negative impact on the control of diabetes.

- There are a couple of recommendations for health care personnel who have contact with subjects with diabetes as a risk factor for developing periodontitis and the negative impact periodontitis has on diabetes control, which are as follows:
- One of the most important points is information that provides education to patients with diabetes as part of a comprehensive program of care.
- To inform that diabetes in all its forms increases the risk of periodontitis and if not treated and controlled is accompanied by complications such as kidney disease and cardiovascular problems.
- Explain that periodontal therapy has a highly positive impact on glycosylated hemoglobin control.
- The physician treating diabetes should inquire in depth about the patient's oral conditions that give an indication of periodontitis such as bleeding, tooth mobility, bad oral odor or suppuration, to have an interconsultation with the primary dentist who will be in charge of treating or referring the patient to the appropriate specialist to have good oral health.
- The dentist who intervenes in a patient with periodontitis should ask if the patient has been diagnosed with diabetes, if the answer is positive, he/she should ask about his/her control and hbA1c levels, if the answer is negative, it is advisable to refer the patient to the general practitioner so that he/she can carry out the pertinent check-ups.
- Patients with periodontal problems should receive appropriate therapy as soon as possible.
- Subjects diagnosed with diabetes and with a considerable amount of dental loss should be oriented for prosthetic rehabilitation of dental pieces, but this cannot be done if the diabetes is not controlled.
- Inform patients that periodontitis, like diabetes, is a chronic disease and should be treated professionally for prolonged periods or even for life.

- Recommend periodic appointments with the dentist at least every 6 months; if less frequent appointments are required, the patient should be informed.[2]

CONCLUSIONS

Based on the information presented in this manuscript and the literature consulted, it can be seen that there is evidence that supports the close relationship between DM2 and periodontitis, placing periodontitis in sixth place as a complication of diabetes; it has been described that in subjects with uncontrolled DM2 the severity of periodontitis is greater and is rapidly progressive.

Studies have shown that periodontal treatment reduces hA1bc levels and that in subjects with low glycosylated hemoglobin levels, thanks to adequate medical treatment, periodontitis could be controlled, suggesting that, in order to avoid future complications, treatment and prevention are fundamental.

DECLARATION OF INTERESTS

The authors declare that the manuscript has been written in the absence of business/financial relationships that could be interpreted as a possible conflict of interest.

REFERENCES

[1] Wu CZ, Yuan YH, Liu HH, Li SS, Zhang BW, Chen W, et al. Epidemiologic relationship between periodontitis and type 2 diabetes mellitus. BMC Oral Health. 2020;20(1):1–15.

[2] Sanz M, Ceriello A, Buysschaert M, Chapple I, Demmer RT, Graziani F, et al. Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. J. Clin. Periodontol. 2018;45(2):138–49.

[3] Löe H. Periodontal Disease: The sixth complication of diabetes mellitus. Diabetes Care. 1976;4:145–53.

[4] Lindhe. Jan Lindhe Niklaus P. Lang - Periodontología Clínica e Implantología Odontológica Médica. 6th ed. México Panamericana. p. 845–980.

[5] Vargas Casillas AP, Yañez Ocampo BR, Monteaguado Arrieta CA. Periodontología e Implantología. 1st ed. México Panamericana. 2016. 430 p.

[6] Valm AM. The Structure of Dental Plaque Microbial Communities in the Transition from Health to Dental Caries and Periodontal Disease. J. Mol. Biol. 2019;431(16):2957–69

[7] Fine DH, Patil AG, Loos BG. Classification and diagnosis of aggressive periodontitis. J. Clin. Periodontol. 2018;45:S95–111.

[8] Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J. Clin. Periodontol. 2018;45:S149–61.

[9] Lang NP, Bartold PM. Periodontal health. J. Periodontol. 2018;89:S9–16.

[10] Albandar JM, Susin C, Hughes FJ. Manifestations of systemic diseases and conditions that affect the periodontal attachment apparatus: Case definitions and diagnostic considerations. J. Periodontol. 2018;89:S183–203.

[11] Mombelli A. Microbial colonization of the periodontal pocket and its significance for periodontal therapy. Periodontol. 2000. 2018;76(1):85–96.

[12] Passanezi E, Sant'Ana ACP. Role of occlusion in periodontal disease. Periodontol. 2000. 2019;79(1):129–50.

[13] OMS. Global oral health status report. Vol. 57, Dental Abstracts. 2022.

[14] Resultados del Sistema de Vigilancia Epidemiológica de Patologías Bucales SIVEPAB 2020. Available from: https://www.gob.mx/cms/uploads/attachment/file/765740/resultadosSIVEPAB_2020.pdf

[15] Medina-Solís C, Cuevas-Suárez C, Lucas-Rincon S, Pontigo-Loyola A, Villagran-Ascencio A, Mendoza-Rodríguez M, et al. Salud bucodental en Hidalgo, México: revisión crítica de la literatura científica. Boletín Informativo de la Coordinación de Investigación-SSH. 2011;42:3-7.

[16] Sutthiboonyapan P, Wang HL, Charatkulangkun O. Flowcharts for Easy Periodontal Diagnosis Based on the 2018 New Periodontal Classification. Clin. Adv. Periodontics. 2020;10(3):155–60.

[17] Cárdenas-Valenzuela P, Guzmán-Gastelum DA, Valera-González E, Cuevas-González JC, Zambrano-Galván G, García-Calderón AG. Principales Criterios de Diagnóstico de la Nueva Clasificación de Enfermedades y Condiciones Periodontales. Int. J. odontostomatol. 2021;15(1):175–80.

[18] Kocher T, König J, Borgnakke WS, Pink C, Meisel P. Periodontal complications of hyperglycemia/diabetes mellitus: Epidemiologic complexity and clinical challenge. Periodontol. 2000. 2018;78(1):59–97.

[19] Harreiter J, Roden M. Diabetes mellitus—Definition, classification, diagnosis, screening and prevention (Update 2019). Wien. Klin. Wochenschr. 2019;131:6–15.

[20] Preshaw PM, Bissett SM. Periodontitis and diabetes. Br. Dent. J. 2019;227(7):577–84.

[21] Aguilar Soto FE, Sosa Morales FJ, Bojórquez Anaya Y, Fontes García Z. Periodontitis una enfermedad multifactorial: Diabetes Mellitus. Rev. Iberoam. Cienc. Salud. 2017;6(11):61.

[22] American Diabetes Association. Standards of Medical Care in Diabetes—2018 Abridged for Primary Care Providers. Clinical Diabetes. 2018;36(1):14–37.

[23] Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. The Lancet. 2017;389(10085):2239–51.

[24] Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat. Rev. Edocrinolo. 2018;14(2):88–98.

[25] International Diabetes Federation Diabetes Atlas 10th edition 2021. Available from: https://diabetesatlas.org/

[26] INEGI. Estadísticas a propósito del día mundial de la Diabetes (14 de noviembre). Datos nacionales. Comunicado de Prensa No 645/21 2021;(645/21):1–5.

[27] Care D, Suppl SS. Classification and diagnosis of diabetes: Standards of medical care in Diabetesd2018. Diabetes Care. 2018;41:S13–27.

[28] López-Gómez SA, González-López BS, Scougall-Vilchis RJ, Pontigo-Loyola AP, Márquez-Corona M de L, Villalobos-Rodelo JJ, et al. Tooth loss in patients with and without diabetes: A large-scale, cross-sectional study of Mexican adults. J. Am. Dent. Assoc. 2020;151(4):276–86. [14

[29] Hajishengallis G, Chavakis T. Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities. Nat. Rev. Immunol. 2021;21(7):426–40.

[30] Amano A. Host-parasite interactions in periodontitis: Subgingival infection and host sensing. Periodontol. 2000. 2010;52(1):7–11.

[31] Artese HPC, Foz AM, Rabelo MDS, Gomes GH, Orlandi M, Suvan J, et al. Periodontal therapy and systemic inflammation in type 2 diabetes mellitus: A meta-analysis. PLoS. One. 2015;10(5):1–14.

[32] Chapple ILC, Genco R. Diabetes and periodontal diseases: Consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J. Clin. Periodontol. 2013;40(14):106–12.

[33] D'Aiuto F, Gkranias N, Bhowruth D, Khan T, Orlandi M, Suvan J, et al. Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial. Lancet. Diabetes Endocrinol. 2018;6(12):954–65.