

FINAL DEGREE PROJECT

Degree in Dentistry

**EXPLORING THE CONNECTION BETWEEN DIABETES
MELLITUS AND PERIODONTAL DISEASES**

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ABSTRACT

Introduction: Diabetes mellitus and periodontal disease represent two interconnected global health crises that share a strong biological and clinical link. Recognised as the “sixth complication” of diabetes, periodontitis functions within a complex bidirectional relationship, where chronic hyperglycaemia leads to oral tissue destruction, while persistent oral inflammation negatively affects metabolic stability.

Materials and Methods: This narrative review synthesised findings from clinical trials and meta-analyses published between 2020 and 2025 to evaluate the impact of non-surgical periodontal therapy on glycaemic control, measured through glycated haemoglobin levels. **Results:** The results demonstrate that scaling and root planning reduces glycated haemoglobin levels, typically by 0.43% to 1.0% within a period of 3 to 6 months. This clinical improvement is comparable to adding a second antidiabetic medication. The underlying pathophysiological mechanisms involve the accumulation of advanced glycation end-products and reactive oxygen species, which activate pro-inflammatory pathways such as Nuclear Factor Kappa-light-chain-enhancer of Activated B Cells. These processes stimulate the overproduction of cytokines like Tumour Necrosis Factor-alpha and Interleukin-6, interfering with insulin signalling and promoting bone resorption through the RANKL/Osteoprotegerin system. While adjunctive treatments show some benefit, they remain less effective than mechanical debridement alone. **Conclusion:** Managing oral health is an essential component of diabetes care. Multidisciplinary collaboration is necessary to improve screening, enhance patient awareness, and ultimately optimise long-term clinical outcomes and quality of life.

KEY WORDS: Diabetes mellitus, Periodontitis, Glycated Haemoglobin, Non-surgical periodontal therapy, Collaborative care.

RESUMEN

Introducción: La diabetes mellitus y la enfermedad periodontal representan dos crisis globales de salud interconectadas que comparten un fuerte vínculo biológico y clínico. Reconocida como la “sexta complicación” de la diabetes, la periodontitis mantiene una relación bidireccional compleja, donde la hiperglucemia crónica provoca destrucción de los tejidos orales, mientras que la inflamación persistente afecta negativamente la estabilidad metabólica. **Materiales y Métodos:** Esta revisión narrativa sintetizó estudios clínicos y metaanálisis publicados entre 2020 y 2025 para evaluar el impacto de la terapia periodontal no quirúrgica en el control glucémico, medido mediante hemoglobina glucosilada. **Resultados:** El raspado y alisado radicular reduce los niveles de hemoglobina glucosilada entre un 0,43 % y un 1,0 % en 3 a 6 meses, un efecto comparable al de añadir un segundo fármaco antidiabético. Los mecanismos implican la acumulación de productos finales de glicación avanzada y especies reactivas de oxígeno, que activan vías proinflamatorias como el Factor Nuclear Kappa B. Esto favorece la producción de citocinas como el Factor de Necrosis Tumoral alfa e Interleucina-6, interfiriendo con la señalización de la insulina y promoviendo la resorción ósea mediante el sistema RANKL/Osteoprotegerina. Los tratamientos adyuvantes aportan beneficios limitados frente al desbridamiento mecánico. **Conclusión:** La salud oral es esencial en el manejo de la diabetes. La colaboración multidisciplinaria mejora el cribado, la concienciación y los resultados clínicos a largo plazo.

PALABRAS CLAVE: Diabetes mellitus, Periodontitis, Hemoglobina Glucosilada, Terapia periodontal no quirúrgica, Atención colaborativa

INDEX OF ABBREVIATIONS:

- **PICO:** Population, Intervention, Comparison, Outcome.
- **BMI:** Body Mass Index.
- **CHW:** Community Health Worker.
- **DM:** Diabetes Mellitus.
- **T1DM / T1D:** Type 1 Diabetes Mellitus.
- **T2DM:** Type 2 Diabetes Mellitus.
- **GDM:** Gestational Diabetes Mellitus.
- **CKD:** Chronic Kidney Disease.
- **HbA1c:** Glycated Haemoglobin.
- **FBG:** Fasting Blood Glucose.
- **AGEs:** Advanced Glycosylation End Products.
- **ROS:** Reactive Oxygen Species.
- **RAGE:** Receptors for Advanced Glycation End-products.
- **TLR:** Toll-Like Receptor.
- **MyD88:** Myeloid Differentiation Primary Response 88.
- **NF- κ B / NF-KB:** Nuclear Factor Kappa-light-chain-enhancer of Activated B Cells.
- **MAPK:** Mitogen-Activated Protein Kinase.
- **RANK:** Receptor Activator of Nuclear Factor-KB Ligand
- **OPG:** Osteoprotegerin
- **TNF- α :** Tumour Necrosis Factor-alpha.
- **IL-1 β :** Interleukin-1beta.
- **IL-6:** Interleukin-6.
- **IL-39 / IL-40:** Interleukin-39 and Interleukin-40.
- **MMPs:** Matrix Metalloproteinases.
- **CRP:** C-Reactive Protein.
- **hsCRP:** High-Sensitivity C-Reactive Protein.
- **HDL:** High-Density Lipoprotein ("good" cholesterol).
- **LDL:** Low-Density Lipoprotein ("bad" cholesterol).
- **WBCs:** White Blood Cells.
- **RBC:** Red Blood Cell.
- **GAD:** Anti-glutamic acid decarboxylase.
- **NETs:** Neutrophil Extracellular Traps.
- **eGFR:** Estimated Glomerular Filtration Rate.
- **NSPT:** Non-Surgical Periodontal Therapy.
- **SRP:** Scaling and Root Planing.
- **aPDT:** Antimicrobial Photodynamic Therapy.
- **ILIB:** Intravascular Irradiation of Blood.
- **CAL:** Clinical Attachment Level.
- **PD / PPD:** Probing Depth / Probing Pocket Depth.
- **BOP:** Bleeding on Probing.
- **PDL:** Periodontal Ligament.
- **PI / PLI:** Plaque Index.
- **GI:** Gingival Index.
- **VPI:** Visible Plaque Index.
- **GBI:** Gingival Bleeding Index.
- **OHI-S:** Oral Hygiene Index Simplified.

- **GOHAI:** General Oral Health Assessment Index.
- **OHQoL:** Oral Health-Related Quality of Life.
- **WHO:** World Health Organization.
- **IDF:** International Diabetes Federation.
- **ADA:** American Diabetes Association.
- **AAP:** American Academy of Periodontology.
- **EFP:** European Federation of Periodontology.

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1. INTRODUCTION

1.1. Diabetes Mellitus

1.1.1. Epidemiological context

Diabetes mellitus is a major risk factor for periodontitis and significantly contributes to the increased pathogenicity of the inflammatory response between the host and periodontal tissues. According to the IDF Diabetes Atlas, there were 537 million individuals with diabetes mellitus worldwide in 2021, and this number is projected to rise to 783 million by 2045 (1).

1.1.2. General definition of diabetes mellitus

It is a disease that affects multiple organs, and it can coexist with other chronic complications affecting multiple organs, including vascular diseases, nephropathies, and neuropathies (1). It is defined by the lack of insulin production in the body or by the inability of the body to use the insulin it produces. This results in elevated blood glucose levels (hyperglycaemia), leading to serious damage to the body and its organs.

1.1.3. Clinical symptoms

The symptoms of diabetes mellitus can go many years unnoticed, and they include: thirst, needing to urinate more than usual, blurred vision, feeling tired, and losing weight unintentionally. For those patients, a high glucose microenvironment enhances the pathological accumulation of advanced glycosylation end products (AGEs) and reactive species (ROS) (2).

1.1.4. High-glucose microenvironment and biological alterations

The vascularization mechanism of action in order to have a loss of bone or vascularisation in diabetes, goes as follows, AGEs and ROS levels increases, binding to their receptors and activating an immune signalling pathway composed of TLR, MyD88 and NF- κ B, inducing another increase of inflammatory substances such as TNF- α , IL-1 β and MMPs. When ROS levels increase, immune cells like neutrophils, release a lot of NETs (neutrophil extracellular traps) which prevent the healing system to function properly. Moreover, ROS activate the p38 MAPK pathway, provoking the bone loss through osteoclast activation (3). Thus implying that diabetes mellitus brings a favourable environment to the an increased risk of developing periodontitis (4).

1.1.5. Impact on quality of life

In everyday life, diabetes mellitus has a strong impact on the quality of life, impacting the physical but also social and psychological aspects (5). Patients affected by this disease suffer the direct consequences of the insulin insufficiency but also the indirect ones, such as obesity, hypertension and cardiovascular complications, which further compromise mental and functional well-being. Maintaining a healthy lifestyle is important for the overall satisfaction of one's life and can improve the glycemic control. Conversely, an unhealthy lifestyle can worsen psychological factors such as anxiety, depression. Reducing the treatment adherence, creating a vicious cycle between poor glycemic control and psychological distress, further exacerbating insulin resistance. Improving the quality of life, requires a multidisciplinary approach, combining pharmacological treatment, psychological counselling and lifestyle modification. Garg and Duggal (2022) suggest that integrating psychosocial care can help improve overall diabetes mellitus management (6,7).

1.2. Classification of Diabetes Mellitus

Diabetes mellitus is classified into types based on etiology, pathophysiology, and clinical presentation. The World Health Organization (WHO) established an initial classification in 1980 and revised it in 1985 and 1999, distinguishing four main forms: Type 1 diabetes, Type 2 diabetes, gestational diabetes mellitus (GDM), and other specific types (8).

1.2.1. Type 1 Diabetes Mellitus

Type 1 diabetes mellitus (T1DM) is an autoimmune condition in which the body's immune system attacks and destroys the pancreatic beta-cells, leading to an absolute deficiency of insulin. It's also called insulin-dependent diabetes mellitus, and predominantly in children, adolescents, and young adults.

The autoimmune process involves the presence of autoantibodies, like anti-glutamic acid decarboxylase (GAD) and islet cell antibodies, and insulin autoantibodies. Although the exact cause remains unclear, viral triggers and genetic susceptibility have been suggested as contributing factors. Because endogenous insulin production is severely diminished or absent, lifelong insulin therapy is required. In this type of diabetes, treatment is typically exogenous insulin intake for a lifelong period.

1.2.2. Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is the most common type of diabetes, marked by the body's resistance to insulin. combined with a progressive defect in insulin secretion. Formerly known as "non-insulin-dependent diabetes mellitus," it is closely linked to obesity, sedentary lifestyle, and increasing age, unlike type 1. A meta-analysis demonstrated that there is a higher risk, practically double, if someone has T2DM to develop periodontitis (9).

Patients often exhibit hyperinsulinemia and insulin resistance in peripheral tissues, leading to relative insulin deficiency. T2DM is frequently accompanied by metabolic disturbances, including hypertension, microvascular and macrovascular complications. Although the onset is typically gradual, the long-term consequences may include nephropathy, neuropathy, retinopathy, and cardiovascular disease, possibly leading to drastic and invasive treatments such as amputations.

1.2.3. Gestational Diabetes Mellitus and other specific types

Gestational diabetes mellitus (GDM) is a condition where glucose intolerance is first detected during pregnancy in individuals without a prior history of diabetes. Hormonal changes during pregnancy can impair insulin action and elevate blood glucose levels. Other specific types include fewer common forms of diabetes caused by identifiable genetic, pancreatic, endocrine, or drug-induced abnormalities. These forms represent less than 10% of all diabetes cases (10).

1.3. Microvascular and Macrovascular Complications of Type 2 Diabetes Mellitus

1.3.1. Microvascular Complications

Type 2 Diabetes Mellitus (T2DM) is marked by long-term high blood sugar levels that progressively damage the microvasculature, leading to three major complications: diabetic retinopathy, neuropathy, and nephropathy. These complications arise due to endothelial dysfunction, oxidative stress, and inflammatory responses that alter vascular integrity and blood flow within small vessels.

1.3.2. Diabetic Retinopathy

Diabetic retinopathy is among the most common complications affecting small blood vessels of T2DM, resulting from microvascular abnormalities in the retinal capillaries. Mansour et al. (2023) identified several genetic loci associated with this complication, including ACVR1C, ZFHX4, WNT9B, SHANK3, ZSCAN5A, and DCP1B. These genes are linked to factors such as lipid profile, glycaemic control, and vascular stiffness. The SHANK3 gene, for instance, has been related to platelet count and fibrinogen levels, both of which increase the risk of thrombus formation and retinal ischemia. Similarly, ZSCAN5A influences monocyte activity, promoting inflammatory cytokine release that damages the blood-retinal barrier and exacerbates neovascularization (11).

1.3.3. Diabetic Neuropathy

Diabetic neuropathy arises from chronic microvascular injury to peripheral nerves, leading to demyelination and axonal degeneration. Mansour et al. (2023) reported associations with GFY, ADH4, LRFN2, PKHD1, SLC11A1, MATN4, and PPARA genes. The ADH4 gene, expressed in the liver, was linked to fibrinogen and apolipoprotein A1 levels, key contributors to inflammation and coagulation processes that impair nerve blood supply. SLC11A1 affects iron metabolism, which, when dysregulated, promotes oxidative stress and macrophage activation in nerve tissue, further worsening neural injury, showing us the strong link between the genetic component and the neurological pathway. Moreover, a reduced flow of saliva has been observed with diabetes medications, and neuropathy affecting the salivary glands may provoke caries (12).

1.3.4. Diabetic Nephropathy

Diabetic nephropathy represents another significant microvascular complication of T2DM, characterised by glomerular hypertrophy, basement membrane thickening, and progressive renal failure. According to Mansour et al. (2023), nephropathy was associated with multiple genetic markers, including TTN, PI16, PPP1R3A, ZNF136, and HSPA12B. The PPP1R3A gene helps regulate glycogen production in kidney tubules, and when too much builds up inside cells, it can contribute to kidney problems. The ZNF136 gene encodes a zinc-finger protein expressed in renal tissues, and its variants have been linked to chronic kidney disease progression via tubular atrophy and inflammatory infiltration.

1.3.5. Macrovascular Complications

In type 2 diabetes, macrovascular complications can involve cardiovascular, cerebrovascular, and peripheral vascular diseases that result from endothelial dysfunction and accelerated atherosclerosis. These complications are a major cause of morbidity and mortality among diabetic patients. Mansour et al. (2023) identified significant genetic loci associated with cardiovascular complications, including PKHD1, MAST1, GFY, SEPT14, PCNT, and RILPL2.

The PKHD1 gene, previously associated with metabolic and cardiac disorders, plays a crucial role in heart function. GFY was linked to carotid plaque formation, implicating it in atherosclerotic processes that compromise arterial elasticity. The PCNT gene, expressed in the heart, is involved in microtubule organisation and cardiomyocyte stability; its mutations have been linked to increased mechanical stress and cardiac dysfunction. Finally, RILPL2 is associated with obesity-related markers, such as BMI and waist-to-hip ratio, reinforcing the role of metabolic dysregulation in macrovascular disease (11).

1.4. **Metabolic and inflammatory biomarkers**

Biomarkers play an essential role in understanding the pathophysiological mechanisms of Type 2 Diabetes Mellitus and its complications. The review conducted by Le et al. (2024) analysed clinical data from over 24,000 participants to identify consistent biological changes across four main biomarker profiles: haematological, protein, cytokine, and lipid that played an important role in the diagnosis of diabetes mellitus (13).

1.4.1. Hematological Biomarkers

The haematological profile in T2DM reflects systemic inflammation and altered oxygen transport. Patients with T2DM exhibited increased counts of white blood cells (WBCs) compared to non-diabetic controls (Le et al., 2024). Elevated WBCs indicate an active inflammatory response, while higher platelet counts suggest enhanced thrombotic activity and increased risk of vascular complications. In contrast, red blood cell (RBC) and haemoglobin (Hb) levels were significantly decreased, resulting in reduced oxygen-carrying capacity and impaired tissue oxygenation and thus inducing microvascular complications such as retinopathy and nephropathy. Increased platelet activation markers also contribute to endothelial dysfunction and atherosclerosis in diabetic patients (14).

1.4.2. Protein Biomarkers

The proteic profile of T2DM patients demonstrates both metabolic dysfunction and chronic inflammation. Serum albumin levels were consistently reduced (–10.8% on average), reflecting insulin deficiency and hepatic

dysfunction. Albumin, known for its antioxidative and anti-inflammatory properties, inversely correlates with T2DM risk. In contrast, acute-phase proteins were significantly elevated, indicating chronic low-grade inflammation(14).

1.4.3. Cytokine Biomarkers

The cytokine profile in T2DM reveals a disruption in immune balance, with an overexpression of pro-inflammatory cytokines and suppression of anti-inflammatory mediators. Elevated tumour necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and interleukin-6 (IL-6) promote insulin resistance by impairing insulin receptor phosphorylation and inducing beta-cell apoptosis. Overall, the cytokine profile highlights chronic immune dysregulation seen in diabetes(16).

1.4.4. Lipid Biomarkers

Alterations in lipid metabolism are key contributors to the cardiovascular risk profile of T2DM patients. The study by Le et al. (2024) reported a specific pattern of abnormalities: while levels of high-density lipoprotein (HDL), often referred to as “good” cholesterol, are characteristically reduced, levels of triglycerides and low-density lipoprotein (LDL), known as “bad” cholesterol, are elevated. These lipid abnormalities underscore the metabolic disturbances and pro-inflammatory environment typical of diabetic dyslipidaemia (14).

1.5. Periodontal diseases

1.5.1. Definition and clinical features

In recent years, periodontitis has also been redefined by the joint AAP/EFP 2018 classification, which is now the worldwide reference. This system evaluates the disease in two complementary ways: the stage, which reflects the extent of tissue destruction, and the grade, which helps estimate how quickly the condition is likely to progress and how strongly it may be influenced by systemic factors such as diabetes. This approach provides a more complete picture of the disease and allows clinicians to adapt diagnosis and treatment planning more precisely (15). Research has shown that the connection between diabetes mellitus and periodontal disease goes both ways. Because of this close interaction, periodontal disease is now often described as the sixth major complication linked to diabetes (16). In addition, periodontitis can influence the prevalence of diabetes, the progression of the condition, and its clinical management (17,18). Periodontal diseases are inflammatory conditions that affect the structures supporting your teeth, including the gums, periodontal ligament (PDL), cementum, and jawbone. Clinically, periodontitis is characterised by gingival inflammation, periodontal pocket formation, clinical attachment loss, and alveolar bone resorption, and can

lead to tooth mobility and tooth loss (19). The periodontal lesion develops through interactions between pathogenic bacteria, such as Actinobacteria and Fusobacterium (1), in the dental biofilm and the host immune-inflammatory response, resulting in progressive destruction of periodontal connective tissues and bone. In periodontitis, vascular damage and increased inflammatory cell infiltration are evident, leading to irreversible degradation of collagen Fibers and alveolar bone (3). Osteoblast activity becomes inhibited while osteoclast-mediated bone resorption persists, creating an imbalance that favors tissue destruction(20).

1.5.2. Pathogenesis of Periodontitis

The pathogenesis of periodontitis involves microbial imbalance and an exaggerated host immune response. Pathogenic bacteria initiate inflammation, but host-mediated pathways are responsible for most of the connective tissue and bone damage. As inflammation progresses, immune cells contribute to the release of pro-inflammatory cytokines and matrix metalloproteinases(MMPS)(16), which degrade extracellular matrix components. Additionally, Numerous mediators are upregulated in periodontal tissues and amplify inflammation. These cytokines also influence osteoclastic activity, promoting bone resorption(3) (21)

1.5.3. Structural Components Affected in Periodontal Disease

Periodontal tissues undergo profound structural and functional alterations during disease progression. The gingiva exhibits increased vascular permeability, inflammatory infiltration, and degradation of collagen Fibers. Within the PDL, fibroblasts—normally responsible for collagen synthesis and tissue remodelling, exhibit altered behaviour under inflammatory conditions. They increase the response of inflammatory-associated genes such as CXCL1 and CXCL13, contributing to the amplification of local inflammation.

Cementum and alveolar bone are also significantly affected. Osteoblast inhibition combined with sustained osteoclast activity leads to progressive bone loss.

1.5.4. Interaction Between Periodontitis and Systemic Health

Periodontal disease has been associated with several systemic conditions, including diabetes mellitus (22), cardiovascular diseases, respiratory diseases, certain types of cancer, and adverse pregnancy outcomes(3). Systemic inflammatory mediators originating from periodontal infection may exacerbate the symptoms of diabetes.

The link between diabetes and periodontal disease is particularly well established. Chronic periodontitis can worsen glycaemic control by increasing systemic inflammatory burden, while poorly controlled diabetes,

significantly increases the prevalence, severity, and progression of periodontitis. Conversely, it has been showed that there has been an average reduction in HbA1c of -0.46% after non-surgical periodontal treatment (25). This bidirectional relationship highlights periodontitis as both a complication of diabetes and a modifying factor that can influence this disease and exacerbate the progression of each other (24).

1.5.5. Interaction Between Diabetes and Systemic Health

In diabetic patients, the high-glucose microenvironment highly alters the behaviour of periodontal cells. Hyperglycaemia promotes the formation of advanced glycation end-products (AGEs), which accumulate in periodontal tissues and bind to their receptors (RAGE). This interaction stimulates activation of the TLR/MyD88/NF-KB pathway, resulting in increased release of TNF-alpha, IL-1beta, and MMPs, all of which contribute to tissue degradation at the end (3). AGEs also impair fibroblast function by inhibiting type I and type III collagen expression and reducing cell migration ability, thereby limiting tissue repair.

Additionally, ROS production increases dramatically in a high-glucose environment, exacerbating inflammatory damage. The combined effects of oxidative stress, inflammation, and immune dysregulation hinder bone regeneration by inhibiting osteoblastic differentiation of periodontal ligament cells.

2. OBJECTIVE

Based on these observations, this narrative review aims to evaluate the impact of periodontal treatment on glycaemic control in diabetic patients using recent data and articles on periodontitis and diabetes mellitus. Specifically, it aims to explain the pathophysiological link between diabetes mellitus and periodontal disease by summarising recent clinical and meta-analytical studies assessing HbA1c variation after periodontal therapy. Another aim is to identify possible mechanisms underlying the improvement in glycaemic control after periodontal treatment. Finally, it aims to discuss the clinical and interdisciplinary implications for patient management (25).

3. MATERIAL AND METHODS

3.1. Study design

This work was developed as a documentary review with a comparative and analytical focus. The goal was to explore recent scientific findings on the two-way relationship between diabetes mellitus and periodontal disease, and to evaluate how periodontal treatment affects blood sugar control, particularly changes in HbA1c levels. The study will follow a structured approach based on the PICO framework:

P	I	C	O
<u>Population:</u> Adults diagnosed with either Type 1 or Type 2 diabetes mellitus.	<u>Intervention:</u> Periodontal treatment, including non-surgical periodontal therapy (NSPT).	<u>Comparison:</u> Diabetic patients without periodontal therapy, or clinical conditions prior to treatment.	<u>Outcome:</u> Glycemic control parameters (primarily HbA1c) and periodontal clinical indicators.

The guiding research question was formulated as follows: “In adult patients with diabetes mellitus, how does periodontal therapy, compared with no periodontal intervention, influence glycaemic control and periodontal status?”

3.2 Sources of information

The review was based exclusively on secondary data extracted from scientific literature published between 2020 and 2025. To ensure reliability, only peer-reviewed articles and official institutional documents were considered. The primary sources included Biomedical databases such as PubMed, Scopus, Google Scholar, SciELO, and clinical journals accessed through the university’s online library. We also used institutional and scientific guidelines like World Health Organization (WHO), American Diabetes Association (ADA) and European Federation of Periodontology (EFP). Finally meta-analyses, systematic reviews and clinical trials examining periodontal disease, diabetes mellitus, and glycaemic biomarkers. No unpublished data, blogs, or non scientific sources were included.

3.3 Search strategy

A structured search strategy was developed using combinations of controlled vocabulary and free-text terms.

Search strings were adapted to each database. The main search equation used in PubMed and Google Scholar was: “Diabetes mellitus” AND “periodontitis” AND (“periodontal treatment” OR “non-surgical therapy”) AND (“HbA1c” OR “glycaemic control”) AND (“bidirectional relationship” OR “systemic inflammation”). All searches were conducted between October and December 2025.

3.4 Inclusion and exclusion criteria

To ensure consistency and scientific validity, the following criteria guided the selection of the literature:

Inclusion criteria:

- Articles published between 2020 and 2025.
- Studies involving adult humans diagnosed with diabetes mellitus.
- Research reporting periodontal parameters and/or HbA1c outcomes.
- Clinical trials, cohort studies, and in-vitro studies explaining biological mechanisms.
- Publications available in English
- Available free articles

Exclusion criteria:

- Case reports, editorials, letters to the editor.
- Studies involving animals when no links to human physiology was provided.
- Articles focusing exclusively on gestational diabetes without periodontal variables.
- Studies lacking clinical or biochemical data relevant to the research question.
- Studies reported of more than 10 years.

3.5 Data extraction

A structured extraction sheet was designed to record the relevant parameters obtained from each selected publication extracted information included the type of study, year, and sample characteristics, the diagnostic criteria for diabetes and periodontal disease, an overview of the periodontal treatments carried out, highlighting the biomarkers assessed—like HbA1c, inflammatory mediators, and oxidative stress markers—and the observed results, such as changes in clinical attachment level (CAL), probing depth (PD), and bleeding on probing (BOP), and finally measured variations in glycaemic control. Whenever available, methodological details, such as follow-up time and the severity of periodontal disease, were also recorded.

3.6 Data synthesis

Due to the heterogeneity of the included studies, designs, populations, and treatment protocols, a narrative synthesis approach was adopted. Findings were grouped into thematic categories corresponding to the major axes of the TFG:

1. Pathophysiological mechanisms linking diabetes and periodontal inflammation.
2. Systemic impact of periodontal therapy on glycemic markers.
3. Role of inflammatory, protein, lipid, and cytokine biomarkers in the interaction between both diseases.
4. Clinical implications for interdisciplinary patient management.

The data were compared qualitatively to identify convergences and the strength of the evidences.

4. RESULTS

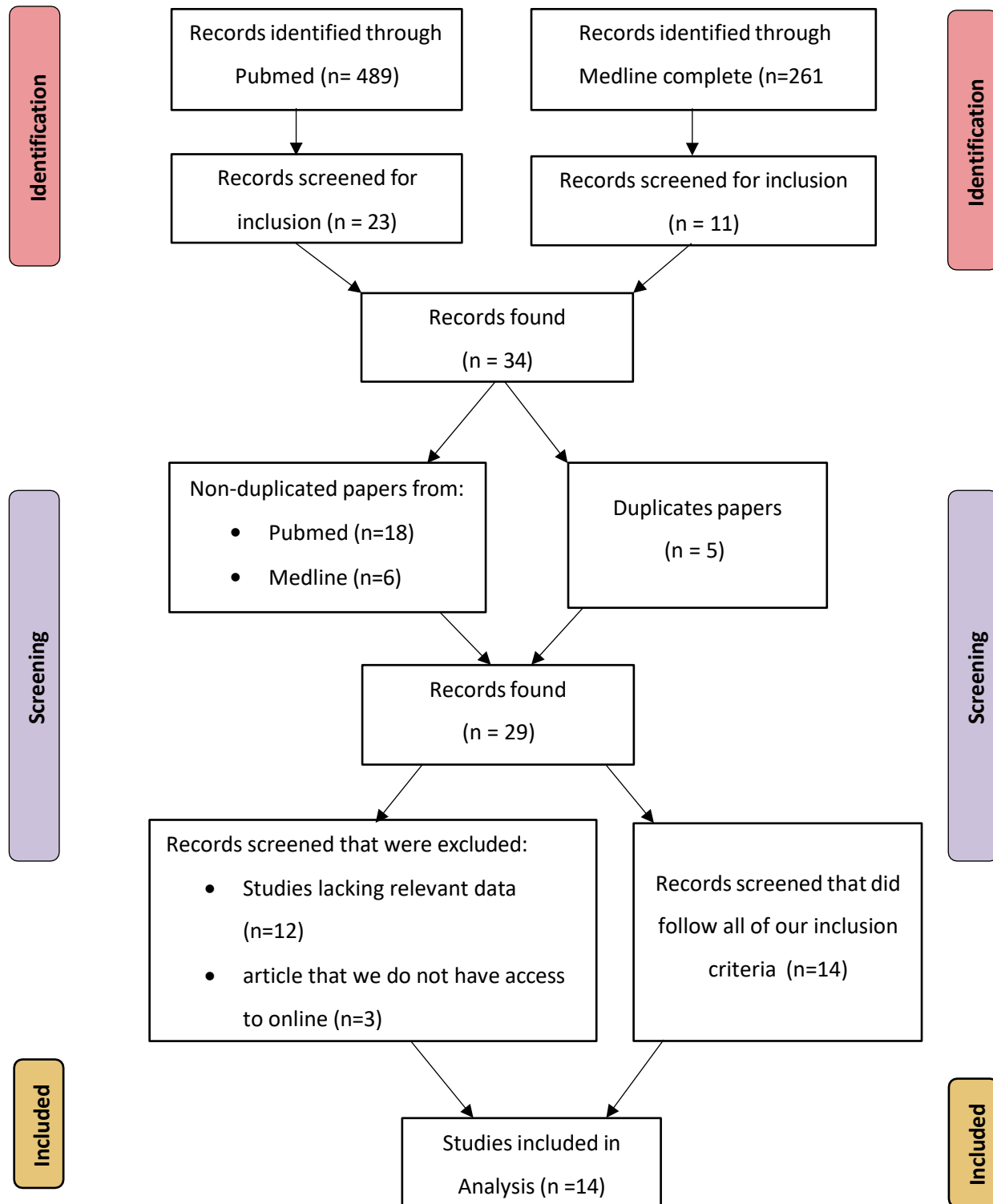


Figure 1: Data Extraction Flow Diagram (self-made)

	Articles	Authors	Study type	Study sample	Observations
1	The effect of antimicrobial photodynamic therapy (aPDT) on periodontal disease and glycemic control in patients with type 2 diabetes mellitus	Sara Brinar, Rok Schara, et al.	Randomised single-blinded controlled clinical trial	n=24 patients with T2DM	• aPDT group achieved significantly greater bleeding on probing reduction. • Microbiological analysis showed lower presence of <i>T. forsythia</i> after aPDT. • Intergroup differences for HbA1c reduction were not significant.
2	Community interventions improve diabetes management and oral health in type 2 diabetes patients with chronic periodontitis	Zhang Yi, et al.	Randomized Controlled Trial (multistage stratified cluster random sampling)	n=784 T2DM patients with chronic periodontitis	• Comprehensive intervention (G3) significantly improved HbA1c control rates (fasting plasma glucose and HbA1c control rates). • G3 showed superior improvements in self-efficacy and quality of life. • Oral issues (bleeding, mobility, halitosis) were most reduced in G3.

3	Adjuvant antimicrobial photodynamic therapy improves periodontal health and reduces inflammatory cytokines in patients with type 1 diabetes mellitus	Cunha Paula, et al.	Randomized Controlled Trial	n=38 patients (18 T1D, 20 normoglycemic)	• aPDT significantly reduced probing depth at 3 months for T1D. • TNF-α levels in crevicular fluid decreased in aPDT groups. • Normoglycemic patients showed better clinical gains than T1D patients.
4	Periodontal health intervention for oral health-related outcomes in older type 2 diabetes patients: a	Chunxiu Xiao, et al.	Randomized controlled trial (single-blind, single-center, randomized controlled trial)	n=108 older Chinese patients with T2DM	• Intervention significantly improved : plaque index, debris index and calculus index were significantly reduced (PLI and OHI-S scores.) • Periodontal health knowledge, behaviors were enhanced. • Quality of life (GOHAI) scores showed no intergroup difference.

	randomized controlled trial in a Chinese tertiary hospital				
5	Levels of peripheral CD4 + and CD8 + T cells and glycaemic control level in patients with both type 2 mellitus diabetes and stage III-IV periodontitis: a randomized controlled trial in Chinese population	Fan Yadan, et al.	Randomized controlled trial	n=51 Chinese patients with T2DM and periodontitis	• SRP improved clinical parameters in 6 months. • Uncontrolled patients (HbA1c $\geq$ 7.5%) showed 0.74% HbA1c reduction. • CD4+/CD8+ ratio normalized in the hyperglycemic group. • There were no notable differences in clinical attachment levels between the groups.

6	Inflammatory Status and Glycemic Control Level of Patients with Type 2 Diabetes and Periodontitis: A Randomized Clinical Trial	Biagio Rapone, et al.	Randomized clinical trial (single center double-blind with two parallel-groups, randomized controlled trial)	n=187 T2DM patients with periodontitis	• Median HbA1c significantly reduced from 7.7% to 7.2% after non-surgical periodontal therapy (NSPT). • C-reactive protein (CRP) levels were significantly lower in the intervention group. • NSPT effectively improves both glycaemic control and systemic inflammation.
7	Influence of physical activity on periodontal health in patients with type 2 diabetes mellitus. A blinded, randomized, controlled trial	K Wernicke, et al.	Randomized controlled trial	n=37 non-insulin-dependent T2DM patients	• 6 months of physical activity significantly reduced BOP and severity. • The active group showed a notable drop in HbA1c levels. Systemic inflammation (hsCRP) increased in the inactive control group.

8	The Effect of Periodontal Therapy on Renal Function and Diabetes Control in Patients With Chronic Kidney Disease. A Randomised Controlled Clinical Trial	Spyridon Kouris, et al.	Randomised controlled clinical trial	n=53 CKD patients with periodontitis	• NSPT significantly increased eGFR and decreased hsCRP at 6 months. • HbA1c levels decreased by 0.54% in the diabetic subgroup. • NSPT provides a protective effect against kidney function decline.
9	Clinical Outcomes and Oral Health-Related Quality of Life after Periodontal Treatment with Community Health Worker (CHW) Strategy in Patients with	Yuan-Jung Hsu, et al.	Randomized controlled study	n=68 patients with T2DM	• CHW strategy improved 1-month PD and CAL more than control. • Long-term oral health quality of life (OHQoL) improved significantly. • Experimental patients were more likely to adopt proper self-care.

	Type 2 Diabetes: A Randomized Controlled Study				
10	Clinical efficacy of scaling and root planing with and without metronidazole on glycemic control: three-arm randomized controlled trial	Ambrina Qureshi, et al.	Randomised controlled clinical trial	n=150 T2DM patients with moderate-severe periodontitis	• Significant reductions occurred in BOP, PPD, CAL, HbA1c, and FBG. • SRP improved glycemic control regardless of antibiotic use. • Metronidazole showed no significant added benefit.
11	Research efficacy of gaseous ozone therapy as an adjuvant to periodontal treatment on oxidative stress mediators in patients with	Biagio Rapone, et al.	Randomized clinical trial	N=180 T2DM patients with periodontitis	• Both groups showed significant reduction in clinical parameters. • No significant differences were found in oxidative stress mediators. • Ozone did not enhance the systemic antioxidative effect of NSPT.

	type 2 diabetes: a randomized clinical trial				
12	Salivary asprosin, IL-39, IL-40, and IL-1 β levels in diabetic patients with periodontitis: A cross-sectional analysis.	Ayşe Oruc, Humeýra, et al.	Cross-sectional study	n=88 participants (healthy, diabetic, and/or periodontitis)	• Periodontal parameters (BOP, PD, CAL, GI, PI) were significantly higher in the periodontitis groups. • Salivary IL-1beta, IL-40 and asprosin levels were increased in individuals with periodontitis. • IL-1beta showed the strongest correlation with periodontal parameters such as CAL and PD. • Asprosin levels were positively associated with BMI and HbA1c • IL-39 did not show significant differences between the groups.
13	Efficacy of ILIB on periodontal clinical parameters and glycemic control in patients with periodontitis and type II diabetes-	Francisco Junior, et al.	Randomized clinical trial.	n=21 patients with periodontitis and T2DM	• Both groups showed significant improvement in periodontal parameters (VPI, GBI, BOP, PD and CAL) after treatment. • no statistically significant difference between the test and control groups was found. • ILIB laser therapy did not provide additional periodontal benefit compared with conventional periodontal therapy alone.

	randomized clinical trial.				HbA1c and fasting blood glucose did not significantly improve in either group.
14	Effects of D ₃ K ₂ With Periodontal Therapy in Diabetes Mellitus and Stage I-II Periodontitis Patients.	Aydogan Tolga, et al:	Randomized double-blind placebo-controlled clinical trial	n=38 participants with DM and periodontitis	- Periodontal clinical parameters improved significantly in both groups after treatment. - No significant differences between the groups were observed for periodontal outcomes. - HbA1c levels decreased slightly during follow-up but the difference was not statistically significant. - Vitamin D levels increased in the test group after supplementation. - Overall, vitamin D supplementation provided limited additional benefit compared with periodontal therapy alone.

Figure 2: Table of results (self-made)

5. DISCUSSION

The main objective of this research is to evaluate the extent of the bidirectional relationship between diabetes mellitus and the periodontal disease, alongside the impact of the periodontal treatment and other additional interventions on the glycaemic control and the periodontal health of patients with diabetes mellitus. The results found after the analyse and reading of the articles confirmed the existence of this close relationship between these 2 chronic conditions (26). However, the impact on glycaemic control appears to be more variable between studies.

I. The efficiency of the non-surgical periodontal treatment on the HbA1c

The scaling and root planning (SRP) is the treatment of choice for the cleaning of the periodontal tissue(26–28). Many of the studies that we included in this documentary research have demonstrated a significative reduction in the amount of glycated haemoglobin (HbA1c) that can go from 0,22% to 1% depending on the population and the initial level of glycaemic control (29). For example, Rapone et al. observed a decrease in median HbA1c from 7.7% to 7.2% after six months of treatment. And Qureshi et al. reported a reduction of over 1% in HbA1c at the 6-month follow-up, suggesting that SRP is effective in improving glycaemic control(30).

However, the impact of SRP on the glycaemic control is not uniform. Our sources suggested that the advantage is more marked in patients presenting an initial badly controlled hyperglycaemia (HbA1c > 7,5%). On the other way, the SRP treatment on patients with controlled diabetes (HbA1c < 7%), the effect of the periodontal treatment seems minimal (31). This divergence underline that the SRP acts mostly by reducing the systemic inflammatory charge, which improves the sensibility to insuline. It is also important to mention that some studies like the “Diabetes and Periodontal Therapy Trial (DPTT)” have found no reduction of the HbA1c, that may be explained by the studying of patients with a limited improvement potential or a not long enough trial (26,30,31).

II. The place of Adjuvant therapies.

Many new therapies have been tested to face the difficulty of curing the periodontal diseases in patients with diabetes mellitus (32).

1. Antimicrobial photodynamic therapy (aPDT): it appears to be a promising option to reduce inflammatory cytokines like TNF-alfa in the gingival fluid (33). It helps reducing the depth of the periodontal pockets in patients with diabetes mellitus type 1 (DT1) and 2 (DT2) in the short terms.

Nonetheless, the impact on the reduction of HbA1c is still controversial and not significant enough compared to the SRP alone (33).

2. Systemic antibiotics (Metronidazole): the addition of metronidazole to the SRP treatment does not seem to add advantages significantly high enough to the glycaemic control. This suggests that the mechanical removal of the plaque is what brings the most improvement (30).
3. Ozone and Laser ILIB: The results encountered in the ozone gaseous therapy and the intravascular irradiation of the blood (ILIB-M) are rather deceiving. Those techniques unfortunately did not show improvement of none of the parameters regarding periodontal diseases nor diabetes mellitus (32,34).
4. Nutritional supplements (vitamin D3K2): The vitamin D has a significant role in the modulation of the inflammation. However, the supplementation in D3K2 have shown a limited benefice in diabetic patients (35).

III. Communitary approach and behavioural changes

The treatment success is closely related to the patient compliance and lifestyle. Programs based on Pender's Health Promotion Model involving community health workers have shown very good results (31,36). These direct approaches increase patient's knowledge and efficacy but also sustainably improve their oral health in the long term. For example, personalized education promotes better use of Bass brushing technique, which is important in the maintenance of clinical improvements after SRP.

Additionally, regular physical activity has shown to be very effective in reducing both the severity of periodontitis and HbA1c levels through the reduction of oxidative stress and systemic inflammation(37).

IV. Immunologic perspectives and biomarkers.

The interaction between periodontitis and diabetes mellitus is manifested through an unregulated immunity complex. The peripheral ratio between CD4+/CD8+ is altered in diabetic patients. Surprisingly, the ratio tends to normalise after an efficient periodontal treatment in those patients, suggesting a partial restauration of the immunitary function(26).

Researches about salivary biomarkers has shown that molecules like asprosin, IL-40 and IL-1beta are significantly high when the patient has periodontitis and diabetes(38). Then saliva can become a precious tool for the follow-up of the inflammation in those patients.

Finally, the improvement of the renal functions through the raise of the eGFR observed after an SRP in patients with chronic renal malfunction and diabetes strengthen the idea that the periodontal health is a crucial for the systemic health (39).

V. Limits of the analysed studies

Firstly, many of the randomised controlled trials presented a reduction in the sample size on whom the researches have been conducted. Which can hidden differences that are important enough to notify (26). Then, the majority of the studies are limited to 3 or 6 months, which can be a limited amount of time in the follow-up of trial regarding the control of the glycaemia after an SRP. Once should know that the inflammation of the periodontal tissue reappears if not maintained rigorously (26,30).

Finally, variable data like diet, socio-economic stress and the duration of diabetes are not always controlled even though they are of an influence on the HbA1c. To conclude, the periodontal treatment through non-surgical methods must be considered as an important part of the treatment of diabetes, and especially with patients that have a badly controlled diabetes. If chemical or technologic adjuvants like lasers and ozone therapy have shown to be bringing none noticeable benefices, Interventions focusing on behaviour, physical activity and education seem to offer more significant and durable results(30).

6. CONCLUSION

The primary purpose of this current research is to confirm that the relationship between diabetes and periodontitis is defined by a cycle of systemic inflammation and immune dysfunction through clinical evidence. One of the central findings is to identify that poorly controlled blood glucose levels exacerbate the destruction of the periodontium with oxidative stress and the pathological accumulation of advanced glycation end-products. Conversely, the chronic inflammation of periodontitis worsens insulin resistance by interfering with normal insulin signalling pathways (40,41). Additionally, non-surgical periodontal therapy (SRP) is a potent non-pharmacological tool for improving glycemia, with clinical benefits observed in patients with initially poorly controlled diabetes. However, therapeutic success is often undermined by a significant lack of patient awareness regarding this bidirectional link; studies show that approximately 70% of diabetic individuals have never received information about their periodontal risks. Finally, this work seeks to advocate for a transition to a multidisciplinary model in which dental professionals screen for diabetes risk and physicians prioritise oral health management. This study serves to justify the inclusion of periodontal care. Strengthening this collaborative work is essential for breaking the inflammatory loop and improving long-term clinical outcomes for patients living with these chronic conditions(42,43).

7. SUSTAINABILITY

The systematic integration of periodontal care into diabetes management is essential for the long-term sustainability of healthcare systems. From an economic perspective, diabetes care currently consumes approximately 12% of global healthcare expenditures, making the cost-saving preventive measures a necessity. Empirical data indicate that providing periodontal treatment to diabetic patients leads to a measurable reduction in overall healthcare costs, estimated at roughly €12 per quarter per patient(44). These savings are particularly significant for individuals on insulin therapy and are put into evidence by a decrease in hospitalisations(45). Furthermore, treating periodontitis contributes to "sustainable systemic health" by lowering the inflammation that influences other chronic diseases, such as cardiovascular and renal diseases. We must address the socioeconomic barriers and knowledge gaps that currently prevent patients from seeking routine dental check-ups by implementing oral health screenings within primary care and promoting low-cost education. Healthcare providers can reduce the impact of chronic disease in a manner that is both clinically effective and financially possible(46).

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