



## **GRADUATION PROJECT**

### **Dentistry Degree**

# **INFLUENCE OF DIABETES IN ORAL HEALTH AND DENTAL TREATMENT**

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## **ABSTRACT**

**Introduction:** One of the most encountered diseases by dentists is diabetes mellitus due to its high prevalence worldwide. Diabetes is a metabolic disease that affects various aspects of health, including oral health, it's one of the major sites in the body where diabetes can cause devastation.

**Objectives:** The intent of this review is to describe the association of diabetes with oral health and to evaluate diabetes related emergencies that might be seen in dental clinic.

**Methodology:** A methodological analysis of scientific articles was performed as this type of resource is credited and legitimate. The research was conducted in English through Medline Complete, PubMed. Results from the last eleven years have been considered, providing relevant information about oral manifestations in diabetic patients. In addition, we have considered the influence of diabetes on dental treatments. 33 studies met the inclusion criteria and were analyzed for their credibility.

**Results:** The most encountered oral manifestation in diabetics patients are periodontitis, dry mouth, dental caries, oral candida infections, oral cancer, and taste disturbances. At least one of those oral manifestation in diabetic patients were superior to healthy patients. No relevant difference was found in the treatment (implant rehabilitation, extraction, orthodontic treatment) of well controlled diabetic patients and healthy patients. However, an acute complication may occur during the treatment such as hypoglycemia, and dentists should be conscious of it and must be able to react appropriately.

**Conclusion:** Diabetes might cause oral complications. Dentists can contribute to maintaining the optimal health of patients with diabetes if they take a proactive role in diagnosing and treating oral conditions that are associated with diabetes. Patients who have a well-controlled form of diabetes can receive dental treatment at a dental office similarly to healthy patients.

**Keywords:** Dentistry, Diabetes, Oral manifestation, Dental treatment, Oral Health.

## RESUMEN

**Introducción:** Una de las enfermedades más encontradas por los odontólogos es la diabetes mellitus debido a su alta prevalencia en todo el mundo. La diabetes es una enfermedad metabólica que afecta a varios aspectos de la salud, incluida la salud oral.

**Objetivos:** La intención de esta revisión es describir la asociación de la diabetes con la salud oral y evaluar las urgencias relacionadas con la diabetes que podrían verse en la clínica dental.

**Metodología:** Se realizó un análisis metodológico de artículos científicos ya que este tipo de recurso está acreditado y legitimado. La investigación se realizó en inglés a través de Medline, PubMed. Se han considerado los resultados de los últimos once años, que aportan información relevante sobre las manifestaciones orales en pacientes diabéticos. Además, se ha considerado la influencia de la diabetes en los tratamientos odontológicos. 33 estudios cumplieron los criterios de inclusión y se analizó su credibilidad.

**Resultados:** Las manifestaciones orales más frecuentes en diabéticos son periodontitis, boca seca, caries dental, infecciones orales por *Candida*, cáncer oral y alteraciones del gusto. Al menos una de esas manifestaciones orales en diabéticos fue superior a la de pacientes sanos. No se encontraron diferencias relevantes en el tratamiento (rehabilitación de implantes, extracción, tratamiento ortodóncico) de pacientes diabéticos bien controlados y pacientes sanos. Sin embargo, puede producirse una complicación aguda durante el tratamiento, como hipoglucemia, y dentistas deben ser conscientes de ello y deben ser capaces de reaccionar adecuadamente.

**Conclusiones:** La diabetes puede causar complicaciones orales. Dentistas pueden contribuir a mantener la salud óptima de los pacientes con diabetes si adoptan un papel proactivo en el diagnóstico y tratamiento de las afecciones bucodentales asociadas a la diabetes. Pacientes con diabetes bien controlada pueden recibir tratamiento odontológico en un consultorio dental de forma similar a los pacientes sanos.

**Palabras clave:** Odontología, Diabetes, Manifestación oral, Tratamiento dental, Salud oral.

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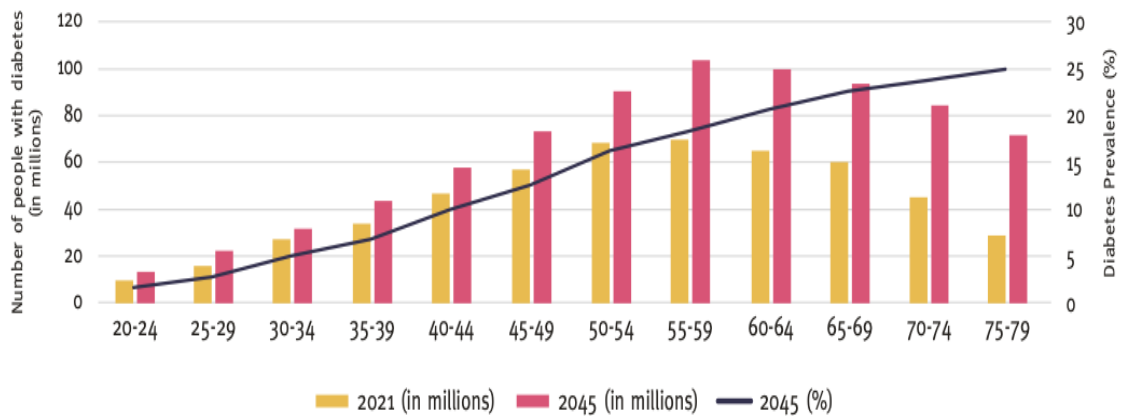
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# I. INTRODUCTION

## 1.1 Diabetes

### 1.1.1. Epidemiology

There are 7.9 billion people in the world, according to the International Diabetes Federation, 537 million adults have diabetes worldwide. 6.7 million people died of diabetes in 2021 (1). By 2030, the World Health Organization predicts that it will be the 7th leading cause of death worldwide. In 2045, the international diabetes federation predicts that 783 million adults will have diabetes worldwide. This increase in the number of diabetics in 2045 is due to the aging of the population, early detection, and improved life expectancy of people treated which contribute to an increase in the numbers. But it is mainly due to social and environmental factors (linked to our lifestyles) that explain this constant increase: overweight, obesity, eating habits, lack of physical activity, and a sedentary lifestyle are the main causes of diabetes. Europe has 61 million people with diabetes or one in eleven Europeans has diabetes (1,2,3).



**Figure 1:** Number of adults people with diabetes (from 20-79 years old) by age group in 2021 and the estimated prevalence in the same group of age in 2045 (3)

### 1.1.2. Definition of diabetes

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. In addition to stimulating cells to absorb glucose from the bloodstream, insulin is secreted by beta cells of the islets of Langerhans converting glucose into energy (3).

The management of diabetic patients in dental practice is becoming increasingly common due to the growing prevalence of diabetes in the population.

It is therefore important to define the influence of diabetes in oral health and dental treatment to allow the dentist to deliver the finest treatment possible for their patient.

## **2.1 Oral health**

A person's oral health includes the health of their teeth, gums, and the entire oral-facial system that allows them to eat, speak, and smile. Oral health refers to the overall health of the mouth, regardless of age (4).

It has been demonstrated that oral health may have systemic multi-organ ramifications. These implications range from endocrine disease to cardiovascular, respiratory, or even neurodegenerative pathology.

Patients with poor oral health are subject to the development of systemic diseases such as pneumonia, high blood pressure, stroke, and diabetes (5,6).

A criterion for general health and welfare is having good oral health.

Caries, periodontal disease, and oral cancer are the most common diseases that negatively affect oral health, but diabetes also negatively affects oral health.

In addition to affecting immune cell function, diabetes mellitus upregulates pro-inflammatory cytokines from monocytes and polymorphonuclear leukocytes and

downregulates macrophage growth factors, predisposing to chronic inflammation, progressive tissue disruption, and diminished tissue repair capacity.

There are several oral complications of diabetes mellitus caused by this immune phenotype, including xerostomia, delayed wound healing of oral mucosa, candidiasis, increased incidence of dental caries, periapical infections, and periodontitis (6).

## **II. OBJECTIVES**

### Principal Objective:

-To describe the association of diabetes with oral health conditions.

### Specific Objectives:

- To examine the most common diabetes-related oral health disorders that are identified in the oral cavity.

- To understand diabetes-related emergencies that might be seen in the dental clinic.

## **III.MATERIAL AND METHODS**

To carry out the following literature review about the influence of diabetes in oral health and dental treatment, exhaustive research has been realized using reliable scientific databases, such as scientific journals, books, literature review studies, and theses. They were found on platforms such as PubMed, Medline. An ascending research was also carried out from the bibliographies of these sources of information.

The following websites such as the World Health Organization, International Diabetes Federation, and the World Dental Federation were also screened for definitions and guidelines.

The realization of the results and the discussion of my work were obtained using the research method PICO. In order to obtain the most relevant results.

The systematic search of my sources of information was established through the advanced search equations in the databases of PubMed.

The formulation of the research questions are the following:

- “Diabetes” MeSH AND “Oral manifestation” (all fields).
- “Dentistry” (all fields) AND “Diabetes” (all fields) AND “Dental treatment” (all fields).
- “Diabetes” MeSH AND “Dental implant” MeSH.
- “Diabetes” MeSH AND “Orthodontic” MeSH.
- “Diabetes” MeSH AND “Tooth extraction” MeSH.
- “Diabetes” MeSH AND “Periodontal treatment” MeSH.

Keywords: Diabetes, Dentistry, Oral Health, Oral manifestation, Periodontal treatment, Orthodontic treatment, Extraction, Implant.

Inclusion and exclusion criteria were established (Table 1). These criteria were used to filter the results on the platform during the search (date of publication, language, article type, species)

Only manuscripts published within the last 11 years were included.

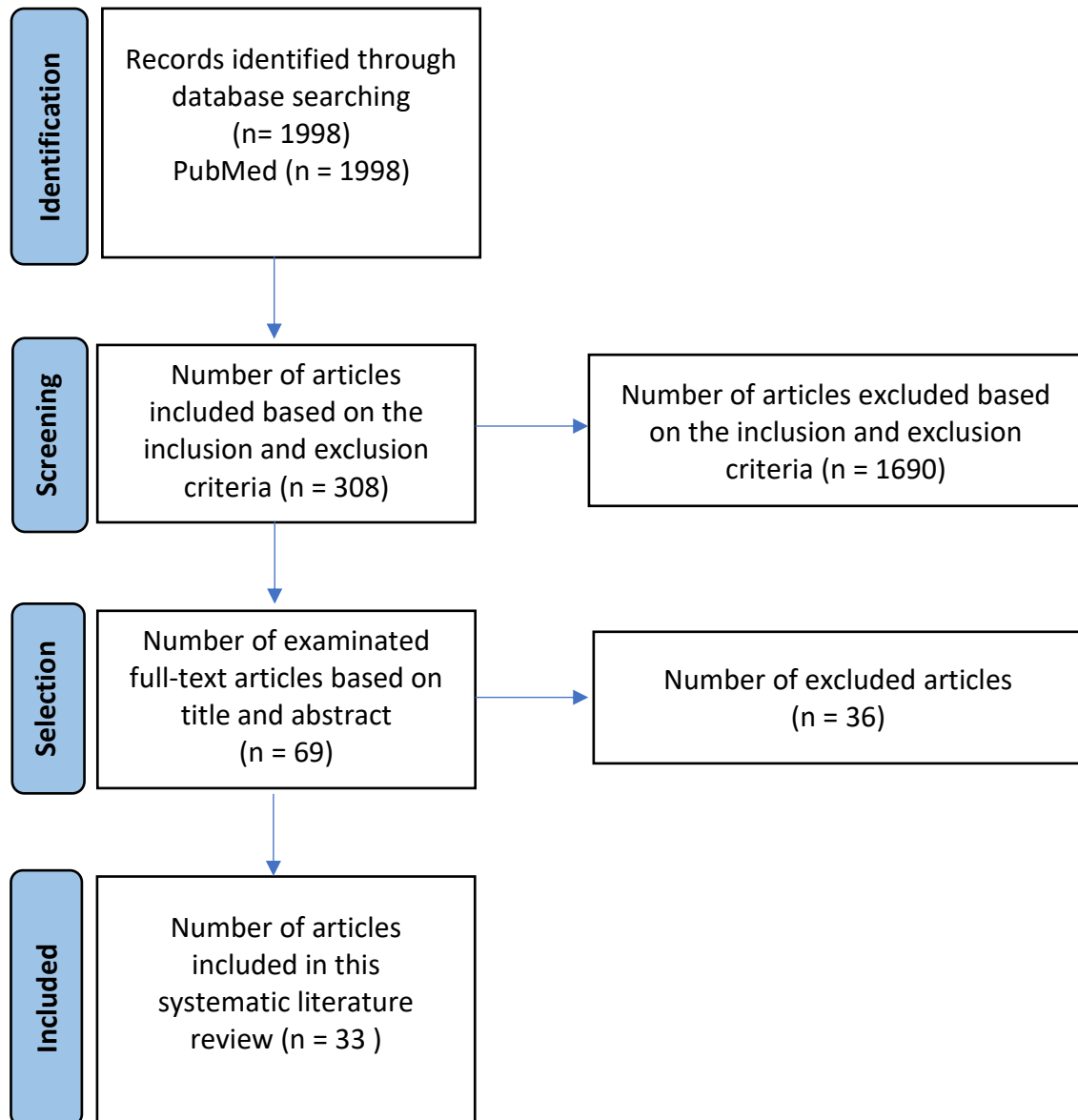
Criteria	Inclusion criteria
Article type	Review, Books, Systematic review, Retrospective clinical study, Clinical study, Randomized control clinical trial, Cross-sectional studies, Meta analysis
Year of publication	From 2012 until 2023
Text availability	Full text and Free full text
Keywords	Title of the article with one of the following terms: Oral health, diabetes, dental treatment, implant, periodontal treatment, orthodontic treatment, extraction.
Language	English, Spanish
Species	Human

**Table 1** : Inclusion criteria of the research



#### IV. RESULTS

**Figure 2:** Flowchart of this systematic literature review.



The results of the other studies used can be found in Annex 1.

**Table 2:** Summary of the descriptive characteristics of articles-based prevalence of oral manifestation in diabetic patients.

Year, Author	Country	Study design	Sample	Treatments	Evaluation	Results
Ahmad P, et al 2019 (8)	Malaysia	Review	63 articles	No treatment was performed.	Evaluation of the most encountered oral manifestation in diabetic patients.	The most common witnessed oral manifestation in diabetic patients include gingivitis, periodontitis that leads to xerostomia, dental caries, oral infections, tongue abnormalities and taste impairment.
Jacob LE, et al 2019 (9)	India	Cross-sectional study	1000 adults (30-77 years)  Divided into 5 groups according to their age	No treatment was done, and an oral examination was carried out with a mouth mirror, tweezers, gauze, tongue depressor, and under electric light.	Evaluation of the most encountered oral manifestation in diabetic patient according to the age group.	The most frequent oral manifestation in order was periodontitis, fissured tongue, xerostomia, candidiasis, burning mouth syndrome, taste alteration, angular cheilitis, oral ulcer, sialadenosis, oral lichen planus, sialorrhea, and geographic tongue.  The group of 60-69 years is the group where oral manifestation was the

						most prevalent. Oral manifestations were less encountered in group of 30-39 years.
Ghadiri-Anari A, et al 2020 (10)	Iran	Cross-sectional study	362 adults (20-70 years)  <u>Group 1:</u> 181 diabetic patients  <u>Group 2:</u> 181 healthy patients	No treatment was done, and an oral examination was carried out under adequate light, lips, and cheeks were retracted during the oral explorations. All the mouth regions were explored by an oral medicine specialist.	Evaluation of oral manifestations including candidiasis, lichen planus, periodontitis, xerostomia, delayed wound healing, geographic tongue, gingival hyperplasia, fissured tongue, and burning mouth syndrome. Diagnosis of the lesions are based on the clinical appearance and patients' history. In case of doubt a biopsy was realized.	The prevalence of oral candidiasis, oral lichen planus, periodontitis, delay oral wound healing, geographic tongue, and xerostomia were significantly greater in diabetic patients than in healthy patients. No significant statistical differences were found for gingival hyperplasia, fissured tongue, and burning mouth syndrome between diabetic patients and healthy patients.
Al-Maweri SA, et al 2021 (16)	Saudi Arabia	Comparative cross sectional study	103 peoples (15-70 years)  <u>Group 1 :</u> 50 diabetic patients  <u>Group 2 :</u>	No treatment was done.	Saliva flow was assessed with the spitting method and xerostomia was assessed with a questionnaire of 4 questions.	Diabetic patients referred a lower salivary flow (0,33+/- 0.16) compared to the group of healthy patients (0,59+/-0,54). No statistical differences were found, but there is a higher proportion of

			53 healthy patients			diabetic patients suffering from xerostomia (60%) comparing to healthy patients (52%).
Lopez-Pintor RM, et al. 2016 (17)	Spain	Review	15 articles	No treatment was performed.	Evaluation of xerostomia and salivary flow in diabetic patients.	All studies reported an increase prevalence of xerostomia in diabetic patient comparing to non-diabetic patients 12,5%-53,5% versus 0-30%.  Studies that determinate the saliva flow have reported a higher flow rate in non-diabetic patients comparing to diabetic patients.
Mauri-Obradors E, et al. 2017 (18)	Spain	Systemic review	19 articles Total of 3,712 patients (2,084 diabetics)	No treatment was performed.	Evaluation of the most encountered oral manifestation in diabetic patients.	14 studies (74%) established a greater prevalence of oral manifestation in diabetic patient and 5 studies (5%) did not admit relevant difference between diabetic patients and healthy patients.

						<p>All studies investigating taste alterations and xerostomia admit a higher incidence of these alterations in diabetic patients comparing to healthy patients.</p> <p>40% of the studies admit an association between caries and diabetes while 60% of the studies didn't admit it.</p> <p>50% of the studies found an associated between mucosal lesion and diabetes while the 50% didn't admit it.</p>
Shenoy MP,et al. 2014 (11)	India	Comparative study	<p>90 peoples</p> <p><u>Group A:</u> 30 diabetic patients (type 1)</p> <p><u>Group B:</u> 30 diabetic patients (type 2)</p>	No treatment was performed.	Evaluation of the oral candidal species carriage in diabetic patients and non-diabetic patients and their oral manifestation. Saliva samples are collected using oral rinse technique.	<p>A positive growth of candidal colonies was found in 30% of the group A, 33% in the group B and 7% in the group C. There is a statistical significance in candidal growth in group a and B compared to group C.</p>

			<p><u>Group C:</u> 30 healthy patients</p>			<p>The mean candidal CFU/ml is positive in group A with 3022,22CFU/ml in group B with 29540,00 CFU/ml and in group C with 6,00 CFU/ml.</p> <p>CFU/ml values of group A and B are significant compared to group C.</p> <p>Erythematous lesions, fissured tongue, atrophic lesion in the tongue , pseudomembranous candidiasis and burning sensations were reported in group A and B.</p>
Gong Y,et al. 2015 (26)	China	Meta-analysis of observational studies	<p>13 articles</p> <p>4 case-control</p> <p>9 cohort</p>	No treatment was performed.	Evaluation of the risk of oral cancer and precancerous lesion in diabetic and non-diabetic patients.	<p>Studies found out an increase incidence of oral cancer in diabetic patients compare to non-diabetic patients.</p> <p>An increase in oral cancer mortality was demonstrated in diabetic patients.</p>

						A positive association between diabetes and risk of oral precancerous lesions was demonstrated.
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**Table 3:** Summary of the descriptive characteristics of articles based on the update of the relation between dental implant survival and diabetic patients.

Year, Author	Country	Study design	Sample	Treatments	Evaluation	Results
Eskow CC, et al. 2017 (34)	USA	Observational cohort study	24 adults (Over 18 years old)	Placing of two or more transgingival implant in diabetic patients.	The survival rate of implants after 1 year and after 2 years in diabetic patients.	<p>The survivals rate of implants after a period of one year in diabetic patients was 98,6%. Out of 72 implants assessed 71 implants remain.</p> <p>The survival after 2 years was assessed on 59 implants and 57 implants remain. According to the study, the survival rate of implants for diabetic patients after a two-year period is 96,7%.</p> <p>29% of the implants have suffered from biological complications the most frequent was peri-implant mucositis.</p>

						<p>The incidence of complications or mucositis was not enforced with HbA1c.</p> <p>Patients with poor glycemic control who underwent implant therapy for two years showed high survival rates with limited complications.</p>
Orto B, et al 2022 (37)	Italy	Retrospective clinical study with 10-year follow-up	47 adults	Full arch rehabilitation with implant prosthetic in patient with diabetic disorder and without	<p>The survival rate for implants, the marginal bone loss, and the clinical complications (wound infection, bleeding, and edema) in diabetic patients and in patients without diabetes. The follow-up period was achieved 1 week after the surgery, at 3 and 6 months and again once a year for the next 10 years.</p>	<p>The survival rate for implants in diabetic patients as 94,74% and 96,72% in patients without any systemic disease. Survival rates for implants were no important statistical difference between both groups.</p> <p>The marginal bone loss had no important statistical difference between both groups too.</p> <p>Concerning the clinical complications, diabetic patients are referred to more wound infection, bleeding, and edema than patients without any systemic disorders. But the statistical difference was too low to prove it.</p>



Katsiroumpa A, et al 2022 (36)	Greece	Systematic review	29 articles	Rehabilitation with dental implants.	To study the repercussion of diabetes mellitus on the osseointegration and stabilization process of dental implants.	<p>4 studies reported a significant increase in implants failure in the group of diabetic patients.</p> <p>5 studies established a higher proportion of implants failing in the group of diabetic patients however not statistically importance was found.</p> <p>10 studies reported a statistically non-significant increase in implants failing in patient not suffering from diabetes.</p> <p>7 studies established no difference in implants survival.</p> <p>3 studies recorded a statistical importance in the increase of implants stability patient not suffering from diabetes.</p>
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**Table 4:** Summary of the descriptive characteristics of articles based on the relation between conventional periodontal treatment and diabetes

Year, Author	Country	Study Design	Sample	Treatments	Evaluation	Results
Sinha S, et al 2021 (31)	India	Clinical study	50 adults  <u>Group 1</u> Diabetic patients  <u>Group 2</u> Non- diabetic patients	Conventional periodontal treatment (Scaling and root planning (SRP)) on diabetic patients compared to non-diabetic patients.	The outcome of SRP on diabetic patients at the start and after 3 and 6 months.  The measured parameters are: -Metabolic assessment (fasting blood sugar, and HbA1c) - Clinical measurement: probing depth, gingival index, plaque index, sulcus bleeding index, and clinical attachment level.	Metabolic assessment:  A significant statistical reduction of the fasting blood sugar level has been registered from the start until 6 months after in the diabetic group.  A significant statistical reduction of HbA1c has been observed from the start until 3 months after and from the start until 6 months but no significant statistical reduction between the 3 and 6 months for diabetic patients.  A significant statistical reduction has been recorded in every clinical measurement for diabetic patients.
Preshaw PM, et al 2012 (19)	UK	Review	95 articles	Periodontal treatments	The relationship between diabetes and periodontitis and the effect of periodontal treatment on diabetic patients.	Studies confirmed that diabetes increases inflammation in the periodontal tissues.  Several studies registered a reduction of HbA1c between 0.40-0.66% 3-9 months

						after conventional periodontal treatment. Patients who underwent a surgical periodontal treatment had HbA1c level that were 0.25% lower than patient with conventional periodontal treatment.
Zhang H, et al 2013 (29)	China	RCCT	75 adults <u>Group 1</u> Treatment group  <u>Group 2</u> Control group	Scaling and root planning (SRP) and Enhanced root planning (ERP)	To figure out the repercussion of SRP and ERP on the periodontal status (bleeding on probing, plaque index, probing pocket depth, clinical attachment loss), and on the glycemic control of diabetic patients. Patients were inspected 3 days before and after the predeterminate time.	Significant statistical amelioration of the periodontal status in the treated group, the probing pocket depth reduction was greater with ERP than with SRP. The reduction of the level of HbA1c and plasma blood glucose levels in the treated group was higher than in the control group.
Bian Y, et al 2021 (30)	China	RCCT	72 adults <u>Group 1</u> SRP  <u>Group 2</u> Root planning  <u>Group 3</u>	SRP or Root planning or Periodontal curettage or Cleansing	The evaluation parameters: fasting blood glucose, plaque index (PI), gingival index (GI), probing depth (PD), attachment loss (AL), serum levels of inflammatory factors were evaluated 3 months before the therapy and 3 months after the therapy.	There is a significant improvement of the clinical measurement (PI, GI, PD, AL) in the group 1 compared to the other one.  There is a significant reduction of the fasting blood glucose in the group 1 compared to the other one.

			Periodontal curettage  <u>Group 4</u> Cleansing			There is a significant reduction in serum levels of inflammatory factors in the group 1.  Group 4 is the one presenting the minor improvement.
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**Table 5:** Summary of the descriptive characteristics of articles based on orthodontics treatment in diabetic patients.

Year, Author	Country	Study Design	Sample	Evaluation	Results
Bampiolaki M, et al. 2022 (25)	Greece	Review	60 articles	Evaluation of the impact of diabetes on orthodontic treatment.	Diabetic patients show a decrease in skeletal maturation and growth parameters in comparison to non-diabetic patients.  The flexibility and joint (TMJ) mobility in diabetic patients are reduced.
Rizvi SO, et al. 2014 (24)	India	Review	10 articles	Evaluation of the impact of diabetes on orthodontic treatment.	A delay in bone regeneration (due to a decrease in the osteoblastic activity or an increase osteoblastic activity), and a weakening of the periodontal ligament were found in diabetic patients

					<p>especially in uncontrolled or poorly controlled.</p> <p>Uncontrolled diabetic patients need an antibiotic prophylaxis when placing orthodontics bands or separator due to the risk of bacteremia.</p>
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**Table 6:** Summary of the descriptive characteristics of articles based on the healing process after tooth extraction in diabetic patients.

Year, Author	Country	Study Design	Sample	Treatment	Evaluation	Results
Power DJ, et al 2019 (32)	Australia	Prospective controlled observational study	105 patients (Average age was 58 years old) <u>Group 1</u> 56 diabetic patients  <u>Group 2</u> 49 non-diabetic patients	Tooth extraction	The healing difference after a dental extraction between diabetic patients and non-diabetic patients. Patients had a follow-up appointment 1 week after the extraction.	If diabetes is well controlled, there is poor but not significant statical difference in the healing process post-extraction between diabetic and non-diabetic patients.

Gazal G. 2019 (35)	Saudi Arabia	Review	36 articles	Tooth extraction	To determine the acceptable level of blood glucose for a tooth extraction in a diabetic patient. To determine the management of diabetic patient when performing an extraction.	180mg/dl (before meals) and 234mg/dl (2 h after a meal) blood glucose level are the maximal acceptable value to realize extractions on diabetic patients. Extraction that was realize with a blood glucose higher than 240mg/dl lead to severe infection and delay in the socket healing.
Huang S, et al. 2013 (33)	Australia	Prospective cohort study	456 patients (18 years old and over) <u>Group 1</u> 224 diabetic patients  <u>Group 2</u> 232 non-diabetic patients	Tooth extraction	The healing difference after a dental extraction between diabetic patients and non-diabetic patients. Follow up period of 4 weeks.	Delay in the healing process was reported in 12 diabetic patients and in 16 non-diabetic patients. No significant statistical difference has been found between both groups.

## **V. DISCUSSION**

### **5.1 Oral manifestation associated with diabetes**

#### **5.1.1. Oral infection**

Diabetic patients are more likely to develop infections and oral infections are one of them. One of the most common oral infections is Oral candidiasis. Candida is a yeast genus with the common species being candida albicans. Candida albicans may be encountered on the skin and other mucosal surfaces such as the oral cavity. The presence of this pathogen does not imply the presence of a disease, most healthy individuals present it as a commensal organism in their oral environment but do not exhibit clinical symptoms. It can cause opportunist infections in individuals with compromised immune systems such as diabetic patients (4,7).

Candida-related oral lesions can have several expressions such as median rhomboid glossitis, angular cheilitis, and chronic atrophic candidiasis but the most common is chronic hyperplasticity candidiasis.

- Chronic hyperplasticity candidiasis is due to the penetration of candidal organisms in the mucosal surface, which produce a hyperplasticity response. The most afflicted areas in the oral cavity are the dorsum of the tongue, the buccal mucosa, the palate, and the labial commissures. Lesions are characterized by an erythematous zone (zone of loss of mucosa), and a white, gray superficial.
- Angular cheilitis is a chronic erosive condition that appears at the corners of the lips as red erosions with central fissures that may ulcer.
- Median rhomboid glossitis is characterized by a depapillated and erythematous dorsal surface of the tongue.
- Chronic atrophic candidiasis or also known as denture stomatitis is defined as an asymptomatic erythematous lesion on the palate of patients wearing a complete or partial prosthesis.

Numerous studies (7-10) have proved that diabetic patients are more susceptible to developing an oral candida infection. Infection due to candida species in diabetic patients mainly results from chronic hyperglycemia which causes a decrease in the immune response: there is a defective response of the polymorphonuclear lymphocyte, neutrophils chemotaxis, and phagocytosis (2). During hyperglycemia phases, the rise in glycoside metabolites in oral epithelial cells may increase the number of candida receptors (11). The reduction of the salivary pH, and salivary flow encourages the establishment of candida in the oral medium (7,9,12). Furthermore, reduced salivary flow leads to a decrease also in secretory immunoglobulin A (sIgA) which has the capacity to hinder the binding of the candida cells to the epithelial cells (9,11). Glycated hemoglobin also known as HbA1c can be used as a predictor of oral candida infection (8,11).

#### 5.1.2. Xerostomia and salivary glands dysfunction

Oral and systemic health are dependent on salivary function (13). The six main functions of saliva can be classified as follows: antibacterial action, preservation, restoration of the tooth integrity and mucosal tissues, digestion, taste protection, and lubricant (8,13).

Several studies have shown that 40 to 80% of diabetic patients have described salivary dysfunction and or xerostomia (7,10,14-18).

An unstimulated whole saliva flow rate lower than 0,1mL/min collected for 5 to 15 minutes, and a chewing-stimulated whole saliva flow rate lower than 0,7mL/min collected for 5 minutes can be classified as salivary glands hypofunction or hyposalivation. Xerostomia also referred as dry mouth is a subjective feeling of dryness in the oral cavity (7).

The salivary flow is regulated by the autonomic nervous system. One of the theories is that reduced salivary flow rate and dry mouth symptoms may be related in some way to diabetic neuropathy (7,18). The ability of salivary glands to react to a salivary stimulus is altered due to autonomic neuropathies. The feedback of hormonal and neural stimulation of the salivary glands is modified due to microvascular changes.



According to studies (7,8,10,15-17) diabetic patients present several alterations of the salivary glands such as injuries in the gland parenchyma, modification of the microcirculation, and asymptomatic bilateral enlargement of the parotid gland who is the largest gland responsible for saliva secretion in the oral cavity. One research has established a link between glycosylated hemoglobin also known as HbA1c and xerostomia. According to it, a decrease in the salivary flow is associated with a high HbA1c (16).

Further research is needed to determine the exact pathological mechanism of diabetes mellitus on the salivary gland.

A disturbance of the salivary flow will cause other complications such as alterations of the mastication, an increase in caries, and oral infections.

### 5.1.3. Dental caries

Dental carie (tooth decay or cavities) is described as the localized destruction of susceptible dental hard tissues (enamel, dentine, and cementum) by acidic by-products from bacterial fermentation of dietary carbohydrates such as sucrose, fructose, and glucose. The equilibrium between the tooth minerals and the bacterial biofilm is present in a healthy environment. If this balance breaks, bacteria in the dental biofilm, such as *Streptococcus mutans* and other closely related *Streptococci* as well as *Lactobacilli*, generate a sticky polysaccharide matrix and acids, demineralizing the hard tooth tissues that lead to dental caries (7).

The pH of the oral cavity, which is generally maintained at 7.2 due to the buffering capacity of saliva, influences the development of dental plaque. If the pH of the oral cavity is less than 5, it encourages the formation of dental plaque and the degradation of tooth hard tissues such as enamel, dentine, and cementum. ANNEX 2. Factors such as hygiene and manner of life also play a role in developing dental caries (8).

Some studies have demonstrated that diabetic patients have a greater proclivity to develop dental caries than non-diabetic patients due to poor glycemic control (7,13,15).

Other studies showed that uncontrolled diabetic patients have a greater proclivity to develop dental caries than patients with controlled diabetes. Moreover, studies reveal that poorly

managed diabetes individuals have a greater number of streptococci and lactobacilli than controlled diabetic patients due to lowered immune defenses. Since these two germs are the most prevalent in caries, a rapid increase of caries in diabetes individuals will be explained (7).

Diabetic individuals, as previously stated tend to suffer from periodontitis which produces gingival recession (15).

This is linked to gingival recession, which exposes tooth-root surfaces, making them vulnerable to developing root caries. Diabetes patients frequently have reduced salivary flow rates and changed saliva composition. Since saliva works as a buffer against the acidic byproducts of bacterial carbohydrate fermentation and aids in the remineralization of the enamel, a change in saliva quantity (hyposalivation) or composition might consequently alter that preventive role against dental caries (7,13,15).

All these factors involved seem to be answerable to predisposing diabetic patients to a greater prevalence of dental caries. However, there is no clear tendency in the literature about the association between diabetes and dental caries.

#### 5.1.4. Periodontal disease

Diabetes and periodontal disease have a close relationship. Diabetic complications include periodontitis, which is often referred to as the sixth complication.

There are two types of periodontal disease: gingivitis, which is a reversible infection of the gingiva around the teeth without a loss of support, and periodontitis, which is an irreversible destruction of the supporting structures surrounding the teeth which include root cementum, periodontal ligament, and alveolar bone along with the clinical appearance of gingivitis. When no periodontal treatment has been initiated, this impairing process eventually results in loose teeth and teeth falling out (2,7,15,19).

Diabetes and periodontal disease, have a well-established bidirectional relationship. Periodontitis is now recognized as a complication of diabetes and diabetes is one of the major

risk factors for the development, progression, and severity of periodontitis (it doubles the risk of developing periodontitis (7,19,20)).

Several studies have proven that diabetes and periodontitis are linked by exasperated and dysregulated inflammatory responses, with the hyperglycemic state resulting in pro-inflammatory effects throughout the body, such as the periodontium.

Adipocytes produce inflammatory mediators, including TNF- $\alpha$ , IL-6, and leptin. By binding the receptor for AGE (RAGE) in the periodontal tissues, hyperglycemic conditions cause AGEs to be deposited in the periodontal tissues, which in turn triggers the release of cytokines and results in altered inflammation. The diabetic state affects the neutrophil role as well, leading to respiratory burst enhancement and delayed apoptosis (which causes a greater degree of periodontal tissue destruction).

Cytokines produced within periodontal tissues can influence glycemic control and insulin signaling through systemic exposure (7,18,19). All these aspects can explain the bidirectional relationship that exists between diabetes and periodontal disease. ANNEX 3.

#### 5.1.5. Periapical pathology and pulpar affection (infection and necrosis)

Caries failed surgical dental treatments, and trauma can all cause dental pulp infections. Pulpar infection can be considered a polymicrobial infection. Blood vessels enter and leave the periapical foramen, supplying the tooth pulp with oxygen and nutrients. If the pulpal vascular system fails, the pulpal infection leads to complete pulpal necrosis and an infected root canal. The infected root canal is a constant supply of bacterial infections, which trigger an immunological and inflammatory response in the region around the dental root apex, known as the "periapical" zone. A periapical lesion, apical periodontitis, or periapical periodontitis is the term used to describe an endodontic infection that induced an inflammatory response (21).

Diabetes mellitus caused two major biological changes: decreased innate immunity, and hyperglycemia (22).

The activity of innate immune cells is modified, neutrophil phagocytosis is reduced, and

macrophages are activated, producing more pro-inflammatory cytokines (21-23). This results in chronic inflammation, diminishing tissue repair capacity, increasing susceptibility to infections, and delays in the wound repair mechanism (2,18).

Hyperglycemia is said to produce structural changes in the tooth pulp and periapical tissues by compromising collateral blood flow. This causes the pulp to age quicker than in patients that do not have diabetes and may also lead to percussion sensitivity, pulpitis, and pulp necrosis (12,24).

Diabetes increases the incidence of periapical pathologies such as apical periodontitis, also larger periapical osteolytic lesions, a higher chance of asymptomatic periapical infections, and a delay or halts in periapical healing (12,18,21-23). According to the findings of several research, periapical illness may lead to poor metabolic control in diabetes (12,23).

#### 5.1.6. Temporomandibular disorders

Temporomandibular joint dysfunction encompasses issues at both the articular level: bone and joint and the functional level: mastication.

Pain during mastication, dysesthesia, joint sounds, and, or restricted jaw opening are principal clinical features of temporomandibular joint disorder. This study revealed that patients with diabetes may present alterations at the temporomandibular level as well as trigeminal pain which may be associated with diabetic neuropathy (25).

Another theory is that diabetes causes inflammatory reactions and microvascular changes that can affect the body's joints, such as the temporomandibular joint, leading to discomfort, stiffness, and sensitivity changes (dysesthesia) that worsen with jaw movements such as chewing and talking (7).

Further research is needed to determine if diabetes is a key factor in temporomandibular joint disorder.

#### 5.1.7. Oral cancer

Oral cancer refers to cancers of the mouth and of the throat. In addition to the lips, the tongue, the oral mucosa, the gums, the floor of the mouth, and the base of the tongue, oral cancer can also develop in the upper throat area: the oropharynx.

As seen previously in the oral mucosal disorder section diabetic patients are more subject to developing precancerous lesions such as oral lichen planus and oral hairy leukoplakia. As a result, they may also be more susceptible to cancer. Researchers have found that diabetic patients are more likely to develop oral cancer than non-diabetic. It remains unclear how diabetes mellitus and oral cancer are related epidemiologically, but their pathogenesis is complex. Momentarily, the only pathological mechanisms proposed to explain why oral cancer risk is increased are hyperglycemia and dyslipidemia, although these are very limited hypotheses. Research into potential pathogenic pathways for diabetes mellitus and oral cancer is lacking. It is impossible to develop effective prevention and treatment programs for oral cancer until it is known why diabetic patients are at higher risk (7,26).

#### 5.1.8. Taste disturbance

Taste perception is inherited, but it can also be altered by the presence of neuropathy (8).

Taste disturbances can range from complete taste loss to the persistent persistence of phantom sensations, such as a bitter or metallic taste in the absence of any irritating material in the mouth.

There are 4 types of gustatory dysfunction: (7)

- Hypogeusia is defined by a decreased sensitivity to taste modalities
- Ageusia is characterized by a complete loss of the taste
- Dysgeusia is a distortion or alteration in the sense of taste
- Phantogeusia is a phantom taste

Taste is an important aspect of dental health that is negatively altered in patients with diabetes.

Numerous investigations have found that the capacity to discriminate and experience diverse flavors is impaired in both type 1 and type 2 diabetes (7,14,15,18).

The two most common types of taste disturbance in diabetic patients are hypogeusia and ageusia. The exact etiology of taste abnormalities in diabetic people is unknown, however, it is thought to be a congenital or acquired taste disease or due to peripheral neuropathy.

In some circumstances, scientists have seen a reduction in vascularization near the tip of the tongue in diabetic patients, which has the potential to lead to vascular and neural damage (7).

In addition, decreasing salivary flow can also alter taste sense. Saliva plays a crucial function in the preservation of the milieu of taste receptors. It is released in reaction to meals, aiding intake and commencing the digestion of carbohydrates and fats, as well as acting as a solvent for flavor compounds and influencing taste sensitivity. Xerostomia is one of the most important symptoms of diabetes mellitus (14,15).

#### 5.1.9. Burning Mouth Syndrome

There is a neurological and sensory orofacial condition known as burning mouth syndrome that causes persistent, usually bilateral, scorching, scalding pain or paresthesia (8,15,18).

A patient complains of discomfort on the tongue, lips, and other mucous membranes of the mouth, even when clinical symptoms are absent and relevant tests are unconfirmed. Although more than one oral region is frequently afflicted, the anterior tongue, hard palate, and lower lip are the most frequently impacted. The pathogenesis is multifactorial, including systemic, local, and psychological components (stress, anxiety, and depression). There is no single reason that can be pinpointed (7,8,18).

Although diabetes mellitus and Burning Mouth syndrome are frequently associated, a clear link has not been found.

It has been hypothesized that diabetic patient's medication use may cause burning mouth syndrome. Using this anti-diabetic medication would decrease the natural moisture in the oral

cavity, causing vascular alterations in the small blood vessels. In addition to a reduction in pain threshold, vascular alterations can result in persistent scorching, scalding, or paresthesia.

ANNEX 4.

#### 5.1.10. Tongue abnormalities

The tongue has in healthy condition a light pink color due to the proportionate distribution of fungiform and filiform papilla on its dorsal surface. The ventral surface and lateral border are smooth, they do not present papillae and have a darker pink color. Occasionally, conspicuous veins are visible (8). Alteration of the tongue mucosa is one of the most usual oral manifestations of diabetes mellitus after periodontal manifestation.

Abnormalities of the mucosa of the tongue encompass:

- Benign Migratory Glossitis
- Median Rhomboid Glossitis
- Fissured tongue

Benign migratory glossitis also called geographic tongue is an inflammatory disorder that is commonly located on the dorsal and lateral border of the tongue. It is a benign disease defined clinically by single or multiple areas of erythema and erosion surrounded by a white, serpiginous, and hyperkeratotic border(7,8,27). Mucosal pain, itching, and burning sensations are felt by the patient. Diabetic patients tend to suffer more from benign migratory glossitis because of a result of hypoxia and oral microvascular dysfunction.

Median rhomboid glossitis or central atrophic glossitis is the most significant and common tongue alteration due to diabetes mellitus; it arises from a subsection of erythematous candidiasis (8,27). It is characterized by central, oval, or rhomboid-shaped papillae atrophy and an erythematous lesion in front of circumvallate papillae on the dorsal surface of the tongue (8,10). This oval or rhomboid shape lesion is symmetrical and is clearly delimited by a smooth and shining surface.

Diabetes mellitus is associated with median rhomboid glossitis as a result of a predisposing condition: microangiopathy, which is frequent in diabetic individuals (27) .

Fissured tongue is a tongue developmental defect characterized by disruption of the smooth texture of the tongue's dorsal surface by one or more fissures that are mainly found over the length of the tongue. This condition is normally symptomless unless there is a buildup of debris or food in the fissures, which can cause irritation or inflammation and increase the risk of infection. Fissuring occurs as a result of both a decrease in the amount and quality of saliva that can be linked with xerostomia due to diabetes mellitus (8,9,27).

#### 5.1.11. Oral mucosal disease

Any abnormal change in the mucosal surface of the mouth is referred to as an oral mucosal lesion. People with diabetes mellitus may develop oral mucosal lesions, including lichen planus, recurrent aphthous stomatitis, and oral hairy leukoplakia according to studies (7-9,14,15,27).

Oral lichen planus is a dermal disorder that is characterized by the production of lesions in the oral cavity. It is characterized by white areas of the mucosa that do not wipe off and a lacey or patch-like white pattern over an erythematous surface. The associations between oral lichen planus and diabetes mellitus have been suggested by several studies. Oral lichen planus may be caused by immunological defects that result in endocrine dysfunction in diabetes mellitus. Moreover, diabetics have often been prescribed medications that can cause related mucosal changes called lichenoid drug reactions. These medications are antihypertensive and antihyperglycemic. Lichen planus or lichenoid reactions have several symptoms, including a burning sensation in the oral mucosa and an increased sensitivity to acidic foods. A higher risk of dysplastic or malignant transformation is associated with them. To properly evaluate these patients, it is imperative to refer them to a dental surgeon specializing in this area (7-9,14,18).



Aphthous stomatitis is also a mucosal lesion that has been reported in diabetic patients. Aphthae are ulcers on the oral mucosa except on the gingiva and the hard palate. Some studies showed that diabetic patients become more susceptible to changes in the oral cavity due to lower chemotaxis and phagocytosis and reduced blood supply due to reduced microcirculation. It could lead to the development of aphthous stomatitis (14,15,20).

Oral hairy leukoplakia is a predominantly, white lesion, soft, and corrugated forming painless plaques on the lateral borders of the tongue. Oral hairy leukoplakia is typically associated with immunodeficient conditions and is potentially a premalignant lesion. A deficiency in polymorphonuclear neutrophils chemotaxis and abnormal macrophage phagocytosis may be responsible for oral hairy leukoplakia among diabetic patients as is demonstrated in various studies (7,27).

## **5.2 Dental treatments**

### **5.2.1. Precaution when caring for a diabetic patient**

The dental clinic must adopt a series of measures when dealing with diabetic patients (5,28):

- Review the medication the patient is taking for his/her diabetes and any other diseases.
- Check the blood glucose level before treatment with the use of a glucometer. In diabetic patients, the fasting plasma glucose should be around 7,0mmol/L, postprandial plasma glucose and random plasma glucose should be around 11,1mmol/L. If the glucose level is not optimal the procedure will be postponed to another day.
- Early morning appointments are desirable in order to decrease the risk of stress engendering hypoglycemia. The liver can release glucose molecules when stress hormones are released.

- Short appointments will be preferable for diabetic patients.
- Dentists should ask for the last blood work of the patient to control the glycated hemoglobin. Its value should be around 6,5%.
- Dentists must be careful with drug prescriptions. Some drugs can interact with the patient current medication for diabetes and provoke hyperglycemia such as NSAIDs and corticosteroids.
- When facing a hypoglycemic crisis, the dentist and the assistant need to be prepared and aware of the protocol to follow.

#### 5.2.2. Conventional periodontal treatment

Conventional periodontal treatment encompasses scaling and root planing and enhance root planing. Diabetes mellitus and periodontal disease present a bidirectional relationship. Periodontal disease has a negative impact on glycated hemoglobin producing an increase in HbAc1 which lead to uncontrolled diabetes. Glycated hemoglobin has an adverse effect on periodontal disease generating an increase in the disease severity (19).

After a conventional periodontal treatment including Scaling and root planing or enhance root planing a significant improvement has been reported in the periodontal parameters (plaque index, bleeding index, gingival index, probing depth, and clinical attachment level) in diabetic patients. Enhancing root planning reduces periodontal parameters more effectively than scaling and root planning alone. A reduction of 0.4% and stabilization of the glycated hemoglobin have been reported after conventional periodontal treatment (19,29,30).

Periodontal treatment will not cure periodontal disease but will decrease systemic inflammation and stop or reduce tissue and bone degradation. There is an obligation for patients, especially diabetics, to undergo periodontal revisions on a regular basis and maintain proper dental hygiene in order to maintain adequate oral health (31).

### 5.2.3. Extraction

A dental extraction is an invasive act followed by a period of healing of the mucosa membrane and the bone. Diabetic patients due to hyperglycemia may be subject to a delayed healing process, increasing inflammation process, and a higher risk of infection. Several studies have shown that the risk of postoperative complications after dental extraction depends on diabetes control. Dental professionals should order blood work to determine the patient's glycosylated hemoglobin level to determine if their diabetes is well controlled. A patient with controlled diabetes has a glycosylated hemoglobin superior to or equal to 6.5%. Patients with type 1 diabetes or insulin-dependent type 2 diabetes are more likely to have complications such as delayed healing, and a greater risk of infection, but not systematically (32,33,34). Non-insulin-dependent patients can be treated like non-diabetics (34).

However, when a diabetic patient will undergo a dental extraction certain parameters should be checked such as the blood glucose level. Fasting blood glucose level should be around 180 mg/dl for a dental extraction. In case of an emergency dental extraction, the blood glucose level (2 hours after eating) should be around 234mg/dl. Dental extraction will not be performed in diabetic patients with a blood glucose level lower than 70mg/dl. A hypoglycemia crisis could occur in this situation. A glucometer is essential for dental clinics to monitor glucose levels (35).

Antibiotic prophylaxis is not needed before dental extraction in patients with controlled diabetes but in case of uncontrolled diabetes or surgical extraction, antibiotic prophylaxis may be needed (2g of amoxicillin 1 hour before the intervention in case of allergy to penicillin, 500mg azithromycin, or clarithromycin). If the dentist has any doubts regarding the patient's medical condition, he or she should have an inter-consultation with the patient's medical practitioner (8,35).

#### 5.2.4. Dental implant placing

Diabetic patients are more susceptible to periodontal disease, caries, and infectious disorders. Therefore, the risk of losing teeth is greater than in other patients. Dental implants could be a rehabilitation possibility. In order to have a successful rehabilitation, the dental implant needs to have satisfying osseointegration, insignificant bone loss, gingival health, a reduce probing depth, and no presence of infection (peri-implantitis or mucositis) (20,34).

According to several studies, implant placements in diabetic patients can be as successful as in healthy subjects. The failure rate of implants, the marginal bone loss, and the clinical complications such as wound infection, bleeding, edema, and delay in bone healing in diabetic patients are slightly higher than in healthy patients but they are no significant statistical differences. In order to get this type of result diabetic patients need to have a controlled diabetic with an HbA1c of around 7%, irreproachable as well as well-controlled oral hygiene, and attend post-surgical checkups. Rehabilitation with dental implants is not advised in case of uncontrolled diabetes considering the adverse effect of hyperglycemia on bone formation, wound healing, and immune response. Some dentists recommend the use of antibiotic prophylaxis before the surgery to diminish the possibility of infection (amoxicillin 2g 1 hour before or in case of allergy 500mg azithromycin, or clarithromycin) (20,34,36,37).

#### 5.2.5. Orthodontic treatment

Orthodontics is a procedure that aims to correct and treat disorders related to abnormalities in the shape of the jaw and or position of the teeth. The orthodontic principle is established on the remodeling of the alveolar bone upon lengthened application of forces (25).

It's established that diabetes produces a decline of blood flow called microangiopathy in teeth, gum, and bone. Microangiopathy creates ischemia, swelling of the gums, alteration of the vitality of the tooth with percussion sensitivity, and or reversible pulpitis. A reduce osteoblastic activity diminishes bone production and regeneration in diabetes patients.

Furthermore, osteoblasts live cycle is reduced by reason of an intensified apoptosis process. Collapsing of the periodontal ligament can also be a consequence of diabetes. Uncontrolled diabetes can make it exacerbate these manifestations (24,38).

Diabetes and orthodontic treatment do not conflict except in the case of severe uncontrolled diabetes or periodontitis (24,25,38). However, dentists should be informed of the consequences of diabetes on teeth, and periodontium in order to minimize the probable complications of orthodontic treatment. Several considerations should be considered before making the decision to start an orthodontic treatment on a diabetic patient. Discard patients suffering from periodontitis or with uncontrolled diabetes, assure favorable dental health and oral hygiene, and monitor blood glucose. During orthodontic treatment, light forces should be applied in order to avoid overload and negative effects on bone remodeling. Screws, bands, or separators placement are invasive orthodontic procedures, in order to perform these procedures antibiotic prophylaxis is needed to limit the risk of possible infections (amoxicillin 2g 1 hour before or in case of allergy 500mg azithromycin, or clarithromycin). For simple orthodontic procedures, no antibiotic prophylaxis is necessary (24).

### **5.3 Prevention**

#### **5.3.1. Signs, and management of hypoglycemia crisis**

Patients with diabetes can suffer hypoglycemia attacks, which may result in death in 2-3% of cases. Factors favoring the risk of a hypoglycemic attack include medications (insulin, sulfonamides, glinides), kidney disease, pregnancy, and hemoglobin levels below 6.5%. Inadequate insulin or oral hypoglycemic medications are the most common cause of hypoglycemic attacks. Blood glucose levels should range from 3.6 to 5.8 mmol/L in a healthy individual. In diabetic patients, the fasting plasma glucose should be around 7,0mmol/L, and the postprandial plasma glucose and random plasma glucose should be around 11,1mmol/L (28). If the blood glucose level is below 3mmol/L (may vary depending on the patient), the patient may be confused and/or have difficulty concentrating. A dentist must be able to identify the signs and symptoms of hypoglycemic attacks and know how to treat them (2,28).

If the dentist is suspecting a hypoglycemic episode, he should abort the dental treatment immediately.

Tremor, tachycardia, alteration of consciousness, concentration, and blood glucose inferior to 4 mmol/L are signs of hypoglycemia. Symptoms are shakiness and trembling, increased sweating, hunger, and « pins and needles » in the lips and tongue (2,5,28).

The management of the hypoglycemic crisis will depend on the state of consciousness of the patient and their ability to safely swallow.

If the patient is conscious, he/she will receive 10-20g of glucose orally in form of liquid, granulated sugar, or lumps of sugar. After a period of 15 minutes, the finger-stick glucose test is repeated. If the level of blood glucose is still lower than 4 mmol/L repeat the administration of 10-20g of glucose and check blood glucose in 15 minutes. Continue until a blood glucose level is superior to or equal to 4 mmol/L. The patient will fully recover within 20 minutes.

Patients suffering from hypoglycemia owing to insulin or oral anti-diabetic medications should be hospitalized as soon as possible.

If the patient is unconscious medical emergency assistance needs to be alerted. A 1 mg glucagon injection will be given intramuscularly or subcutaneously, followed by a glucose gel being applied internally to the mouth, and check blood glucose in 15 minutes. 5 to 25 grams of 50% dextrose can be given intravenously if access is available. This hypoglycemic episode will be notified to the patient's physician (2,5,28).

### 5.3.2. Signs of hyperglycemia crisis

Because of the prolonged onset of symptoms resulting from diabetic ketoacidosis or hyperosmolar hyperglycemia, these conditions are rarely encountered as dental emergencies. It is difficult for dentists to distinguish between hypoglycemia and hyperglycemia since hyperglycemia can present with symptoms including hunger, nausea, vomiting, weakness, or abdominal pain. Since a small amount of added sugar will not cause significant damage to the

patient, the dentist should assume a hypoglycemic emergency and administer carbohydrates immediately. When a patient experiences a true hyperglycemia emergency, insulin, and medical intervention are essential (2,5).

### 5.3.3. Instructions for diabetics

There are certain recommendations diabetic patients should follow in order to reduce their possible oral manifestations associated with diabetes.

In diabetic patients, oral candidiasis appears to be one of the most common oral manifestations. Preventing oral candidiasis is best accomplished by controlling glycemia. However, if the patient develops oral candidiasis, the prescription of an antifungal medication such as clotrimazole, nystatin, or miconazole is needed.

Dry mouth or xerostomia can be prevented with adequate oral hygiene which consists of brushing the teeth twice a day with fluoride toothpaste and flossing once a day. Having controlled diabetes also plays a key role in preventing dry mouth. Diabetic patients can manage the symptoms of xerostomia by using saliva substitute or saliva stimulant depending on the patient's needs.

They are also subject to dental caries, in order to avoid the development of further pathologies and restore the function and aesthetics of a tooth, dental caries must be treated. The development of dental caries can be prevented with adequate oral hygiene which consists of brushing the teeth twice a day with fluoride toothpaste and flossing once a day. Dietary tips, using a mouthwash containing NaF 2% once a day, applying fluoride varnish (NaF 5%) every 6 months, and having controlled diabetes are measures that reduce the incidence of dental caries.

Despite the fact that periodontal disease cannot be completely cured, it can be controlled if treated efficiently with scaling and root planing. It can be averted with periodic dental revision, controlled diabetes, dietary tips, satisfying oral hygiene brushing the teeth twice a day with fluoride toothpaste, and flossing once a day.

If the patient suffers from a pulpar or periapical pathology an endodontic treatment such as a root canal will be performed. Pulpar and periapical pathologies are hard to prevent but having stable diabetes can be part of a preventive measure (12,18).

## **VI. CONCLUSION**

Diabetes is a very common metabolic disease that affects various aspects of health, including oral health, it is one of the major sites in the body where diabetes can cause devastation. The relationship between diabetes and oral disorders is well established.

Diabetes patients are more prone to oral complications such as periodontitis, dry mouth, dental caries, oral candida infections, oral cancer, and taste disturbances. Several longitudinal studies indicate a temporal relationship between periodontitis and oral cancer. A number of studies suggest that microvascular complications of diabetes can be triggered by the same pathogenic pathways that cause oral complications as well. The generally increased prevalence of oral complications cannot be neglected, even though this is not evident for all of them.

Oral complications have a huge impact on diabetic patients, quality of life, prevention, and early management of oral pathologies. When it comes to managing patients with diabetes mellitus, dentists must pay attention to their patient's needs. Medical professionals should be aware of the signs and symptoms of this disease, so they can address them accordingly. Dental professionals can greatly contribute to maintaining the optimal health of patients with diabetes mellitus if they take a proactive role in diagnosing and treating oral conditions that are associated with diabetes mellitus and are actively involved in the treatment of such conditions. It is imperative that these patients are aware of their increased susceptibility to infections and delayed wound healing.

Patients who have a well-controlled form of diabetes can receive dental treatment at a dental office similarly to patients who do not have diabetes. Morning appointments are preferred over evening ones, and patients must be instructed not to rush, to reduce the possibility of hypoglycemia occurring.



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## VIII. ANNEXES

Annex 1:

Descriptive characteristics of articles-based prevalence of oral manifestation in diabetics patient and management of diabetic patient in dentistry.

Year, Author	Country	Study Design	Sample	Treatment	Evaluation	Results
Cicmil A, et al. 2017 (14)	Bosnia	Cross-sectional	90 adults (45-65years)  <u>Group 1:</u> 60 diabetic patient  <u>Group 2:</u> 30 healthy patients	No treatment was performed.	Evaluation of the oral symptoms and mucosal lesions in diabetic patients.	Diabetic patients (poorly controlled) present a statistically significant higher presence of xerostomia and neurosensory disorders than non-diabetic patients.  Poorly controlled diabetic patients present an increased prevalence of oral mucosal lesions in comparison to controlled diabetic patients and healthy persons. No statistically significant discrepancy was found between the groups.
Nayani S, et al. 2020 (2)	UK	Review	38 articles	No treatment was performed.	The management of diabetic patients experiencing dental treatment.	For surgical procures, the blood glucose should be 6-10mmol/l in order to treat the patient safely.

						Hypoglycaemia is defined as blood glucose below 4 mmol/l.
Menon A, et al 2018 (15)	India	Review	21 articles	No treatment was performed.	Evaluation of the most commonly observed oral manifestations in diabetic patients.	<p>Studies showed that diabetic patients are more susceptible to periodontal disease than healthy patients.</p> <p>Tastes disturbances have been observed in diabetic patients but not all studies have report it.</p> <p>Oral mucosal disorders including lichen planus and recurrent aphthous stomatitis have been observed in diabetic patients but not all studies have report it.</p> <p>Some studies have reported that diabetic patient have more active dental caries than healthy patients.</p>
Wagner A, et al. 2018 (20)	Romania	Review	17 articles	No treatment was performed.	Evaluation of the oral health in diabetic patients.	<p>Periodontitis has a higher prevalence (times two) in diabetic patients in comparison to non-diabetic.</p> <p>Patient with a poorly controlled diabetes have a higher periodontal attachment lost, and more gingival bleeding.</p>

Leite RS, et al. 2013 (13)	USA	Review	45 articles	No treatment was performed.	Evaluation of the most commonly observed oral manifestations in diabetic patients.	<p>Patients with diabetes present a two-fold higher risk of developing periodontal disease compared to healthy patients. Patients with uncontrolled diabetes present an increased inflammatory response.</p> <p>Pathologies such as fissured tongue, lichen planus, recurrent aphtous stomatitis , oral candidiasis are more prevalent in diabetic patients.</p> <p>Xerostomia is linked to a decreased in the salivary flow rates and an increase in HbA1c.</p> <p>Several studies have reported an increase of dental caries in diabetic patients, but no clear association has been found.</p>
Martí Álamo S, et al. 2011 (28)	Spain	Review	25 articles	No treatment was performed.	The management of the strategies use in the dental practice to treat diabetic patients.	<p>When the blood glucose level is between 100 and 200 mg/dl, invasive dental procedure can be performed.</p> <p>Blood glucose level: &lt; 60 mg/dl is reported as a hypoglycemic crisis.</p>

Segura-Egea JJ, et al. 2012 (23)	Spain	Review	38 articles	No treatment was performed.	The association between diabetes mellitus and periapical inflammation.	<p>Studies reported a high prevalence of apical periodontitis and diabetic patients.</p> <p>Studies proposed that chronic periapical disease may contribute to metabolic dyscontrol of diabetes.</p>
Segura-Egea JJ, et al. 2012 (22)	Spain	Review	50 articles	No treatment was performed.	The association between apical periodontitis and diabetes.	<p>Results of studies were not conclusive but a proposition of an association between apical periodontitis and diabetes.</p> <p>Studies have described an increase prevalence of periapical lesions, asymptomatic infections and diabetic patients.</p> <p>Diabetic patients with a poor glycemic control and a high HbA1c are more subject to apical periodontitis.</p>
Verhulst MJL, et al. 2019 (7)	Netherlands	Review	250 articles	No treatment was performed.	Evaluation of all the potential oral complication due to diabetes mellitus.	<p>Cross-sectional studies have investigated candidal manifestations in diabetic and non-diabetic patients. A higher prevalence of median rhomboid glossitis, angular cheilitis patients with diabetes compared to healthy patients.</p> <p>Some studies reported a significant prevalence of xerostomia in diabetic patients (53,5%) compared to healthy patients (28%).</p> <p>Some studies showed a higher prevalence of carie in diabetic patients compared to non-</p>



					<p>diabetic patients, but other studies didn't report it.</p> <p>Studies indicate an increase in prevalence and incidence in diabetic patients.</p> <p>Severe temporomandibular joint (TMJ) dysfunction was significantly more prevalent in the diabetic group (27.3%), compared to non-diabetic patients (15.8%).</p> <p>Studies showed a higher prevalence of oral cancer and precancerous lesions in diabetic patients (8%) in comparison to non-diabetic patients (3,2%).</p> <p>In some studies, hypogeusia was more reported in diabetics patients than in non-diabetic patients.</p> <p>Several studies concludes that diabetic patients are more susceptible to suffers from certain taste alterations.</p> <p>Studies have found a higher prevalence of burning mouth sensation in diabetic patients</p>
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						(18%-40%) than in non-diabetic patients (7%-11,1%).
Kudiyirikal MG, 2015 (12)	UK	Review	75 articles	No treatment was performed.	Determination of the most common oral manifestation of diabetes	Oral infection has an increase prevalence in diabetic patient resulting from salivary dysfunction, hyperglycemia and abnormal immune response. According to several studies, diabetic patients have a higher prevalence of periapical disease, and it can contribute to a poor metabolic control of the diabetes.
Miller A, et al. 2020 (5)	Canada	Review	30 articles	No treatment was performed.	Management ,and dental considerations for diabetic patients.	Dental management considerations for diabetic patient are data collection about blood glucose level, HbA1c level, doses and time of administration of the medication.  Signs and management of hypoglycemic crisis : Tremor, tachycardia, alteration of consciousness. Blood glucose inferior to 4 mmol/L are signs of hypoglycemia. Patient is conscious, he/she will receive 10-20g of glucose orally. Patient is unconscious 1 mg glucagon injection.

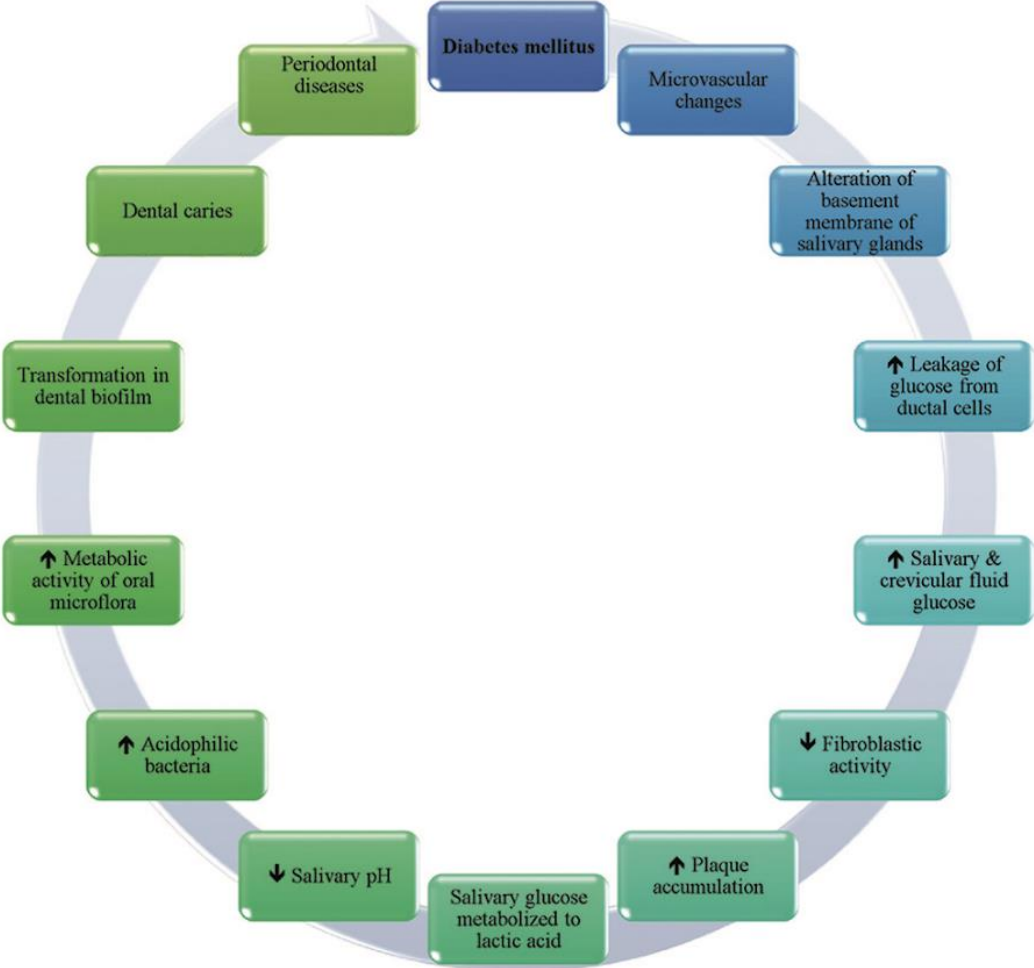
Sasaki H, et al. 2016 (21)	USA	Review	50 articles	No treatment was performed.	The relation between periapical lesion and diabetes.	Diabetes may increase the risk of pulp necrosis and periapical pathologies.
Shetty P, et al. 2021 (27)	India	Review	30 articles	No treatment was performed.	The different types of tongue lesion associated with diabetes.	Diabetic patients are clearly subject to tongue disorders or abnormalities that may lead to diabetic complications such as glossitis, candidiasis of the tongue, oral hairy leukoplakia, geographic tongue and fissured tongue.

Descriptive characteristics of articles based on orthodontics treatment and implant rehabilitation in diabetic patients.

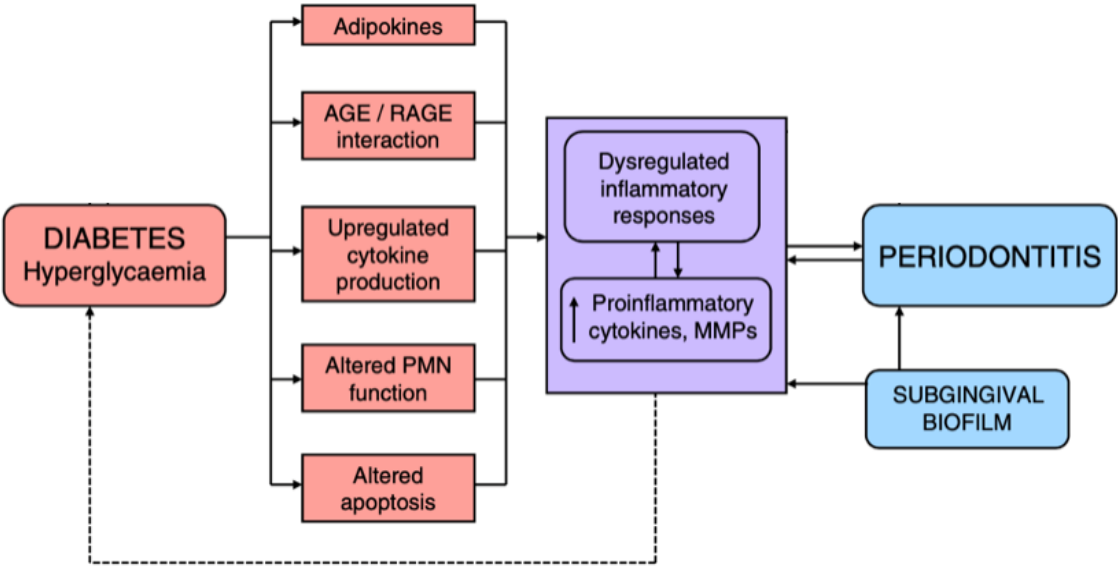
Year, Author	Country	Study Design	Sample	Evaluation	Results
Almadih A, et al. 2018 (38)	Saudi Arabia	Review	10 articles	Evaluation of the impact of diabetes on orthodontic treatment.	<p>A delay in bone regeneration due to a decrease in the osteoblastic activity or an increase in osteoblastic activity, in diabetic patients especially in uncontrolled or poorly controlled.</p> <p>Studies have shown that diabetic patients who undergo orthodontic treatment with a poorly controlled glucose level have a high risk of periodontal ligament rupture.</p>

					Uncontrolled diabetic patients need antibiotic prophylaxis when placing orthodontics bands or separators due to the risk of bacteremia.
Wagner A, et al. 2018 (20)	Romania	Review	17 articles	The success of dental implants in diabetes patients.	<p>Studies reported that diabetic patients with a poorly controlled diabetes had a decreased stability from the 2 to 6 first weeks after one year, no statical differences have been noticed between diabetic (controlled and non-controlled) ,and non-diabetic patients.</p> <p>Implant survival in diabetic patients range from 85% to 96,4%.</p>

Annex 2: Diagram representing the correlation between diabetes mellitus, periodontal disease, and dental caries (8)



Annex 3: Simplified chart of the bidirectional relationship between diabetes mellitus and periodontal disease (19)



Annex 4: The probable connection between burning mouth syndrome and diabetes mellitus (8)

