INSTITUTO UNIVERSITÁRIO EGAS MONIZ

MESTRADO INTEGRADO EM MEDICINA DENTÁRIA

IMPLANT THERAPY FOR PATIENTS WITH DIABETES

Trabalho submetido por
Bader Razzouk
para a obtenção do grau de Mestre em Medicina Dentária

Novembro de 2022

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AGRADECIMENTOS

Terminada uma grande etapa na minha vida gostaria de deixar aqui o meu sincero agradecimento a algumas pessoas que fizeram parte deste percurso:

Ao meu Orientador de tese, Prof. Doutor Ignácio Barbero Navarro.

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RESUMO

A procura de pacientes diabéticos, após a perda de um ou mais dentes, por tratamentos com implantes é crescente. Isso nos leva a refletir sobre a viabilidade da cirurgia de implante e sobre as medidas que devem ser tomadas para garantir e manter o sucesso em pacientes com doenças sistêmicas. Para responder a estas questões, propusemos fazer um estudo de literatura.

As complicações orais do diabetes podem aumentar muito o risco de se tornar parcial ou totalmente desdentado. Existem muitas causas: gengivite, doença periodontal, xerostomia, aumento da suscetibilidade à infeção, cárie e lesões periapicais podem levar ao aumento das taxas de extração dentária. No entanto, a estabilidade do tecido periimplantar e a manutenção da crista óssea são essenciais para a sobrevivência e sucesso a longo prazo dos implantes dentários.

Em modelos experimentais, é demonstrado que pacientes diabéticos que recebem implantes têm uma progressão satisfatória da osteointegração. No entanto, o diabetes prejudica a cicatrização de feridas e diminui a área de contato do tecido em pessoas que têm a doença.

Portanto, é fundamental seguir as recomendações antes da colocação de implantes dentários, que incluem manter um bom controle glicêmico, usar profilaxia antibiótica, usar bochechos com clorexidina e manter uma boa higiene bucal. Todas essas ações são cruciais para a sobrevivência dos implantes dos pacientes diabéticos.

Todos os artigos com mais de 15 anos em inglês, português e francês incluindo os seguintes critérios, serão mantidos:

Meta-análise, Revisões sistemáticas, Ensaios controlados randomizados, Coortes, Estudos caso-controle, Relatos de casos.

Palavras-chave: “diabetes mellitus”, “implante dentário”, “osseointegração”, “periimplantite”.

ABSTRACT

The demand of diabetic patients, after the loss of one or more teeth, for implant therapy is increasingly. This leads us to ask questions about the feasibility of implant surgery and the means to be implemented to guarantee and maintain success on subjects with systemic pathologies. To answer these questions, we proposed to carry out a review of the literature.

The oral complications of diabetes can greatly increase the risk of becoming partially or totally toothless. There are many causes: gingivitis, periodontal disease, xerostomia, increased susceptibility to infection, caries and periapical lesions can all lead to increased rates of tooth extraction. However, peri-implant tissue stability and crestal bone maintenance are essential for both the survival and long-term success of dental implants.

In experimental models, it is demonstrated that diabetic patients who get implants experience a satisfactory progression of osteointegration. However, diabetes is known to impair wound healing and decrease the area of tissue contact in persons who have the condition.

Therefore, it is crucial to go by the recommendations before having dental implants placed, which include maintaining good glycemic control, using antibiotic prophylaxis, using chlorhexidine mouthwash, and maintaining good oral hygiene. All these actions are crucial for diabetic patients' implant survival.

All articles over 15 years old in English, Portugues and French including the following criteria will be retained:

Meta-analysis, Systematic reviews, Randomized controlled trials, Cohorts, Case control studies, Case reports.

Keywords : “diabetes mellitus”, “dental implant”, “osseointegration”, “periimplantitis”.

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INTRODUCTION

Diabetes mellitus (DM) is a significant worldwide health issue that has a significant global patient population. According to information provided by pertinent international organizations, there will be 642 million diabetic patients globally in the next 20 years\. DM has a significant negative impact on overall health in diabetics (especially derived from vascular, cardiac, renal, ocular, or neurological affectation). It also implies a high rate of disease-related mortality and high healthcare spending, which is expected to reach $673 billion yearly (1).

Among the organs and systems that are impacted by DM are the oral cavity. The prevalence of diabetes mellitus (DM) has dramatically increased over the past few decades, mostly as a result of the persistent rise in the incidence of type 2 DM. According to statistics from the World Health Organization, more than 422 million adults worldwide had diabetes in 2014, and it is anticipated that this number will continue to climb (2).

Dry mouth, dental caries, periodontal disease and gingivitis, oral candidiasis, or thrush, burning mouth syndrome, taste disturbances, rhino cerebral zygomycotic (mucormycotic), aspergillosis, oral lichen planus, geographic tongue and grooved tongue, stimulating and traumatic wounds, delayed wound healing and increased incidence of infection after surgery, and salivary gland dysfunction are just a few of the oral health issues and symptoms linked to diabetes (3). Diabetes mellitus (DM) is a common clinical condition that affects 8.3% of the global population (415 million people), 13.1% of the Portuguese population, and remains largely underdiagnosed despite the implementation of screening programs (4).

Diabetes is a globally prevalent metabolic disorder characterized by hyperglycemia. Oral complications with diabetes can greatly increase the risk of becoming partially or completely edentulous. The demand of diabetic patients, after the loss of one or more teeth, for implant therapy is increasingly important. This leads us to ask ourselves questions about the feasibility of implant surgery and the means to be implemented to guarantee and maintain success in subjects suffering from systemic pathologies (5–9).

Dental implants have become one of the most prevalent procedures for rehabilitating patients with single missing teeth or totally edentulous jaws since their development. As implants become increasingly common, it is more crucial than ever to figure out what elements influence osseointegration. Diabetes has been recognized as a medical risk factor that has a deleterious impact on osseointegration (10).

Humans have always had to face the issues associated with tooth loss. In the past, one's survival was at risk if they could not adequately bite and masticate minimally processed food. With improvements in food processing, the fundamental reason to attempt to keep one's teeth or look for solutions to replace lost teeth changed from survival to the capacity to enjoy a variety of cuisines and food textures. Modern dental treatments have made it possible and desirable to replace missing teeth, and facial esthetic considerations have become increasingly important in maintaining one's dentition (11).

The history of the evolution of dental implants is a rich and fascinating travel book through time. Since the dawn of humanity, humans have used dental implants in one form or another to replace missing teeth (12).

The first evidence of the use of dental implants comes from the archaeological discovery of the jaw of a prehistoric person, in the caves of Niaux and Lascaux, in France, which had a badly positioned dental element, which can be interpreted as an attempt to tooth replantation due to a possible traumatic avulsion. Another human jaw was discovered in the Mayan civilization, with shells implanted in the remaining alveoli, showing an attempt to replace dental elements (12).

Implants were created by South American and Egyptian cultures to repair missing teeth. Some were implanted post-mortem, while others were implanted during the patients' lifetimes. The implants were carved from ivory or constructed from the teeth of other animals. It is unlikely that these implants worked without experiencing early failure (11).

Throughout the 17th century, replacing tooth roots was done in Europe with a variety of tools and animals. The following century saw the transplantation of teeth from donors who had sold their natural teeth to people in need of replacements. Because of rejection, these transplants did not work out properly. The issues with early implant designs that were used in the 1800s are discussed by Shulman. These were various gold or lead extraction equipment that was placed there (11).

In 1809, endo-osseous implantology really began. Maglio is the first physician to describe a modern technique, with the placement of a gold implant in a post-extraction socket. The prosthesis being performed after tissue healing (12).

In 1888, Berry developed the principles of biocompatibility and primary stability, establishing the need for immediate implant stability and the use of "safe" materials, preventing the transmission of diseases (12).

At the beginning of the 20th century, Payne and Greenfield became the forerunners of modern implantology, emphasizing the importance of intimate bone-implant contact and promoting a rapprochement to the principles of orthopedic surgery and the concepts of "clean" surgery and deferred activation (12).

In the late 1930s, several studies were carried out on different biomaterials, as well as the introduction of surgical and prosthetic innovations, with the development of three types of implants: end osseous implants I, subperiosteal implants and end osseous implants II (12).

Endosseous implants were created utilizing a variety of retention techniques in the early 1960s. Titanium rods were bored into the bone emerging in the location of the desired crown. Pins were bent and resin was used to fix them. Although titanium rods were also joined intraorally by welding, the long-term effects were unpredictable (11).

For the purpose of replacing lost teeth with implant-supported prostheses, implant dentistry has developed over the past 50 years from an experimental procedure to a very predictable choice (13).

The discovery that implants made of commercially pure titanium could achieve anchorage in the bone with direct bone-to-implant contact 50 years ago served as the catalyst for this advancement in oral rehabilitation (13).

Professor P. I. Branemark from the University of Gothenburg (Sweden), who carried out the initial preclinical and clinical investigations in the 1960s, was the most significant forerunner of contemporary implant dentistry (13).

Later, he coined the word "osseointegration," which is now a frequently used description of the occurrence. The University of Bern (Switzerland Professor) Andre Schroeder, the second pioneer, began investigating the tissue integration of different implant materials in the late 1960s. His team was the first to discover direct bone-to-implant contact for titanium implants in nondecalcified histologic sections. A few years later, he was the first to report on the reactions of soft tissue to titanium implants. Both pioneers were in charge of a group that carried out several preclinical and clinical investigations to create the scientific foundation for contemporary implant dentistry (13).

When implant therapy was made available to patients who were partially dentate, the next stage in implantology began in the middle of the 1980s. Around 1990, the first clinical publications surfaced, and the results associated to implants were positive. Since then, patients with partial dentition have dominated the patient population; in some competence centers, they now account for more than 90% of all implant patients. As a result, meeting the growing demand for implant-supported restorations that are both functional and aesthetically pleasing has become a significant challenge. In response, the industry produced more prosthetic implant components, including angulated abutments, attractive single-tooth abutments, and cementable abutments (13).

The search for the articles is performed using the following search engines: PubMed, Google Scholar, Cochrane, and by combining the following keywords: diabetes mellitus, dental implant, osseointegration, periimplantitis.

All articles over 15 years old in English, Portugues and French including the following criteria will be retained: meta-analysis, systematic reviews, randomized controlled trials, cohorts, case control studies, case reports.

DEVELOPMENT

1. Diabetes Mellitus

Diabetes mellitus is a metabolic disorder characterized by the presence of pathological hyperglycemia due to an insufficient amount of insulin in the plasma, changes in insulin action on target tissues, or a combination of the two. Due to its metabolic effect, this disease affects the metabolism of carbohydrates, lipids, and proteins. This increase in the values of glucose in the blood is responsible for numerous complications including renal, ocular, cerebral and angiopathic damage (14).

1.1 Epidemiology

According to the International Diabetes Federation (IDF), The prevalence of diabetes among adults aged 20 to 79 over the world was predicted to be 10.5% (536.6 million) in 2021 and 12.2% (783.2 million) in 2045. Diabetes prevalence was similar between genders (Figure 1 and Figure 2) and was highest in people aged 75 to 79 (15).

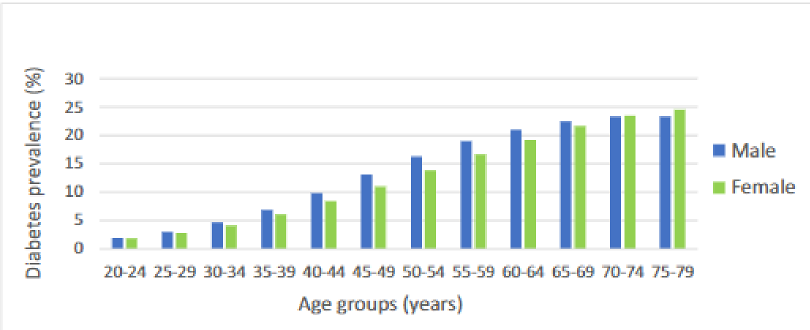

Figure 1 Diabetes prevalence by age and sex in 2021: IDF Diabetes Atlas (15) (with permission of Elsevier, Copyright 2022).

In 2021, the prevalence was predicted to be higher in urban (12.1%) than rural (8.3%) locations and high-income (11.1%) than low-income (5.5%) nations. Between 2021 and 2045, middle-income countries are predicted to experience the largest relative increase in the prevalence of diabetes (21.1%), followed by high-income (12.2%) and low-income (11.9%) countries. In 2021, it was forecast that 966 billion USD would be spent globally on diabetes-related healthcare. By 2045, that amount is expected to rise to 1,054 billion USD (15).

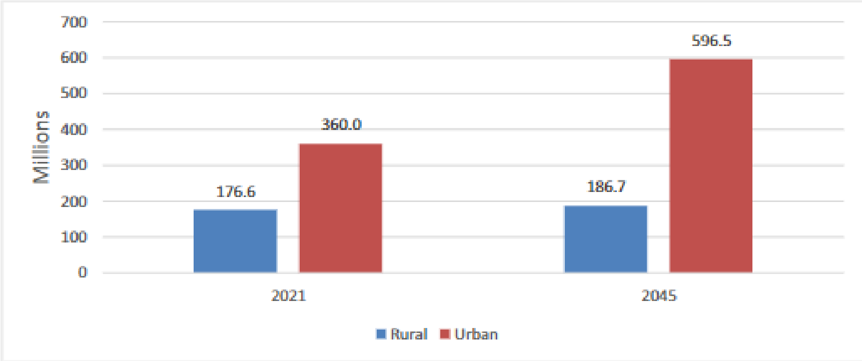

Figure 2 Number of people with diabetes in adults (20–79 years) living in urban and rural areas in 2021 and 2045 (15) (with permition of Elvevier, Copyright 2022).

The number of persons with diabetes worldwide has risen too little over half a billion, its mean more than 10.5% of the adult population have this condition (15).

In Portugal, it is estimated that in 2015 the prevalence of diabetes reached about one million people, or 13.3% of the Portuguese population, with about 44% of cases being diagnosed. This prevalence continues to increase, particularly in men aged between 20 and 79 years (16).

1.2 Classification

The following are the general categories of diabetes:

1) Type 1 diabetes is one of the most common types of diabetes (due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood).
2) Diabetes type 2 (due to a progressive loss of adequate b-cell insulin secretion frequently on the background of insulin resistance).
3) Specific types of diabetes caused by other factors, such as monogenic diabetes syndromes (such as neonatal diabetes and young-onset diabetes), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with the use of glucocorticoids, in the treatment of HIV/AIDS, or after organ transplantation).
4) Gestational diabetes mellitus (GDM) is a kind of diabetes that occurs during pregnancy (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation (17).

1.3 Etiology

Diabetes can have many causes and etiologies, but they all inexorably lead to changes in insulin secretion, sensitivity to hormone action, or both, at some point in its natural history (18).

The etiology of type 1 diabetes is poorly understood. Consider whether the autonomic response that characterizes this kind of diabetes is triggered by environmental, infectious, or nutritional factors. There is also a genetic predisposition, but it is less than for type 2 diabetes (18–20).

There are several factors that contribute to the development of type 2 diabetes. The genetic factor is more important in this case because the majority of patients with type 2 diabetes have a first-degree relative who also has type 2 diabetes (21).

The individual's lifestyles play a significant role in the disease's establishment. This occurs more frequently in people who are overweight, do not engage in any physical activity, and eat a high-calorie diet. People who are overweight have a five-fold higher risk of developing diabetes than those who are normal weight. As a result, obesity is the leading risk factor for type 2 diabetes (22,23).

1.4 Pathophysiology

Type 1 diabetes is caused by the autoimmune destruction of insulin-producing pancreatic β cells in genetically predisposed individuals, resulting in absolute insulin deficiency (24).

This autoimmune process appears about 5 to 10 years before the onset of diabetes. The destruction of pancreatic beta cells is caused by autoantibodies, mainly by the infiltration of CD4 T lymphocytes and CD8 T lymphocytes into the islets (Figure 3). There are four main autoantibodies: anti-islet antibodies; anti GAD (glutamate decarboxylase) antibodies; anti-insulin and anti-IA2 antibodies (23,25,26).

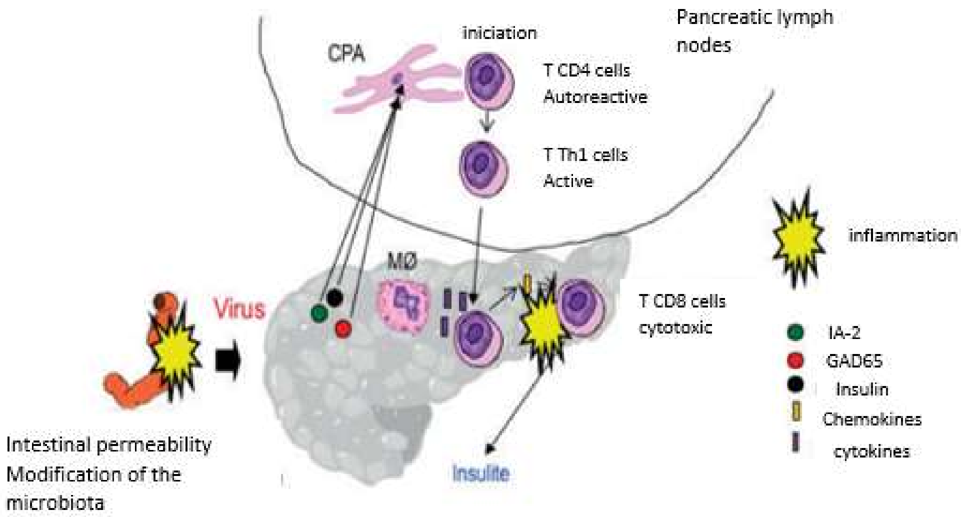

Figure 3 Pathophysiology of type 1 diabetes (23) (e-mail permission was sent to the author).

This form of diabetes is manifested by rapid weight loss, polyuria, polydipsia, and polyphagia (21).

Type 2 diabetes is the result of a combination of various elements whose expression depends on environmental factors (Figure 4), such as excessive consumption of saturated fats and sugars and a sedentary lifestyle. The disease thus occurs as a result of a relative deficiency in insulin, caused by an increase in resistance to insulin by part of peripheral tissues such as the liver, skeletal muscle and adipose tissue (27,28).

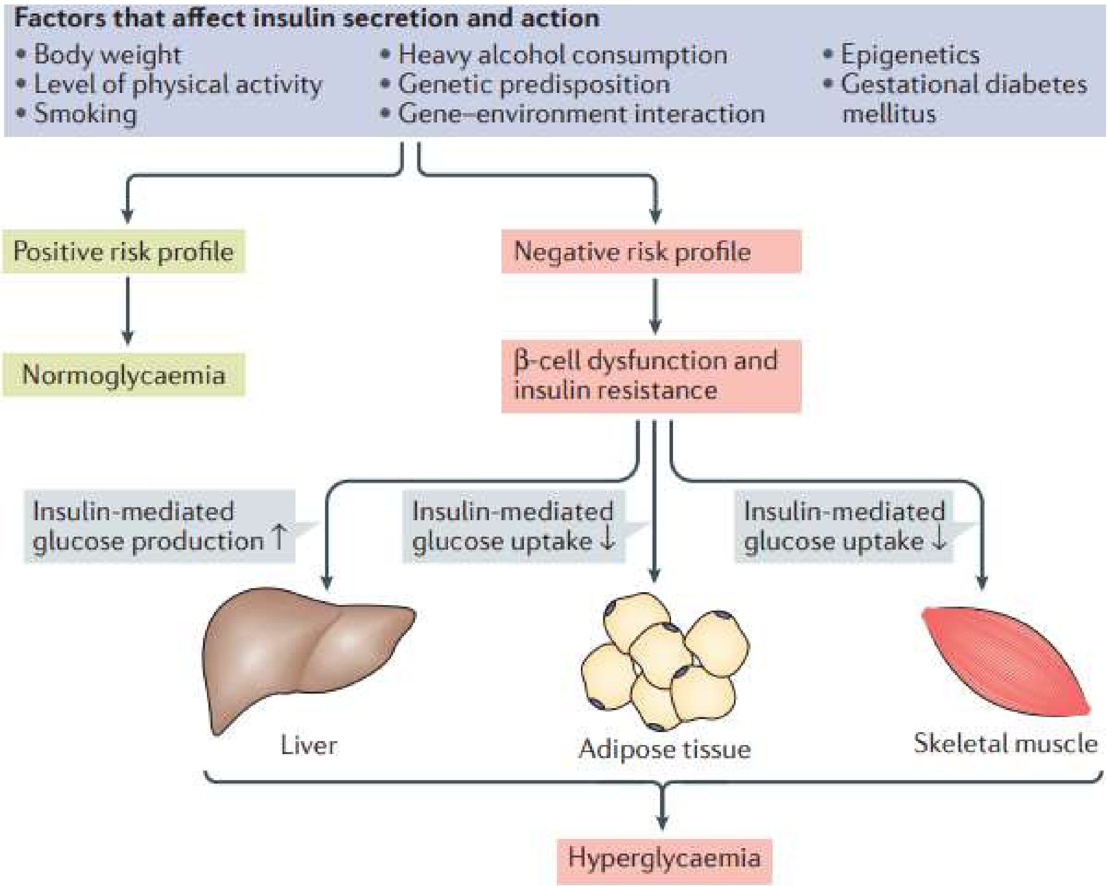

Figure 4 Pathophysiology of hyperglycemia in T2DM (18) (with permission of Springer, Copyright 2017).

Insulin resistance is secondary to excess visceral adipose tissue (Figure 5), resulting in a decrease in insulin sensitivity exerted at the peripheral and hepatic level. Portal flow of free fatty acids promotes hepatic synthesis of triglycerides and stimulates hepatic gluconeogenesis. Free fatty acids are oxidized at the muscle level, resulting in the production of acetyl CoA, which inhibits glucose catabolism enzymes. All these mechanisms lead to chronic hyperglycemia, a key element of diabetes (28). The greatest risk factor for insulin resistance is obesity, abdominal, subcutaneous and visceral fat distribution (28).

The topographic distribution of adipose tissue and the typological variation of muscle tissue depend on hormonal and environmental factors (stress, alcohol and smoking) that favor lipids, while physical inactivity and aging lead to an increase in type 2 muscle fibers compared to type 1 muscle fibers (29).

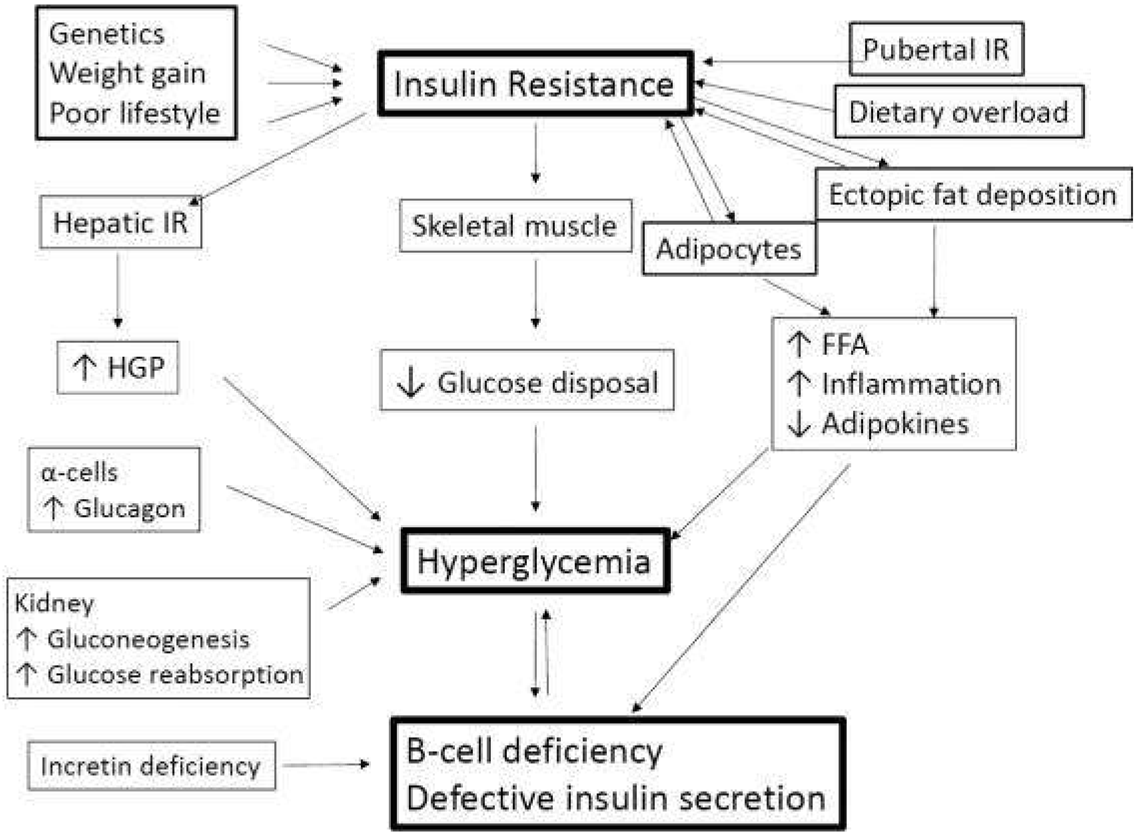

Figure 5 Pathophysiology of type 2 diabetes in children and adolescents (27) (CC BY-NC 4.0).

1.5 Complications of diabetes

There are many complications associated with diabetes (Figure 6). Strict control of blood glucose, dyslipidemia, and blood pressure, as well as tracking the effects on organs most sensitive organs (kidneys, eyes and peripheral nerves), are essential to minimize the damage resulting from permanent hyperglycemia (21,30).

Complications can be divided into: 1) macrovascular: Characterized by atherosclerotic lesions that progressively obstruct large and medium-sized arteries, which can result in coronary insufficiency and stroke and/or peripheral arterial disease (30); 2) microvascular: Diabetic retinopathy, diabetic nephropathy and diabetic neuropathy (21,30). As for the oral complications associated with diabetes, these are diverse, and include tooth loss, gingivitis, periodontitis and oral soft tissue pathologies (31).

The relationship between diabetes and the development of dental caries is still unclear. It is well known that the cleaning and buffering capacity of saliva is diminished in patients with diabetes mellitus, resulting in an increased incidence of dental caries lesion, especially in those patients suffering from xerostomia (31).

Dysgeusia present in some patients with diabetes may result from salivary dysfunction associated with diabetes or from the use of certain oral antidiabetic drugs. Due to the immunosuppression associated with diabetes, there may be an increase in fungal, viral or bacterial oral infections (31).

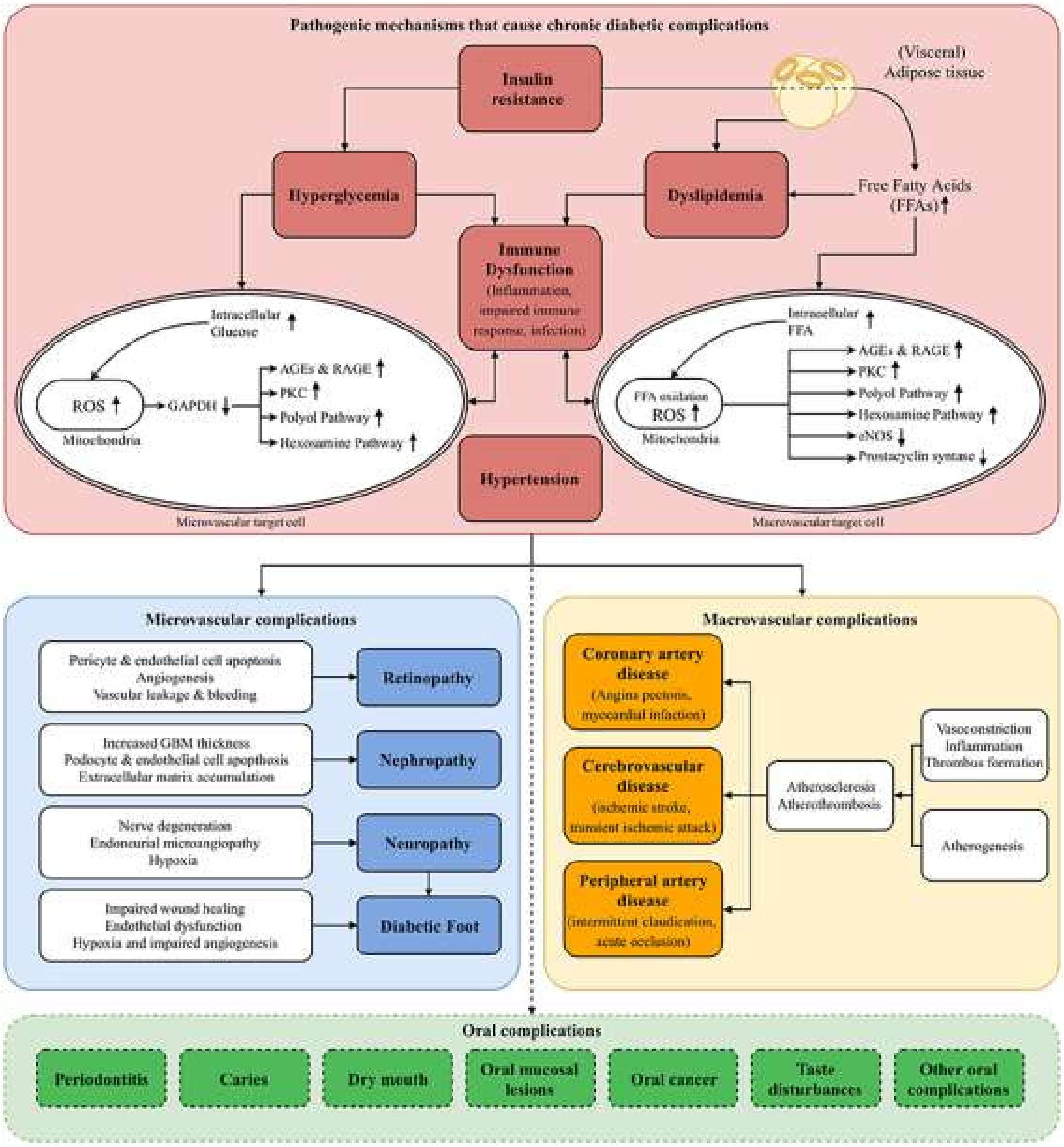

Figure 6 Pathogenesis of diabetic complications (CC BY) (32).

2. Dental precautions for patients with diabetes

Each patient with diabetes must be assisted in a peculiar way, because characteristics of the disease assume a more marked form than others, in each individual (30).

2.1 Anamnesis and clinical examination

During the anamnesis, the dentist, therefore, should obtain information regarding age, dietary patterns, physical activity habits, nutritional status, weight history, diabetes education history and previous treatments (32).

The clinical examination must be rigid and thorough, through the evaluation of the orofacial soft tissues and the completion of the periodontogram and international dental record (32).

2.2 Complementary exams

It is important to ask the patient or his/her attending physician for the most recent laboratory tests such as complete blood count and glycated hemoglobin (Figure 7). If oral surgery is planned, coagulation tests should be requested (30).

The treatment of type 2 diabetes is based on lifestyle changes, diet, physical exercise, glycemic self-monitoring (Figure 8), and pharmacological treatment with oral antidiabetics and/or insulin (30).

1. Good glycaemic control:
   HbA1c < 7%
   Baseline and pre-prandial glycaemia (mg/dL): 80 - 110
   Maximum post-prandial level of glycaemia (mg/dL): < 180
2. Pre-operative antibiotic therapy
3. 0.12% chlorhexidine mouthwash

Figure 7 Recommendation to reduce the risk of implant failure in diabetic patients (34) (e-mail permission was sent to the author).

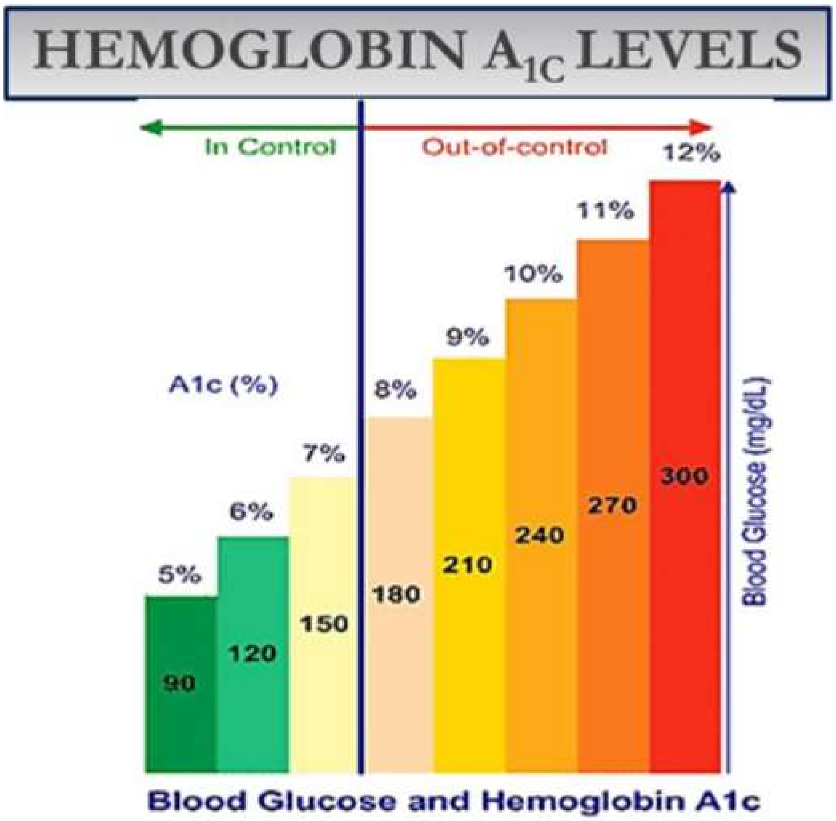

Figure 8 Blood glucose and hemoglobin A1c levels (Public Domain Mark 1.0) (35).

2.3 Specific precautions

Patients with diabetes can be classified according to the severity of their disease:

2.3.1 Low-risk patients

This type of patient is usually asymptomatic and has no neurological, vascular, or infectious complications. Biologically, these patients have minimal glycosuria (0 to 1), no ketonuria, and blood glucose levels below 150 mg/dL.

2.3.2 Patients at moderate risk

This type of patient has no clinical manifestations. However, some complications may be present.

Biologically, glycosuria ranges from 0 to 3, ketonuria is nil, and blood glucose remains below 250 mg/dL.

2.3.3 High risk patients

These patients have multiple complications and poor glycemic control, requiring constant insulin dose adjustments.

Biologically, glycosuria and ketonuria are present and blood glucose levels often exceed 250 mg/dL (14mmol/L) (33).

2.4 Precautions regarding pharmacological prescriptions

The prescription of antibiotics does not require special precautions, in these patients they do not present drug interactions (34).

As for analgesics and anti-inflammatory drugs, corticosteroids should be used with caution in all patients with diabetes, due to the risk of hyperglycemia. In case of prescription, the intake should be for the shortest possible period and blood glucose monitoring and respective therapeutic correction should be reinforced (34).

3. Diabetes and osseointegration

3.1 Definition of osseointegration

According to a thorough systematic review of the literature, the process of creating a direct interface between the implant and the bone without the use of soft tissue is known as osseointegration. The stability and life of the implant depend on this procedure. Through the migration and proliferation of osteoblasts and supporting connective tissue, the surrounding bone is remodeled. The value of implant stability will be determined by this close contact. When the diabetes well controlled , there is no or little effect on implant survival (35).

Since it is now understood that dental implants are merely foreign bodies, the definition of osseointegration has modified to include the tissues' defense mechanism. When titanium implants are sufficiently stable, bone tissue forms around them to protect them from the tissues (36).

3.2 ***Complication of Diabetes on osseointegration***

In light of the findings showing how DM affects the metabolism of bone and wound healing, osseointegration and its maintenance are therefore probably hampered in such circumstances (37).

3.2.1 Changes to the Bone Healing Process

It has been demonstrated that bone resorption is stimulated by chronic hyperglycemia (Figure 9). Diabetes appears to cause less bone development than normal, which appears to be the main contributor to bone loss. Inhibiting osteoblastic differentiation and changing how the parathyroid hormone reacts, which controls how phosphorus and calcium are metabolized, are also effects of hyperglycemia., Additionally, it has a negative impact on the bone matrix and its constituent parts, as well as adhesion, growth, and extracellular matrix accumulation. Numerous experimental models of diabetes have demonstrated that bone growth, osteoid synthesis, and mineral balance are all significantly reduced (38).

The mechanisms of wound healing, which include, 1. an acute inflammatory phase marked by inflammatory cell migration and the release of inflammatory mediators, 2. a proliferative phase where new extracellular matrix (ECM) is deposited, and three. a remodeling phase where the matrix is organized and remodeled, are necessary for successful osseointegration. In metabolically compromised patients, these processes of hemostasis, inflammation, proliferation, and remodeling are negatively impacted by a confluence of decreased vascular supply secondary to microangiopathies, dysfunctional cellular activity associated with exposure to toxic metabolites, and decreased host immune competence associated with the persistent proinflammatory systemic state (39).

The most frequent side effects of hyperglycemia include micro and macrovascular disorders as well as poor wound healing (39).

Figure 9 Alteration in bone healing in diabetic patients (Public Domain Mark 1.0) (35).

3.2.2 Oxidative Stress Phenomenon

When hyperglycemia causes an imbalance between the synthesis of reactive oxygen species and antioxidants, which results in tissue destruction, this phenomenon occurs. Cell death results from the destruction of several biological components, including DNA, lipids, and proteins, by reactive oxygen species such as superoxide anions, hydroxyl radicals, and peroxyl radicals (40).

3.2.3 Diabetes and Periodontitis: An interaction

An essential factor in the association between diabetes and periodontal disorders is the level of glycemic control. People with poor glycemic control had increased prevalence and severity of gingival inflammation and periodontal damage (41).

Periodontitis patients with diabetes and those without diabetes had similar subgingival microbiotas, indicating that changes in the host's immunoinflammatory response to the possible pathogens may be a major factor (42).

Diabetes may impede neutrophil adhesion, chemotaxis, and phagocytosis, allowing bacteria to stay in the periodontal pocket and greatly increasing periodontal damage (43).

3.2.4 Osseointegration impact

A significant increase in the number of metabolically challenged individuals who have either already undergone or will require dental implant therapy and/or maintenance is anticipated given the rising frequency of type-2 diabetic mellitus (T2DM) (13).

Osseointegration and peri-implant bone preservation, which depend on normal bone metabolism, are essential for the success of implant therapy (13).

It has been demonstrated that although the amount of bone generated in diabetic animals and controls is comparable, there is a decrease in the bone implant contact in diabetics. This demonstrates that diabetes prevents osseointegration, a condition that may be corrected by treating hypoglycemia and preserving close to normal glucose levels (44).

Due to microangiopathy, which slows down wound healing and inhibits the immunological response of periodontal tissues to infection, DM is linked to poorer osseointegration of dental implants. A high glucose level can also directly limit osteoblast growth, reduce collagen formation, and increase bone resorption. Additionally, it hinders the adhesion, growth, and accumulation of extracellular matrix and does not promote the development of bone matrix. The associated rise in AGEs stimulates the release of inflammatory cytokines such IL-1, IL-6, and TNF-, which further boosts osteoclast activity, degrades bone quality, and affects osseointegration (Figure 10) (45).

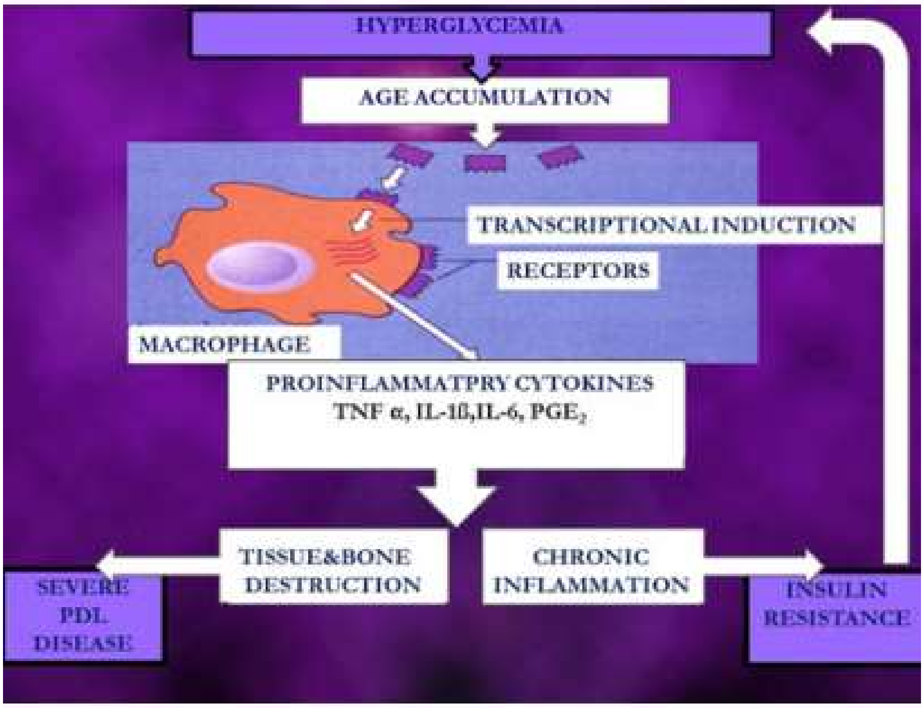

Figure 10 Linkage between diabetes and periodontal disease severity (Public Domain Mark 1.0) (35).

Al-Sowygh et al. have confirmed that people with hyperglycemia and high AGE concentrations have worse bone defects around implants. Additionally, T1DM is more detrimental than T2DM in this regard and is linked to a higher failure rate of implant osseointegration. The mechanism at play as well as the significance of diabetes duration for implant osseointegration are yet unknown currently. Although some researchers have suggested that the duration of diabetes may influence implant failure, others do not believe that this is a major factor, most prior reports have not provided data regarding the timing of the diagnosis of diabetes. Nevertheless, it is generally believed that good glycemic control is necessary for successful osseointegration in patients with diabetes (46).

The activation of various key pathways, which are crucial in starting off processes associated to inflammation, oxidative stress, and cell death, results in the destruction of vascular cells. These pathways include: increased expression of AGE receptors (RAGEs), which cause the production of reactive oxygen species (ROS) and inflammatory cytokines; increased polyol pathway flux; increased formation of advanced glycation end products (AGEs), proteins structurally modified by glycosylation with altered function; and activated protein kinase C isoforms, that stimulate the production of cytokines and inflammation; Significant levels of the pro- inflammatory adipocyte cytokines, and increased hexosamine flow (Figure 11 and Figure 12) (47).

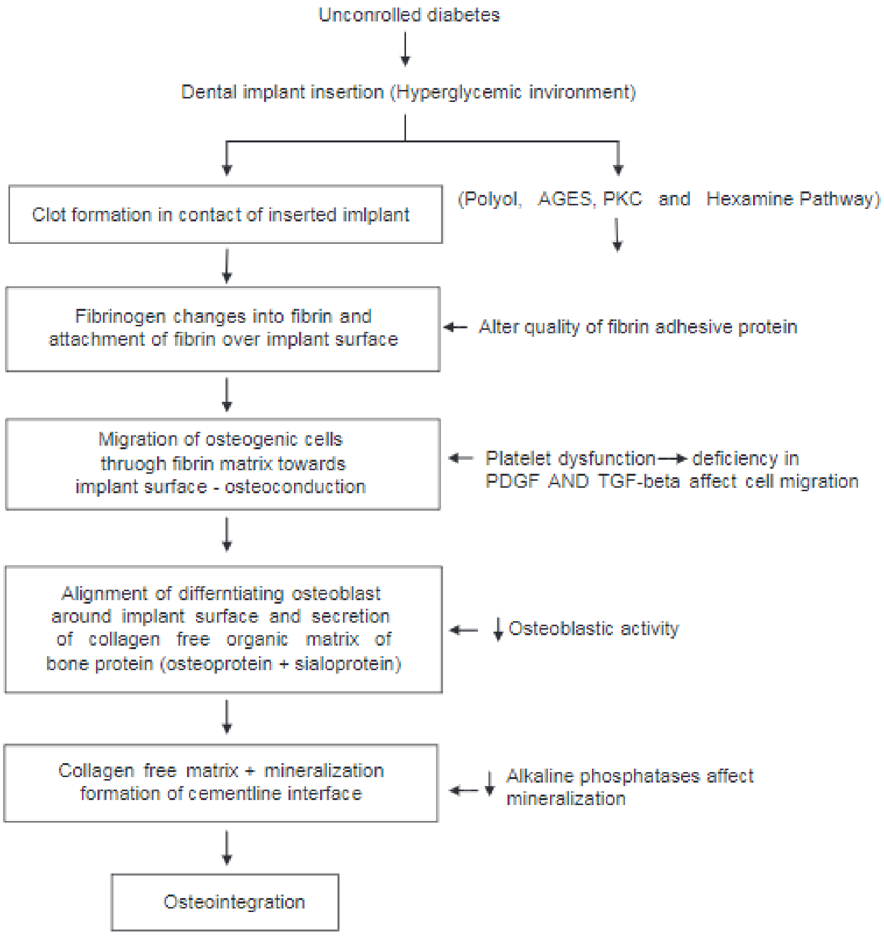

Figure 11 Possible effects of diabetes over mechanism of osteointegration (CC BY-NC-SA 3.0 AU) (50).

Microvascular dysfunction may considerably impede the regeneration process since proper vascularization of the bone implant is essential for recovery (39).

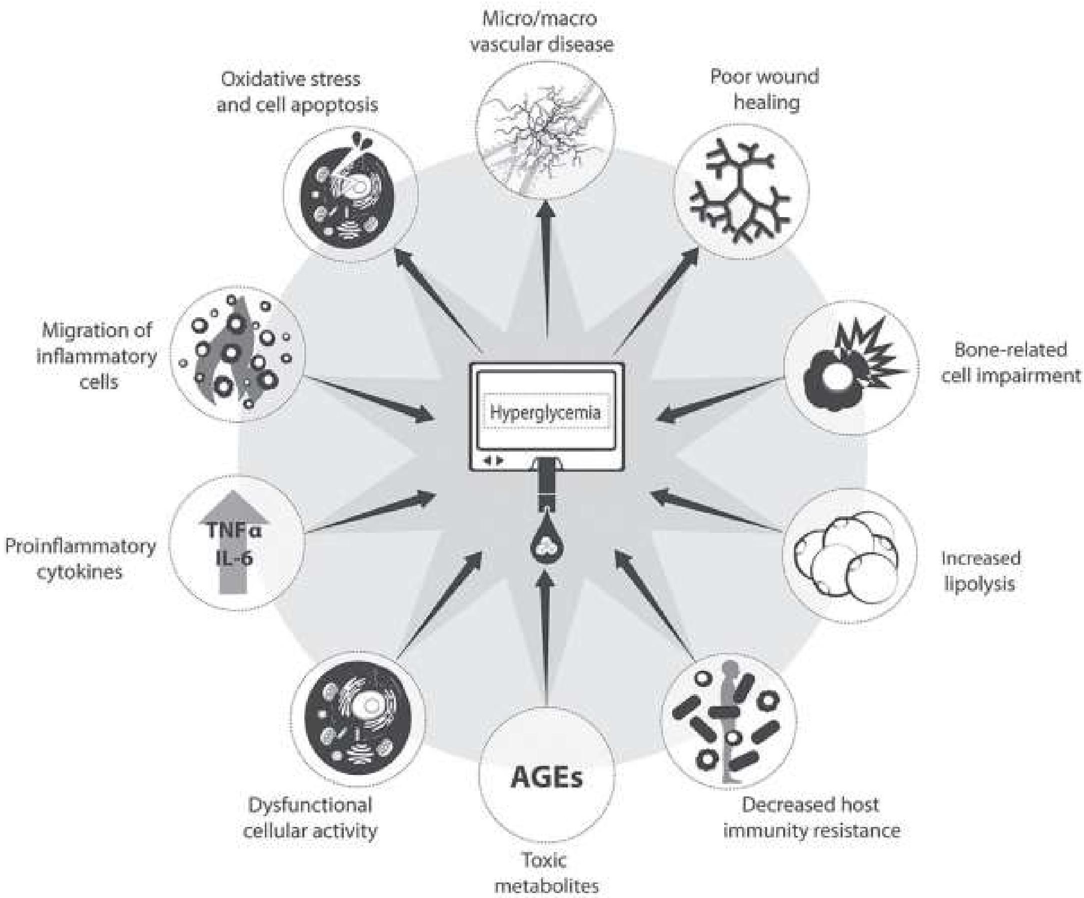

Figure 12 Bone Healing Impairment and Obesity/Metabolic Syndrome and Type 2 Diabetes Mellitus (with permission of Elsevier, Copyright 2020) (42).

4. The success factors

The relationship between diabetes, and implants can exacerbate the latter if diabetes is not adequately controlled. However, certain criteria come into play, such as the type and duration of diabetes and glycated hemoglobin levels (48).

4.1 Type of diabetes

According to the study by Alsaadi et al (2008), 694 implants were placed in non-diabetic patients, twenty-five in patients with type 2 diabetes and one implant in the only diabetic patient with type 1. They distinguished thirteen failures in non-diabetic patients,1 alone in a type 2 diabetic and a failure in a single type 1 diabetic. Despite the important limitations of this study, the authors concluded that implant loss is more common in patients with type 1 diabetes than in patients with type 2 diabetes (38).

A controlled type I diabetes patient population was the subject of a research to assess implant treatment for partial edentulism, 53 patients with type I diabetes were scheduled in Group A, and 53 healthy patients were scheduled in Group B. Clinical and radiological checks were made from the beginning up to 24 months, and all patients had their implants' survival rates, presence of peri-implant tissue infections, and marginal bone loss evaluated. At the 24-month follow-up, 5 and 3 implants failed in diabetes and non-diabetic individuals, respectively (49).

The first findings of this prospective study suggested that implant treatment for edentulism might be a predictable and safe technique for diabetic type I patients when glucose levels are maintained and oral hygiene appointments are frequent (49).

If glucose levels are rigorously controlled and maintained, implants can remain esthetically and functionally stable in type 2 diabetic patients in a way similar to healthy people (50).

4.2 Influence of duration of diabetes disease

In ten of the forty investigations, details about the disease's duration were provided. In every study, the information remained descriptive. Therefore, there was no association between the length of the condition and any potential impact on implant therapy (51).

4.3 Glycated hemoglobin levels

Blood glucose control is reflected by serum HbA1c levels and diabetes is conventionally controlled when HbA1c is < 7% (21).

Stability of glycemic control offers better chances of implant success.

In the group comparison of diabetic patients with a HbA1c 6.1-8% and > 8.1, a significant difference could be seen (51).

Oates 2009, divided a group of type 2 diabetic patients into four groups based on HbA1c values : first group with 6%, the second with a value between 6% and 8%, the third group with a value between 8% and 10% and the fourth group with a value equal to or greater than 10%) (52).

Their results showed a decrease in implant stability in the third and fourth groups, i.e., HbA1c values greater than 8-fold are associated with greater dental implant failure in type 2 diabetes (52).

4.4 Microbiological control and implant survival

Antibiotic prophylaxis reduces the risk of early failure of dental implants and postoperative infection. In comparison to when no antibiotics were given, the administration of a single dose of antibiotics in conjunction with implant placement procedure resulted in a statistically significant lower early implant failure rate (53).

5. The risks of failure

Diabetes mellitus is classified as a risk factor for implant therapy and it has been suggested that severe or poorly controlled diabetes is a contraindication to dental implant therapy (54).

When diabetes is well-controlled, implant procedures are safe and predictable, with a rate of complications comparable to that of healthy patients. For people undergoing treatment with dental implants, a well-managed diabetes condition poses no additional risks (55).

Currently, some studies show that the failures are due to the (31).

- Host factors that prevent healing,

- Type 1 diabetes

- Peri-implant infections

− Association with periodontal disease

− HbA1c > 7%

and the prevalence of periodontal disease is 60% in diabetics (31).

Diabetic patients without adequate glycemic control may be at a higher risk of failure (56).

6. Dental implant surgery

The physiological reactions brought on by the "stress" of a procedure can have an impact on cardiac and diabetes management. As a result, the healthcare provider treating a patient with diabetes mellitus must come up with treatment plans that address the patient's entire health, including their cardiovascular status (44).

6.1 For the Pre-surgical evaluation

6.1.1 Medical Consultation

Patients who have good glycemic control can typically be treated like other patients. If the fasting blood glucose level is either below 70 mg/dL or above 200 mg/dL, or if the HbA1c level is higher than 7%, it is advised that elective treatment be postponed. This recommendation is supported by data showing that people with blood glucose levels below 70 mg/dL are at high risk for hypoglycemic incidents, that blood sugar levels above 200 mg/dL or a HbA1c level above 7% indicate poor glycemic control, and that people with these blood sugar levels are also more likely to have or be developing significant microvascular and/or macrovascular disease , Further medical advice is needed if the anticipated dental therapy could have a negative impact on maintaining excellent glycemic control (5,57).

6.1.2 Diabetes and antibiotic prophylaxis

Antimicrobial prophylaxis is sometimes recommended before dental therapy, especially in individuals with poorly managed diabetes because of the reciprocal association between infection and poor glycemic control (44).

According the study of Morris (2000), the use of 0.12% chlorhexidine mouthwash has demonstrated a clear advantage in addition to antibiotic prophylaxis by lowering the failure rates from 13.5 to 4.4% in type 2 diabetics over a 36-month follow-up period (58). When antibiotics were given prior to surgery, this study's failure rate was found to decrease by 10.5% (44).

The administration of antibiotic prophylaxis and a chlorhexidine mouthwash is now indispensable during any implant surgery in diabetic patients as these significantly increase the success rate (59).

For preoperative take amoxicillin: 2 g orally, single dose 60 minutes before the surgery or clindamycin: 600 mg orally, single dose 60 minutes before procedure (for patients who are allergic to penicillin) , and chlorhexidine digluconate 0.12%: 15 ml for 1 minute; begin 2 days before the procedure. For post-operative Amoxicillin: 2 g per day, twice a day for 7 days,1g 12/12h or azithromycin: 500 mg orally, single dose for 3 days or Clindamycin: 600 mg orally, twice a day for 7 days, and chlorhexidine digluconate 0.12%: 15 ml for 1 minute; for 12 days (59).

Once the indication has been established, surgery in a diabetic patient requires specific precautions given the terrain that is particularly vulnerable to infections. The interest of systematic antibiotic prophylaxis is discussed. Is antibiotic coverage at each implant placement in a diabetic, regardless of his quality of glycemic control, justified (60).

During implant surgery, anaerobic gram-positive cocci and anaerobic gram-negative spirochetes are the pathogens most responsible for disturbing tissue healing. Thus, the antibiotic of choice to prevent complications should be bactericidal and with low toxicity. The antibiotic of choice is therefore amoxicillin given its spectrum of action (60).

In the case of penicillin allergies, the use of related macrolides such as clindamycin, clarithromycin, azythromycin or the first generation of cephalosporins is recommended. A study carried out on type 2 diabetics with good glycemic control found success rates of 97.3% at 1 year and 94.4% at 5 years using 2g of amoxicillin or 600mg of clindamycin per day (60).

6.1.3 Time and duration of appointments

Patients should preferably get treatment in the morning with brief appointments, following the administration of their regular dose of insulin or oral hypoglycemic medication and a typical breakfast. By scheduling the appointment at this time, the patient will be at the dental office before the therapeutic agents' peak activity (i.e., a period of high glucose and low insulin or oral hypoglycemic drug action) is reached. (61).

6.1.4 The application of local anesthetics

When necessary, an oral benzodiazepine, nitrous oxide, or intravenous sedative may be added to the local anesthetic. To prevent rebound hypertension brought on by hypoxia, the doctor should ensure enough oxygenation if nitrous oxide is utilized (35% nitrogen dioxide/65% dioxygen). Recent papers provided a thorough overview of the issues surrounding the use of vasoconstrictors in local anesthetic drugs, with a focus on patients with cardiovascular problems. The important elements for determining the safe use of a vasoconstrictor in patients with DM should be the existence of cardiovascular risk factors in conjunction with dental operations and the patient's functional capacity (61).

6.1.5 Managing postoperative pain

Effective postoperative pain management should also be a part of treatment options. Analgesics based on opioids efficiently suppress pain and frequently promote cardiovascular stability. It has been suggested that patients on insulin may experience an enhanced hypoglycemic impact while taking large dosages of salicylates, and this effect has also been linked to the sulfonylurea chlorpropamide. However, acetylsalicylic acid (ASA) therapeutic levels are typically ineffective, these possible medication interactions are a further reason to check plasma glucose levels after surgery, but they do not completely rule out the use of an opioid/ASA formulation for pain control in the dental environment. In fact, an opioid/ASA formulation is preferable to an opioid/ibuprofen formulation since the latter may interfere with the antiplatelet action of the former given that many patients with DM are using ASA as primary or secondary therapy to prevent cardiovascular events (44).

6.1.6 Implant Selection

According to study Morris (2000), the diabetic patient follows the same fundamental osseointegration principles as those described by Albrektsson et al (62). The screw-shaped design, the implant's surface roughness, and the implant's surface purity are all elements that aid in better osseointegration (44).

6.2 Ways of surgery

There are two ways to perform surgery: a traditional flapped (open) approach, or a flapless procedure. The typical surgical technique for inserting a dental implant is thought to be the conventional flapping technique. Elevating the flap (open flap) is typically favored when placing dental implants by conventional surgery in order to clearly see the recipient site (5).

The flap designs for implant surgery have changed over the past 30 years, and more recently, the idea of placing implants without elevating the flap and exposing the bone structures has been proposed. With tooth extractions and site preservation, flapless methods have previously been utilized for a while and have demonstrated lower morbidity. In addition, in order to maintain the vascular supply and pre-existing soft tissue shapes, surgeons have also thought of a flapless technique for immediate implants. To access the bone, surgeons must first penetrate the gingiva using either rotary instruments or a tissue punch (63).

The review Singh et al. (2019) use 14 articles relating to the survival rate of dental implant placement by conventional or flapless surgery among patients with managed diabetes mellitus were included from the PubMed database, The purpose of this review is to determine the dental implant's survival rate when installed using either of the two techniques, therefore, According to the included studies, the cumulative mean dental implant survival rates using conventional and flapless procedures are 94.2% and 92.3%, respectively, Both traditional and flapless dental implant placement techniques have a similar success rate (5).

One of the more prevalent systemic disorders, diabetes mellitus was formerly thought to be detrimental to dental implant surgery due to its high failure rate and poor wound healing in diabetic patients. Advanced glycation end products (AGEs) are created when nonenzymatic glycation of proteins occurs as a result of elevated blood glucose levels (64).

Advanced glycation of proteins alters the endothelium's permeability, releases growth factors and inflammatory cytokines, changes the endothelium's anti-thrombotic properties, and increases the expression of adhesion molecules and chemokines, all of which can result in microvascular complications like poor circulation and delayed wound healing. These complications may also increase the risk of implant failure in diabetics with poor glycemic control (5).

When calculated using the National Glycohemoglobin Standardization Program (NGSP) certified technique, glycated hemoglobin (HbA1c), a well-known marker for monitoring glycemic management, is now utilized as a diagnostic marker. The ADA recommends a HbA1c value of 6.5% as the diagnostic cutoff for diabetes and a range of 4.0% to 5.7% as nondiabetic. The American Diabetes Association (ADA) advises diabetic patients to keep their HbA1c levels under 7% to reduce their risk of microvascular and macrovascular complications (65).

The study of Yadav (2018) eighty-eight people with type 2 diabetes, these patients were split into two groups at random (Figure 13 and Figure 14) . Patients in group I underwent full thickness flap surgery to insert implants, and patients in group II underwent flapless surgery to install implants. In both groups, the average age, length of diabetes, levels of glycosylated hemoglobin, and the ratio of men to women were matched and statistically compared, dental implants were put followed by delayed loading (4 months) in both groups (66).

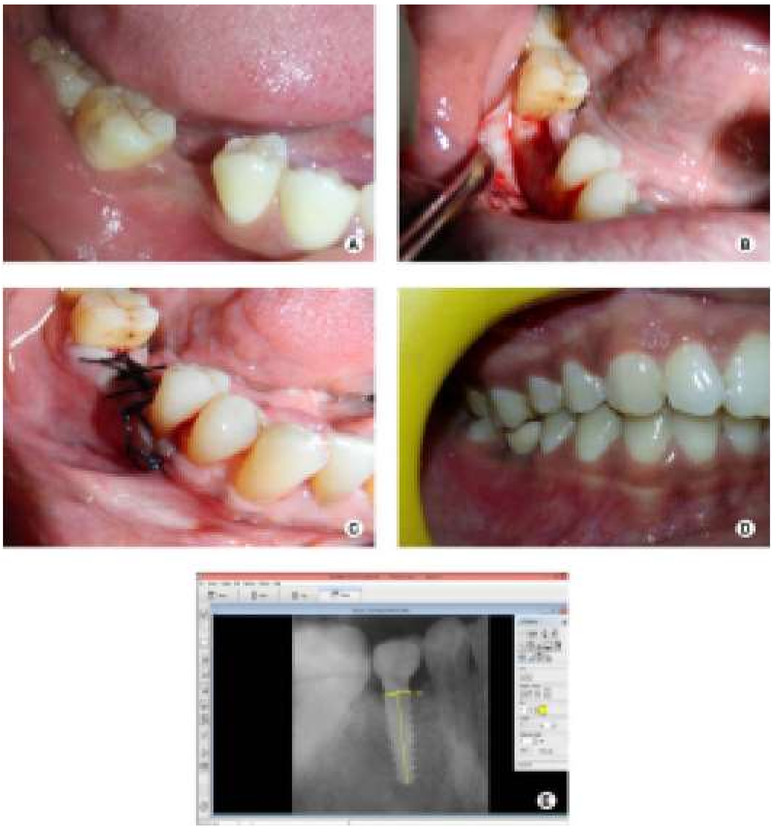

Figure 13 Full thickness flap surgery; (A) Preoperative photograph; (B) Flap reflection; (C) Implant with cover screw; (D) Flap closure; (E) Definitive prosthesis; (F) Measurement of crestal bone level using DBSWIN software (66) (with permission of John Wiley and Sons).

Figure 14 Flapless surgery; (A) Preoperative photograph with circular punch; (B) Bone exposure with punch; (C) Implant with cover screw; (D Definitive prosthesis; (E) Measurement of crestal bone level using DBSWIN software (66) *(with permission of John Wiley and Sons).*

Table 1 Mesial bone level (mean ± SD) of two groups, NA: not applicable (66).

Period	Full thickness flap (n = 40)	Flapless (n = 36)	*p* Value
At baseline	0.00 ± 0.00 mm	0.00 ± 0.00 mm	NA
After 6 months	0.47 ± 0.08 mm	0.36 ± 0.13 mm	0.576
After 12 months	1.56 ± 0.25 mm	1.50 ± 0.22 mm	0.891
p Value	<0.001	<0.001	–

Table 2 Distal bone level (Mean ± SD) of two Groups, NA: not applicable (66)*(with permission of John Wiley and Sons).*

Period	Full thickness flap (n = 40)	Flapless (n = 36)	*p* Value
At baseline	0.00 ± 0.00 mm	0.00 ± 0.00 mm	NA
After 6 months	0.44 ± 0.08 mm	0.35 ± 0.12 mm	0.687
After 12 months	1.57 ± 0.23 mm	1.61 ± 0.22 mm	0.947
p Value	<0.001	<0.001	-

Both groups showed similar mesial and distal crestal bone loss (Table 1 and Table 2) in the intergroup comparison at 6 months and 12 months following baseline (the difference was statistically insignificant) (66).

Since bleeding is minimized, operation takes less time, and patients experience less discomfort, flapless implant surgery is thought to have advantages over the conventional flap technique. However, there aren't any research comparing patient outcome characteristics to back up these hypotheses (63).

Shamsan et al. found that the conventional technique of implant placement resulted in statistically significant higher mean pain severity and duration than the flapless procedure (67).

6.3 Immediate dental implants

With tooth extractions and site preservation, flapless methods have previously been utilized for a while and have demonstrated lower morbidity. In addition, to maintain the vascular supply and pre-existing soft tissue shapes, surgeons have also thought of a flapless technique for immediate implants. To access the bone, surgeons can utilize rotary devices or tissue punches to penetrate the gingiva (63).

When teeth are present, three different sources of blood supply enter the bone: the periodontal ligament, the connective tissue above the periosteum, and the bone itself. Blood no longer comes from the periodontal ligament once a tooth is lost; instead, it now only comes from soft tissue and bone (63).

According to the study by Andrade (2022), to evaluate the success, survival, and physiologic changes that occur around immediately loaded dental implants (ILs) in type

2 diabetic patients (DM2), four studies indicated a 100% success rate of IL in DM2 in this systematic review (68).

7. Oral rehabilitation options for diabetic patients

The mucosa that covers the edentulous ridges and supports them provide support for conventional full dentures. The prostheses are built to maximize any potential retentive pressures while attempting to minimize those that destabilize them. There is tight contact, but no direct attachment, between the prosthesis and the ridges. This is troublesome in such a physically demanding setting, and many patients have trouble getting used to their dentures, especially the bottom one. Edentulism is linked to a diet that is less healthy as well. There is already a sizable body of research proving that implant-supported mandibular dentures significantly improve patients' quality of life and happiness compared to traditional dentures (69).

According to a study Al-Shibani (2019) comparing type 2 diabetes mellitus (T2DM) and non-diabetic subjects' clinical and radiological peri-implant parameters around narrow diameter implants (NDIs; 3.3 mm) and regular diameter implants (RDIs) (Table 3), eighty-six patients who needed posterior mandibular implant surgery were split into two groups (42 T2DM and forty-four non-diabetic individuals). The clinical and radiographic results presented in the current 36-month follow-up study showed consistent clinical behavior with a 100% success rate for NDIs and RDIs, suggesting that both NDIs and RDIs can Osseo integrate in both systemically healthy and T2DM patient (70).

Table 3 Mean (range) crestal bone level around narrow and regular diameter implants in type 2 diabetes mellitus and non-diabetic patients at 18 and 36 months of follow up (70)(with permission of John Wiley and Sons).

	18-months follow up				36-months follow up			
	T2DM (*n* = 42)		Non-diabetic (*n* = 44)		T2DM (*n* = 42)		Non-diabetic (*n* = 44)	
Clinical parameters	NDIs	RDIs	NDIs	RDIs	NDIs	RDIs	NDIs	RDIs
No. of implants	22	20	25	19	22	20	25	19
Mean crestal bone level in millimeters (range)	0.27 (0.2-0.3)	0.23 (0-0.5)	0.1 (0-0.3)	0.1 (0-0.3)	0.35 (0.1-0.6)	0.3 (0-0.55)	0.15 (0.1-0.4)	0.2 (0.1-0.4)
Mean mesial crestal bone level in millimeters (range)	0.1 (0-0.2)	0	0.1 (0-0.3)	0.2 (0-0.4)	0.1 (0-0.3)	0.2 (0-0.4)	0.1 (0-0.4)	0.3 (0-0.5)
Mean distal crestal bone level in millimeters (range)	0.3 (0.2-0.7)	0.4 (0-0.6)	0.3 (0.1-0.6)	0.4 (0-0.5)	0.4 (0.3-0.9)	0.5 (0.1-0.7)	0.4 (0.2-0.7)	0.5 (0.1-0.6)

In order to assess crestal bone loss (CBL) and stability around submerged and non-submerged dental implants in Saudi patients with well- and poorly controlled type 2 diabetes mellitus, an evidence-based rationale for the best use of implant therapy in patients with T2DM was established. This included thirty-five patients with well-controlled T2DM and thirty-two patients with poorly controlled T2DM, 7-year prospective study, when compared to patients with well-managed diabetes, patients with poorly controlled T2DM exhibit inferior peri-implant bone outcomes. The maintenance of HbA1c levels is necessary for the outcomes of effective dental implant therapy to be predictable (46).

7.1 Diabetes and oral rehabilitation with implants

Numerous studies have demonstrated that people with diabetes are far more likely to develop periodontal disease, which can lead to tooth loss. The potential effects of partial or total edentulism on diabetics' ability to maintain a healthy diet due to diminished chewing efficiency are cause for concern. These dietary limitations may have a detrimental effect on glycemic control. In the end, these people may benefit from tooth replacement, and the effective use of implant therapy may significantly enhance the health and wellness of diabetic patients seeking to control their blood sugar levels (9).

In the past several decades, dental implant surgery has been evolved to be the most effective and comfortable tool for dental and oral rehabilitation, but as more implants are being placed, issues are occurring more frequently (51).

According to a thorough systematic review, patients with poorly controlled diabetes mellitus experience peri-implantitis more frequently, especially soon after implantation. Additionally, these patients have longer-term implant loss rates that are higher than those of healthy people. Conversely, success rates under controlled circumstances are comparable. The accepted practice now is perioperative anti-infective therapy, which includes the supportive administration of antibiotics and chlorhexidine and appears to increase implant success, dental implant operations constitute a secure method of oral rehabilitation for those with prediabetes or diabetes mellitus. As a result, patients with diabetes mellitus or prediabetic diseases are still eligible for dental implant surgery under regulated circumstances (51).

8. Complications Post-rehabilitation with implant

Once the implant is osseo integrated, the goal is to maintain this state of implant success over time, to maintain a state of good health, to preserve the implant bone as well as the soft tissues. According to the criteria of implant success, the loss of 2mm around the neck of the implant during the first year of function followed by no more than 0.2mm of lysis each year has long been considered a criterion of success. Thanks to the improvement of surgical techniques, the design of implants and the modification of topographic surfaces, peri-implant bone lysis has been gradually reduced (71).

This means that recent studies have called into question the success criteria and tolerated bone lysis. These studies consider that it is better to take into account bone lysis rates rather than the lysis values themselves in order to enable practitioners to predict peri-implant pathologies (71).

Galindo-Moreno et al. (2015) demonstrated that the lysis rate at 18 months was strongly related to the initial bone lysis rate. If bone lysis is above the threshold of 0.44 mm after 6 months of loading, the progression of bone lysis seems to be significantly greater with a greater risk of implant failure (72).

New success criteria that would include required bone lysis values around implants should be developed, based on bone lysis rates over certain time intervals rather than bone lysis values after a certain time (73).

Results from human studies have shown that peri-implant bone lysis is greater in diabetics compared to non-diabetics. Additionally, animal studies have found that diabetes negatively affects the osseointegration of implants (74–76).

According to a prospective study conducted over three years, marginal bone lysis is dependent on HbA1c values (77). It was found that the group that had the highest HbA1c values was the one that also had the highest bone lysis values. Hyperglycemic conditions are responsible for the alteration of bone physiology. These results are similar to those of previous studies that found greater bone lysis in diabetic subjects compared to non-diabetics (78,79).

This can be explained by an increased production of pro-inflammatory cytokines such as interleukin (IL-1B) and tumor necrosis factor alpha (TNF-α) in the gingival fluid (80).

In another study, the average bone lysis was 0.2mm with a follow-up period of 1 year in a group of type 2 diabetics (81).

This group was subjected to strict control of oral hygiene with learning the correct brushing technique, and follow-up visit with scaling and root planning every 6 months. Comparable bone lysis values were found in a group of diabetics undergoing a 10-year dental prophylaxis program (82).

It is obvious that an optimal control of oral hygiene prevents marginal bone lysis in non-diabetic subjects but also in diabetic subjects. Therefore, it is important for practitioners to educate patients in strict hygiene and to ensure maintenance given the beneficial effects on teeth and implants. Studies have shown that non-surgical periodontal therapies play a major role in reducing periodontal inflammation in patients with chronic hyperglycemia (83).

However, it has been reported that even if periodontal therapy reduced inflammation, it had a non-significant impact on the degree of metabolic control in subjects with chronic hyperglycemia. Two important factors are retained to preserve osteointegration in diabetic patients, good glycemic control with regular monitoring and an adapted and personalized therapeutic approach. Optimal oral hygiene combined with regular follow-up to maintain the results obtained (84).

The use of dental implants can replace missing teeth with a good prognosis, but the high prevalence of peri-implant diseases has emerged as a growing issue that directly threatens the stability and satisfaction of clinical outcomes over the long term (85).

Despite the fact that diabetic patients' implant placement is frequently initially stable, reports suggest that osseointegration is reduced in these patients (37).

Patients are more susceptible to both severe periodontal disease and peri-implantitis (Figure 15). It's also likely that a decreased rate of early osseointegration makes the implant more vulnerable to peri-implantitis in the future (37).

It is known that hyperglycemia can change the microbiome to become more pathogenic and/or increase the local inflammatory response, which can speed up bone loss due to periimplantitis (39).

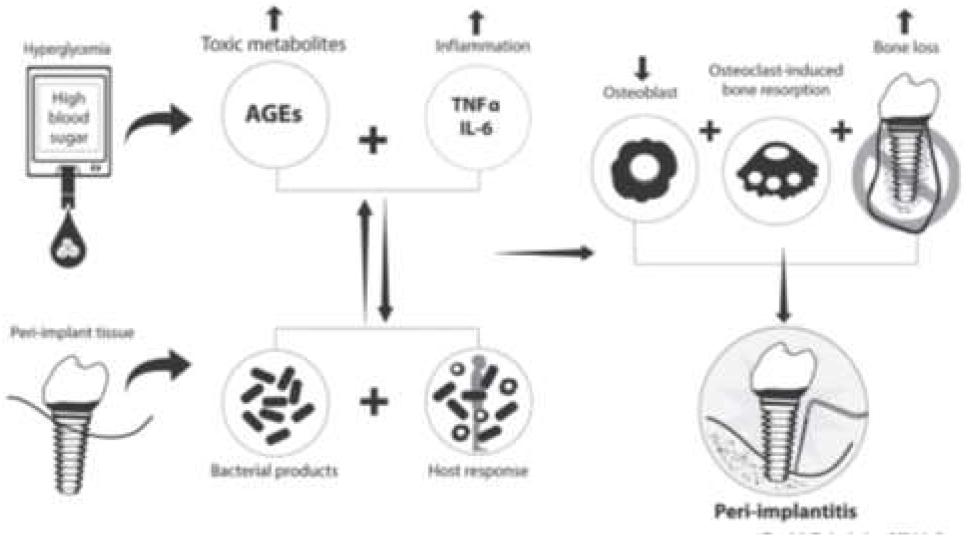

Figure 15 Peri-implant Disease and Obesity/Metabolic Syndrome and Type 2 Diabetes Mellitus (39) (with permition of Elvevier, Copyright 2020).

Patients with diabetes are susceptible to experiencing more pronounced progression of peri-implant disease than people with metabolic health due to altered host response along with environment conducive to increase bacterial plaque buildup as a result of hyperglycemia (86).

The underlying molecular mechanisms that cause poor osseointegration of implants and decreased bone metabolism, as well as the complex signaling cascade that is affected by hyperglycemia, have been thoroughly explored elsewhere (87).

Given the shortage of consistent treatments for managing peri-implant disorders globally, understanding host reaction at the bone to dental implant interface may help identify crucial biomarkers or indicators for early diagnosis and the creation of customized treatments for individuals with metabolic impairment (88).

Although the definition of peri-implant diseases has been tried by several authors, it is still up for debate. The key diagnostic indicator for peri-implant mucositis, according to the Consensus Report of the Seventh European Workshop on Periodontology, is bleeding on gentle probing, whereas peri-implantitis is characterized by loss of the supporting crestal bone and BOP, with or without concurrent deepening of peri-implant pockets or suppuration (89).

Implant success, also known as peri-implant disease-free (PID-free) status, was defined as an osseointegrated implant with no indications of BOP or suppuration (90).

In addition to these circumstances, a bone loss of 2 mm, which is regarded as normal bone remodeling, was also included in the definition (91).

success of an implant defined. All peri-implant sites in a patient with multiple implants have to comply with the aforementioned requirements in order for that patient to be designated as PID-free (91).

8.1 Peri-implant mucositis

As a result of establishing the biologic width, the soft-tissue complex at dental implants grows in 8 weeks, and the supracrestal peri-implant mucosa is made up of connective tissue with an average length of 1 mm and 2 mm junctional epithelium (92).

It should be noted that the development of peri-implant disorders was tightly correlated with microbial colonization and host response, which was consistent with periodontal diseases, one of the most frequent adverse effects of peri-implant dysbiosis at the implant-mucosa interface is peri-implant mucositis, which is thought to be the precursor of peri-implantitis (Figure 16) (26).Peri-implant mucositis affected around 23.9-88.0% of patients and 9.7-81.0% of implants (93).

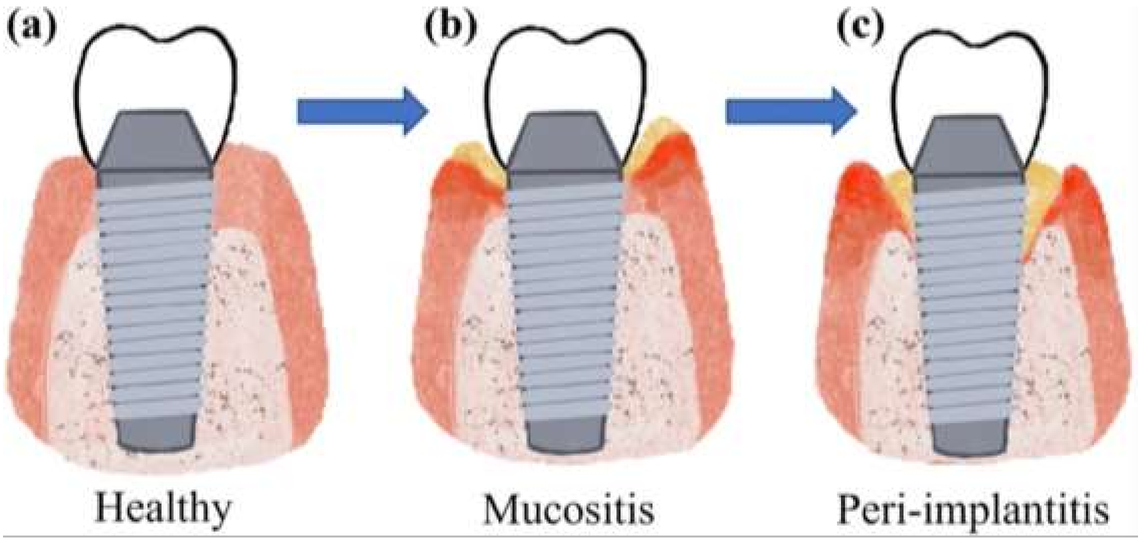

Figure 16 Progression of peri-implantitis (105) (with permission of Elsevier, Copyright 2022).

The important criteria for the definition of peri-implant mucositis are inflammation in the peri-implant mucosa and the absence of continuing marginal peri-implant bone loss. Peri-implant mucositis has been defined as an inflammatory lesion of the mucosa surrounding an endosseous implant without loss of supporting peri-implant bone. bleeding on probing is a clinical indicator of inflammation, and other symptoms could include erythema, edema, and suppuration (94).

Peri-implant mucositis is the inflammation of the mucosa surrounding an implant when there is no evidence of bone loss to support the implant include bleeding on probing and/or suppuration, which are typically associated with probing depths of less than 4 mm and no radiographic evidence of bone loss other than bone remodeling (95).

In Lagunov and colleagues' meta-analysis, Jiang (2020) probing depth (PD) and bleeding on probing (BOP) are regarded as two crucial peri-implant measures for determining the health of peri-implant soft tissue. Diabetes patients had higher BOP than non-diabetic patients in the meta-analysis by Lagunov and colleagues, according to their research, they discovered a statistically significant difference in BOP (P .00001) favoring ND patients between the diabetic and ND groups. This study suggests that T2DM patients were more likely than healthy patients to experience peri-implant mucosa inflammation and found no change in PD between ND and diabetic individuals, suggesting that PD in diabetic patients may be similar to that in healthy patients (17).

8.1.1 Etiologies and pathogenesis

Like gingivitis around natural teeth, peri-implant mucositis describes the inflammatory process that occurs around an implant. Soon after implants are inserted, salivary glycoproteins bind to exposed titanium surfaces, causing microbial colonization (95).

The development of a biofilm is crucial for the development of infections surrounding dental implants and plays a critical role in the onset and progression of peri-implant diseases (96).

Furthermore, Gram-negative anaerobic bacteria identical to those seen surrounding natural teeth in individuals with severe chronic periodontitis have been linked to peri-implant diseases (96).

As is acknowledged that gingivitis is the forerunner to periodontitis, peri-implant mucositis is the condition that precedes peri-implantitis. However, peri-implant mucositis does not always progress to peri-implantitis, much like the causal link between gingivitis and periodontitis. Similar to how "epithelial sealing" around teeth works around tooth implants (95).

In addition, it is determined that there is no proof that any structural variations between natural teeth and implants will materially alter the host's reaction to a bacterial challenge. Furthermore, research suggests that, like gingivitis, peri-implant mucositis can be reversed with adequate treatment. Thus, removal of the biofilm from the implant surface is the major target when treating peri-implant mucositis (95).

8.2 Peri-implantitis

A condition known as peri-implantitis is characterized by an inflammatory response around an implant that includes inflammation of the soft tissues as well as a progressive loss of the supporting bone beyond normal bone remodeling (95).

8.2.1 Prevalence and epidemiology

Dental implants puncture the mucosa, exposing them to the oral microbiota on a constant basis. Dental implant surfaces may develop pathogenic biofilms as a result of oral bacteria colonization (98).

Despite the infectious, it is widely acknowledged that peri-implant diseases have a multiple origin and that certain individuals appear to be more at risk than others are (99).

Dental implants may be less predictable due to various systemic or local factors, which might result in peri-implant inflammation, bone resorption, and ultimately implant loss (100).

Since DM is one of the systemic disorders that affect 9.3% of the world's population, it is common for dental patients to have it, nowadays, there are many publications that evaluate the relationship between DM and dental implants (101).

Similar to the current examination, Rokn et al. (2017) showed no association between diabetes mellitus (DM) and the prevalence of peri-implantitis, the review by Schwarz's conclusion that diabetes is a risk factor for peri-implantitis, Papi et al. reported that there is a 50% higher risk of detecting peri-implantitis in subjects with diabetes/hyperglycemia compared to non-diabetics, while other authors, such as Monje and Papi, considered that DM is associated with an increased risk of peri-implantitis, but not with peri-implant mucositis in their meta-analysis (101).

Although there is not conclusive evidence, there is a relationship between the presence of DM and peri-implantitis, so it is advised for patients to keep their glucose levels under control. In the end, the variability in the results may be due to the fact that patients who visit the dental clinic today are involved not only with their oral health but also with their systemic health (102).

9. Recommendations

9.1. Periodontal maintenance of diabetic patients:

Diabetic patients are at greater risk of oral diseases, namely periodontal diseases. A follow-up with the dentist should be done regularly and the patient should undergo a periodic dental examination, at least twice a year. The dentist plays an important role in raising awareness of the need for an oral examination and in providing information on the relationship between diabetes and periodontal disease (103).

It is essential to teach these patients good oral hygiene technique and perform a complete periodontal evaluation. If necessary, periodontal treatment should be performed followed by a reassessment after three months. This reassessment will determine the need for surgical periodontal treatment or supportive periodontal treatment (103).

9.2. Diabetes management and glycemic balance

The dentist should collect information on health status and glycemic control from the patient or the assistant doctor, as the success of treatments largely depends on the control of diabetes (57).

An exchange of information between the dentist and the endocrinologist/assistant physician is important for the best possible care. In fact, communication must be two-way: the attending physician must be informed about the oral manifestations and complications of the disease to help regulate the blood glucose level, and the dentist must be aware of the glycemic control of the disease to help maintain the patient's oral health (57).

For good glycemic control, it is recommended that HbA1c be kept below 7%. It is recommended to schedule morning appointments to avoid any change in blood glucose, preferably that the patient has had breakfast. For patients treated with insulin, appointments should be scheduled an hour and a half after breakfast to avoid spikes in insulin activity (57).

Currently, conscious sedation with nitrous oxide has an excellent safety record in patients with diabetes and reduces the stimulating effect of stress (adrenaline and corticosteroids) that have hyperglycemic actions. The use of narcotics or barbiturates in these patients is not contraindicated (61).

The placement of a dental implant is a non-urgent surgical procedure. Any non-urgent surgical procedure may be performed after verifying that the treatment has a reasonable prospect of success and determining the risk-benefit ratio. In fact, uncontrolled diabetes affects the patient's ability to heal after surgery and the effectiveness of the immune system, increasing the risk of infection (61).

In addition, regular monitoring and measurement of blood glucose are essential after placement and healing of dental implants. Good oral hygiene and good nutrition remain equally important factors (57).

10. Impact on the quality of life of implant rehabilitation

According to the study of Topçu et al., 2017 focused at analyzing factors that could have an impact on patients' satisfaction levels and perceptions of dental implant treatment. These factors could be both implant site-related and patient-based also addressed potential discrepancies between dental patients' and dental specialists' assessments of aesthetics, 264 anterior esthetic implant sites with supported fixed prosthesis (n = 164) were included, Fixed implant-supported restorations typically offer very high levels of satisfaction and quality of life in terms of oral health (104).

Study of Beresford & Klineberg, 2018, End osseous dental implants were used to restore twelve patients with an edentulous mandible or a failing dentition. Three implants were positioned, and an interim fixed prosthesis with little cantilever was mounted onto them right away. Two Locator attachments were put in place and an overdenture was tried after a 4-month healing period; after another 4-month healing period, a fixed prosthesis was put on the three implants. Using computer-aided design, a titanium framework with a resin base and teeth was created for the fixed prosthesis. A seven-item visual analog scale and a modified version of the 49-item oral health impact profile were used to evaluate patient satisfaction and dental health-related quality of life prior to treatment, following the wearing of the provisional, and following each treatment choice. When compared to a standard complete mandibular removable dental prosthesis, both treatment methods significantly and comparably improved patient satisfaction and oral health-related quality of life (19).

More recent research shows that patients with mandibular implant-supported overdentures are more likely than patients with conventional dentures to positively adjust their diet, especially after nutritional interventions. Contrary to conventional denture wearers, implant over-denture wearers appear to be more satisfied with their prosthesis when pushed to change their diet (69).

Cost is still seen as a very substantial obstacle to the supply of implant assisted prostheses. Even while they are undoubtedly more expensive than traditional dentures, using only two implants can reduce the initial cost. Additionally, spreading out the total cost across the patient's anticipated longevity reveals that the annual cost difference between the two treatment modalities is rather minimal, especially when compared to the initial first-year costs (69).

CONCLUSION

Patients with diabetes mellitus are increasingly frequent in dental clinics around the world. Diabetes mellitus is one of the main risk factors for periodontal and peri-implant diseases. It alters healing, immune capacity, bone remodeling and compromises osseointegration.

Recent research has demonstrated that diabetes is not a contraindication for dental implant placement. In fact, the success of implant depends on several factors, such as glycemic control (HbA1c), the type and duration of diabetes.

Regarding the duration of the disease and the success rate, the authors opinions differ, with some suggesting that success is greater if the duration of the disease is short, due to its association with micro and macro-vascular complications. Other authors argue that the duration of diabetes does not negatively influence implants when diabetes is controlled.

In conclusion, there are contradictory reports in the scientific literature about the factors that influence the success of implants in patients with diabetes. However, they all converge on the fact that the placement of dental implants is possible and predictable if blood glucose is well controlled.

More studies of high quality level are still required to define clinical guidelines for implant therapy for patients with diabetes.

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