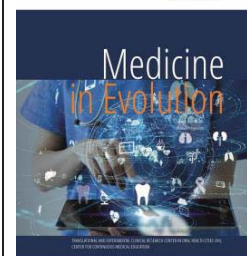# Interdisciplinary approaches to preventing oral complications in diabetic patients: a systematic literature review

Galuscan A., Balean O., Dumitrescu R., Alexa V., Sava-Rosianu R., Floare L., Jumanca D. E.

Department of Preventive, Community and Oral Health Dentistry, Faculty of Dental Medicine, University of Medicine and Pharmacy Timișoara "Victor Babeș", Translational and Experimental Clinical Research Center in Oral Health (TEXCE-OH)

Correspondence to:
Name: Octavia Balean
Address: Department of Preventive, Community and Oral Health Dentistry, Faculty of Dental Medicine, University of Medicine and Pharmacy Timișoara"Victor Babeș, Splaiul Tudor Vladimirescu 14A
Phone: +40 748677191
E-mail address: balean.octavia@umft.ro

Abstract

In the last three decades the number of people with diabetes has doubled. The global prevalence of diabetes mellitus (DM) is rapidly rising as a result of population aging, urbanization and associated lifestyle changes. Among the complications in the oral sphere of diabetes were reported: periodontal disease (PD) (the most important oral disease correlated with diabetes), xerostomia, oral candidiasis, glossodynia, slow healing of the tissues of the oral cavity, as well as other conditions for which it would be necessary to implement early prophylactic and therapeutic measures.

This systematic literature review was conducted to answer the following questions: The primary question: What are the ways to prevent periodontal disease and oral mucosal diseases in DM patients? And the secondary questions were: How were these methods evaluated in the studies included in the research? What is the level of knowledge of both patients and diabetologists regarding the prevention of these oral complications in diabetic patients?

436 bibliographic references were identified and were centralized in a file. The studies were evaluated according to their title and abstract, following the extent to which they correspond to the inclusion criteria. After analyzing the titles, 351 articles were excluded and the remaining 86 had their abstracts evaluated. 25 articles were selected and read in full, two of which were excluded because they proved not to be relevant to the chosen topic. Thus, finally, 23 studies were included in the systematic review.

The most important conclusion was that: an interdisciplinary collaboration is necessary between health specialists, dentists and diabetologists alike, with the aim of developing programs to educate diabetic patients about the oral complications of DM and their prevention.

Keywords: Diabet, prevention, oral diseases, parodontitis, gingivitis, xerostomia, oral cancer

INTRODUCTION

In recent years, researchers have closely studied the correlation between the state of oral health and systemic ailments, in the context of wanting to update the information already present in the literature. Thus, a special interest was given to diabetes, one of the most common ailments encountered in the general population, given the fact that the number of people with diabetes, worldwide, has doubled in the last three decades. The global prevalence of DM is rapidly rising because of population aging, urbanization and associated lifestyle changes [1].

Among the complications in the oral sphere of diabetes were reported: periodontal disease (the most important oral disease correlated with diabetes), xerostomia, oral candidiasis, glossodynia, slow healing of the tissues of the oral cavity, as well as other conditions for which it would be necessary to implement early prophylactic and therapeutic measures. Regarding periodontal disease, it is necessary for diabetic patients to be aware of the fact that maintaining oral health and good glycemic control contributes to reducing the progression of this disease. In this sense, both the dentist and the diabetologist must communicate effectively with the patient so that he understands the importance of prevention.

The chosen theme aims to better understand the effects of diabetes on the body, particularly in the oral cavity, with the objective of identifying ways to prevent periodontal disease and oral mucosal diseases and evaluating these methods. The research method employed in this paper is the systematic review. A synthesis of the most recent and relevant articles from the literature will be pursued.

Diabetes Mellitus (DM)

According to the IDF (International Diabets Federation), DM is a chronic condition that occurs when the pancreas is no longer able to produce insulin or when the body cannot properly use the insulin it produces [2]. In other words, diabetes is a metabolic disorder determined by multiple etiological factors. It is characterized by chronic hyperglycemia accompanied by disturbances in the metabolism of carbohydrates, fats and proteins resulting from defects in insulin secretion and/or reduced insulin sensitivity of some tissues [3]. Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of pancreatic β-cells with consistent insulin deficiency to abnormalities leading to insulin resistance. Impaired insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which, if any, abnormality is the primary cause of hyperglycemia [4].

Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, and many patients do not fit easily into a single class [4]. That is precisely why it is necessary to know the criteria on the basis of which a correct diagnosis can be made, as well as the types of DM. Over time there have been numerous attempts to classify DZ. In 1997, the American Diabetes Association (ADA) proposed a classification of DM. This was later taken over by the WHO in 1999 [5]. The most recent classification belongs to the ADA, in 2020 and is illustrated in table 1.

Table 1. DZ classification (ADA, 2020) [6]

Type 1 diabetes - due to autoimmune destruction of β-cells, which usually leads to absolute insulin deficiency
Type 2 diabetes -due to progressive loss of adequate insulin secretion by β-cells often in the setting of insulin resistance
Gestational diabetes - diagnosed during pregnancy, in the second or third trimester. Specific types produced by:

- genetic defects of beta cells.
- genetic defects of insulin action.
- diseases of the exocrine pancreas: pancreatitis, tumors, cystic fibrosis.
- endocrinopathies: hyperthyroidism, Cushing syndrome, aldosteronism, glucagonoma.
- induced by drugs or chemical substances: Dilantin, vacor, nicotinic acid, glucocorticoids, thyroid hormones, thiazides, alpha interferon, pentamidine.
- infections: congenital rubella, cytomegalic virus.
- rare autoimmune forms.
- genetic syndromes.

Type 1 diabetes, also called insulin-dependent diabetes, represents only 5-10% of all cases with this metabolic disorder. It is caused by cell-mediated autoimmune destruction of pancreatic β-cells, in which case the administration of exogenous insulin is mandatory [4].

Type 2 diabetes accounts for approximately 90% of all diabetes cases. This chronic condition is characterized by insulin resistance with relative insulin deficiency. (insulin is secreted, but not enough to overcome insulin resistance) [3]. In this condition, insulin is ineffective and is initially counteracted by an increase in insulin production to maintain glucose homeostasis, but over time, insulin secretion decreases, resulting in type 2 diabetes [7].

Diagnosing diabetes is particularly important because it influences the establishment of the appropriate treatment plan for each clinical case. If it is easier in symptomatic patients, in asymptomatic people once the test result is abnormal, it must be confirmed by an additional test. This is increasingly important as screening programs expand and also because 30-50% of people with diabetes are asymptomatic and do not know they have the disorder [3]. Complications of diabetes: Patients with diabetes have a high predisposition to a series of complications that constitute serious health problems [2]. High blood glucose levels can cause serious conditions such as cardiovascular diseases, neuropathy, retinopathy, nephropathy and complications in the oral cavity [10].

Oral complications of diabetes: Regarding the oral complications, they are the point of interest for the topic of this paper. The correlation between diabetes and oral diseases has been, in recent decades, an important topic for researchers given the increasing number of patients suffering from this metabolic disorder. In most studies, periodontal disease was highlighted as the most important oral complication of DM [10]. If blood glucose is not properly managed, there is an increased risk of inflammation of the gums (gingivitis) which can later evolve into periodontitis. Periodontitis is the main cause of tooth loss, being associated with an increased risk of cardiovascular disease. The prevention of this oral disease consists in performing regular dental consultation to ensure an early diagnosis, in the case of patients with previously undiagnosed diabetes, and also for the regular monitoring of any oral complications in people with diabetes [2]. Other potential oral complications described in the literature are: carious lesions, xerostomia, oral candidiasis, lesions of the oral mucosa, oral cancer, glossodynia, taste disturbances, delayed healing of oral lesions, apical periodontitis and peri-implantitis [10].

It should be mentioned that these changes are not always present, as they are not specific conditions nor pathognomonic for diabetes. In addition, they are unlikely to be seen in patients with well-controlled diabetes. Patients with controlled DM have a normal tissue response, a properly developed dentition with a reduced incidence of caries and a normal defense against infections [11].

Periodontal disease has been described as the sixth complication of diabetes, in addition to microvascular disease and macroangiopathy. Many factors, such as increased numbers of specific glucose-demanding bacteria, neutrophil dysfunction, inhibition of

collagen synthesis, adipokines and advanced glycation end products (AGEs) have been associated with higher susceptibility to periodontal disease in diabetic patients [12]. Diabetes has been recognized as a risk factor for periodontal disease since the beginning of 1990, the chances of developing this oral disease being 2-3 times higher in patients with poorly controlled diabetes compared to healthy ones [13]. Reduced defense mechanisms and increased susceptibility to infections were the major changes observed in patients with uncontrolled diabetes [11]. The severity of periodontal disease was closely correlated with the degree of metabolism, control and duration of diabetes. Pathogenic mechanisms that establish the link between diabetes and periodontal disease: Impairment of neutrophil adhesion, chemotaxis and phagocytosis, can facilitate the persistence of bacteria in the gingival groove thus causing significant periodontal damage. While neutrophils are often hypofunctional in diabetes, patients may have a hyper-responsive monocyte/macrophage phenotype, resulting in significantly increased production of cytokines and proinflammatory mediators. This hyper-inflammatory response results in high levels of pro-inflammatory cytokines in the crevicular fluid. Elevated levels of inflammatory mediators, including PGE2, IL-1β and TNF-ἀ in gingival exudates, are associated with increased severity of periodontal disease in patients with diabetes and AGE-enriched gingival tissue, who exhibit greater vascular permeability, greater breakdown of collagen fibers and an accelerated destruction of connective tissue and bone [14]. Studies have shown that chronic periodontitis can induce an increase in the systemic chronic inflammatory state, reflected in increased serum C-reactive protein, IL-6 and fibrinogen levels [14]. The increased level of C-reactive protein (hsCRP) may be a stronger predictor of acute myocardial infarction than cholesterol, being an important index in the accurate assessment of cardiovascular disease risk [15].

Gingivitis is inflammation of the gingival tissues without loss of attachment or bone. Being the first stage of periodontal disease, gingivitis can also be influenced by systemic factors, one of them being diabetes. In many cases, the clear signs of gingival inflammation that occur in these patients are seen in the presence of relatively small amounts of bacterial plaque. Therefore, the long-term prognosis for these patients depends not only on the control of the bacterial plaque, but also on the control or correction of the systemic factor [11].

Periodontitis represents the inflammatory disease of the periodontal tissues, being caused by the presence of microorganisms or specific groups of microorganisms, resulting in the progressive destruction of the periodontal ligament and the alveolar bone accompanied by an increase in probing depth and the appearance of gingival recession [11]. In patients with type 1 diabetes, periodontitis begins after the age of 12, and is five times more common in adolescents than in children. Thus, in patients aged between 13-18 years, the percentage is 9.8% and increases to 39% in those older than 19 years [11]. The level of glycemic control is essential in determining the risk of periodontitis in DM patients.

Similar to the other complications of diabetes, the risk increases with poor glycemic control. Evidence has emerged to support a bidirectional relationship between diabetes and periodontitis; that is, diabetes increases the risk of periodontitis, and periodontitis increases the risk of complications of diabetes and makes glycemic control more difficult. Furthermore, it has been found that there is a possibility to improve glycemic control by treating periodontitis [13]. In diabetic patients, glycemic control is complicated by the constant reservoir of gram-negative anaerobic bacteria that are located deep in the gingival sulcus producing infection and inflammation throughout the body. An important aspect of the link between periodontal disease and DM is the fact that chronic periodontitis causes systemic inflammation, which results in increased insulin resistance and hyperglycemia.

Because patients with DM, especially those with poor glycemic control, accumulate high levels of AGEs in tissues, including the periodontium, this interaction may account for the marked increase in crevicular fluid levels of IL-1β and TNF observed in patients with

diabetes compared to those without diabetes and may contribute to the increased prevalence and severity of periodontal disease in diabetics [14]. It should be mentioned that the sites affected by periodontitis in diabetic patients contain the same bacterial species as the sites affected in patients without metabolic disorders. The similar composition of the subgingival flora could indicate that the increased prevalence and severity of periodontitis in DM patients is influenced by the host response [14]. Periodontal treatment aimed at eliminating periodontal pathogens and reducing inflammation has been shown to have a positive impact on glycemic control by restoring insulin sensitivity in patients with poorly controlled diabetes. Also, an effective control of periodontal infection in patients with diabetes can reduce the level of AGEs in the serum. Thus, it can be concluded that the prevention and control of periodontal disease should be considered an integral part of diabetes [14].

Xerostomia: Patients with diabetes, especially those with poor glycemic control, can present, as an oral complication, damage to the salivary glands. This complication manifests itself clinically through reduced salivary secretion thus causing xerostomia with an impact on hard and soft oral tissues [16]. Xerostomia is the subjective sensation of dryness of the mouth, this definition being based on the absence or presence of the individual sensation of dry mouth and not on precise measurements of saliva flow. Compared to xerostomia, hyposalivation is an objective decrease in salivary flow [17,18]. Both type 1 DM and type 2 DM have been associated with xerostomia. A series of studies have highlighted a decrease in salivary flow in diabetic patients compared to clinically healthy patients. Changes in the microcirculation of the salivary glands, damage to the gland parenchyma, dehydration and disturbances in glycemic control could be some causes of low salivary flow [17]. The consequences of xerostomia on the oral cavity are: disturbance of masticatory function and speech, inflammation of the oral mucosa, accumulation of bacterial plaque, decrease in the buffering capacity of saliva, fungal infections (Candida Albicans) and, last but not least, severe degradation of oral tissues [18].

Glossodynia and taste disorders: Glossodynia or Burning Mouth Syndrome is an oral complication found in patients with DM and not only, being described as an oral burning sensation lasting at least 4-6 months. Most commonly involving the tongue, sometimes it can also extend to the lips or in certain areas of the oral mucosa. It can be accompanied by dysgeusia (taste alteration) and subjective xerostomia (dry mouth) [19]. In patients with diabetes, burning sensation in the mouth has been attributed to poor glycemic control, metabolic changes in the oral mucosa, angiopathy and neuropathy. Thus, it is believed that a good control of the metabolism could lead to amelioration of symptoms. According to studies, the correlation between diabetes and glossodynia has been considered quite controversial. It has been suggested that type 2 diabetes plays a role in the development of BMS (Burning Mouth Syndrome). In contrast, other studies reported a lack of association between these two conditions [20].

Oral candidiasis: The correlation between candidiasis and diabetes has been much studied over time, especially due to the increased susceptibility of diabetic patients to fungal infections compared to those without DM [21,22]. Oral candidiasis is an opportunistic, common infection of the oral cavity caused by the overgrowth of Candida species, particularly Candida albicans. Numerous risk factors such as poor oral hygiene, tongue lesions, sex, age, smoking, unbalanced diet, salivary pH disturbance, xerostomia and wearing dental prostheses contribute to the occurrence of oral candidiasis in patients with diabetes [21,22]. In the last decade, the large number of immunocompromised patients has led to an increase in the prevalence of oral candidiasis, which is one of the most common fungal infections. The diagnosis of oral candidiasis is based on changes in the oral mucosa in the form of erythematous, pseudomembranous (oral thrush) or hyperplastic plaques [21,22]. The dorsal surface of the tongue is the point of initiation of infection for most clinical forms of oral

candidiasis [23]. Among the reasons why diabetic patients are more susceptible to oral candidiasis are high salivary glucose levels, reduced salivary flow, impaired chemotaxis and defective phagocytosis due to the deficiency of polymorphonuclear leukocytes [21]. Oral manifestations of oral candidiasis can generally be classified into three main categories, namely: acute manifestations, chronic manifestations, and chronic mucocutaneous candidiasis syndromes [23].

Stomatitis, glossitis and angular cheilitis. Denture-induced stomatitis is mainly observed in ill-fitting full denture wearers, with diabetes being a systemic contributing factor. The clinical manifestations are represented by erythema, edema, decubitus lesions, with deposits of Candida albicans present on the oral mucosa. Median rhomboidal glossitis represents the chronic inflammation of the tongue manifested by the atrophy of the filiform papillae located on the midline of the lingual dorsal surface. It appears as a well-defined, symmetrical, rhomboid-shaped area, red in color, with a smooth and shiny appearance. Angular cheilitis can be seen at the level of the oral commissures as an erythematous lesion. The lesion has been reported to occur in diabetic patients with poor glycemic control [24].

Lesions with malignancy potential, premalignant oral lesions and oral cancer.

Oral **lichen planus** is a chronic inflammatory disease with a higher incidence among women than men. The prevalence of this potentially malignant lesion in the general population varies from 1% to 2% [25]. The relationship between oral lichen planus and diabetes was first described in 1966, and since then numerous epidemiological studies have demonstrated this association. It has been highlighted that endocrine dysfunction in DM patients can be a determining factor of immunological changes. These changes contribute to the development of oral lichen planus [26]. According to studies, oral lichen planus occurs more frequently in patients with type 1 diabetes compared to patients with type 2 diabetes. The argument is that type 1 diabetes is considered an autoimmune disease, and oral lichen planus is based on a whole mechanism autoimmune In addition, acute hyperglycemia alters the immune response. Atrophic-erosive forms of oral lichen planus are the most common in patients with diabetes [24].

Leukoplasia is the most common premalignant lesion of the oral mucosa. The WHO defined it as a white spot or plaque that cannot be removed by wiping and that cannot be classified under any other pathology. The etiology of this lesion is not very clearly established, however, there are certain risk factors such as: smoking, HPV-16 and HPV-18, Candida albicans or certain localized traumas. Most leucoplakias (80%) are benign; the remaining 20% are malignant or premalignant and only 3% of these progress to carcinoma [11].

Patients with DM have a higher risk of developing oral cancer compared to subjects without DM [10]. Oral cancer which is a subtype of head and neck cancer and is defined as any cancerous tissue with localized development in the oral cavity. Except for the already known risk factors (smoking, alcohol and infection with the oncogenic human papillomavirus (HPV)), certain studies have shown that glucose metabolism abnormalities and diabetes can also have an influence on the development of neoplasia's. In conclusion, if DM is associated with an increased risk of oral cancer, it is very important to focus on prevention [27].

Aim and objectives

The purpose of this paper is to identify, through a systematic review, the methods of preventing periodontal disease and oral mucosal diseases, the evaluation of the effectiveness of these methods, as well as the evaluation of the level of information of both patients and diabetes specialists regarding the prevention of these oral complications in diabetic patients.

MATERIAL AND METHODS

This systematic literature review was conducted to answer the following questions:

The primary question:

What are the ways to prevent periodontal disease and oral mucosal diseases in DM patients?

Secondary questions:

- How were these methods evaluated in the studies included in the research?

- What is the level of knowledge of both patients and diabetologists regarding the prevention of these oral complications in diabetic patients?

Given the fact that numerous relevant articles were found for this study, it was decided to perform a systematic review in order to find answers to the questions formulated above.

The review followed a clear protocol, detailed in the article by Shamseer L. et al (2015) entitled "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation" [28].

Search strategy for bibliographic sources

For the systematic search of the scientific literature, the following electronic databases were used: ScienceDirect, PubMed, Google Scholar and SpringerLink. Initially, a search was performed in the PubMed database applying the search terms "diabetes mellitus", "prevention of oral manifestations", "prevention of periodontal disease", "gingivitis", "gingival bleeding". With the help of the "Publication Date" filter, the 10 years option was chosen, in the search result only studies from the last 10 years (published between 2011 and 2021) are present.

Another search was then performed using the Google Scholar database. Combinations of keywords such as: "awareness", "diabetic patients", "periodontal therapy", "oral mucosal diseases", "xerostomia", "oral candidiasis", "taste disturbance", "oral cancer" or "burning mouth syndrome" were used to ensure a more objective and comprehensive search. Studies published since 2011 were selected.

Other scientific articles were identified through the Science Direct and SpringerLink databases using the same search terms. Also, some studies were obtained from the reference lists of review articles. The keywords used were identified following a random literature search.

Criteria for selecting scientific articles.

The selection of specialized articles was made based on the inclusion and exclusion criteria. The studies included in this paper met the following criteria: (1) studies published between 2011 and 2021 in scientific journals, (2) studies conducted on more than 20 subjects with diabetes diagnosed at least 6 months before, (3) age of participants over 14 years, (4) participants with DM type 1 or 2, (4) studies evaluating the level of knowledge of medical specialists regarding the oral complications of DM. Studies older than 10 years, animal studies, in vitro studies, studies performed on less than 20 patients, studies on pregnant women or patients with uncontrolled systemic diseases or mental illnesses were excluded.

Data collection. 436 bibliographic references were identified and were centralized in a file. The studies were evaluated according to their title and abstract, following the extent to which they correspond to the inclusion criteria. After analyzing the titles, 351 articles were excluded and the remaining 86 had their abstracts evaluated. 25 articles were selected and read in full, two of which were excluded because they proved not to be relevant to the chosen topic. Thus, finally, 23 studies were included in the systematic review. The graphical representation of the data collection protocol was illustrated in Fig. 1
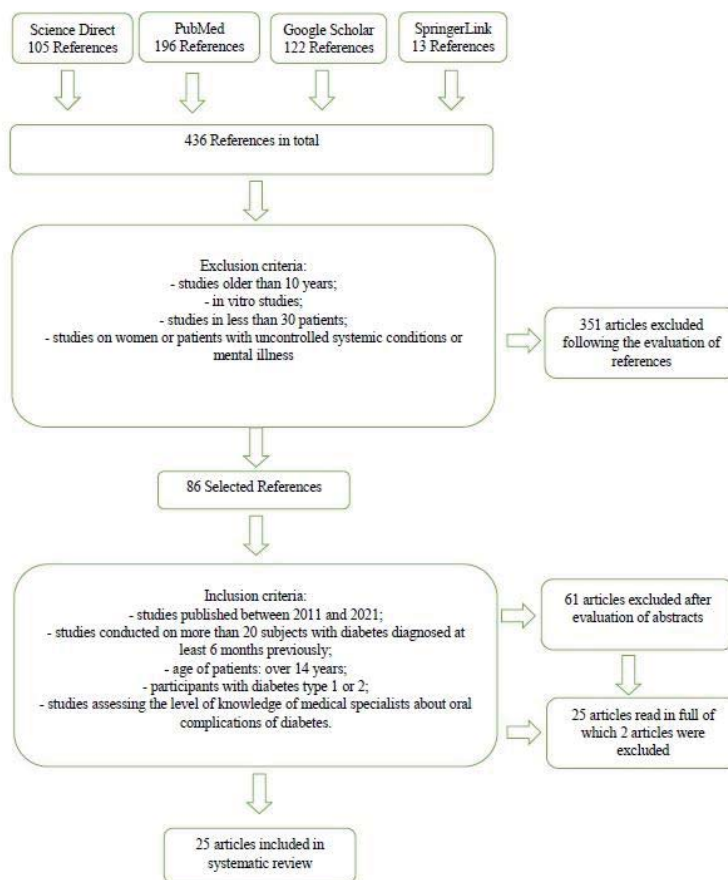
Figure 1. Data collection protocol

Data analysis: After analyzing the data from the 23 selected articles, we obtained the following results.

RESULTS

Following the selection of studies based on the inclusion and exclusion criteria, 23 articles resulted that were analyzed in the systematic review. Of these, 74% were cross-sectional studies, 8.7% randomized clinical trials and 17.3% in vivo experimental studies. The articles were published in English. A large part of the studies (60.8%) was carried out in Asian countries, 19.6% in Europe, 15.3% in America and 4.3% in Africa. Two studies were conducted among family doctors [46] and endocrinologists and diabetologists [44].

In 66% of the articles, the participants were selected from the Diabetes Centers or from the Departments of Diabetes, Nutrition and Metabolic Diseases of the Regional Hospitals, and in 34% of the articles, the participants were in the records of the Periodontology Departments of the Universities.

Regarding the type of DM of the participants, in 36.7% of the studies patients with type 1 and 2 diabetes were included, in 4.3% only DM, type 1 and in 59% only DM, type 2. In two studies [15,22] patients had uncontrolled diabetes.

Fourteen (14) studies were conducted based on a questionnaire. Of these 8 studies [29,30, 40, 42,43,45,49,50] aimed to evaluate the level of knowledge of diabetic patients regarding periodontal disease and other oral complications. Two (2) studies [31, 39] focused

strictly on the changes occurring in the oral mucosa, 2 studies [32, 38] addressed xerostomia and 2 studies [44, 46] evaluated the attitude of family doctors and diabetologists towards oral health of diabetic patients. The rest of the studies [33,34,35,36,37,41,47,48,51] were based on different specific therapies for periodontal disease and for the other oral complications of DM.

Assessment of patients' knowledge level: Many patients with DM were not aware of the bidirectional relationship between DM and periodontal disease [30, 40,43]. However, Al Amassi B. Y. et al, 2017 highlighted in his study that 75.9% of participants knew that diabetes is an important risk factor in the onset of periodontal disease [42]. Regarding the signs of gingival diseases, bleeding during brushing and gingival inflammation were frequently mentioned by patients [29,30].

Xerostomia was one of the most recognized oral complications of DM. In the study conducted by Kakooei S. et al, 2020 on a sample of 433 diabetic patients from Iran, 90% of them mentioned xerostomia as one of the main oral complications of diabetes [50]. Similar results were obtained in the studies of Bowyer V. et al, 2011 [30] and Çankaya H. et al, 2018 [45].

Regarding visits to the dentist, in the study conducted by Bahammam M. A., 2015, only 12.6% of patients went to the dentist in the last year, although 80.2% went to the diabetologist in that year [40]. Similar results were obtained in other studies included in the systematic review [29,42,43]. The participants came to the dental office only if they had a problem.

Regarding oral hygiene, the results of the studies were divided. In a limited number of studies [30,43,50], more than 50% of the participants answered that they brush their teeth twice a day, and regarding the use of dental floss and mouthwash, the percentage was in average below 20% in most items.

Evaluation of the level of knowledge of health professionals

In the study conducted by Obulareddy V. T. et al, 2018, all participants (specialists in endocrinology, general medicine and diabetology) agreed that there is a correlation between oral health and general health, but only 43.2% were aware of the relationship bidirectional, and the remaining 56.4% reported diabetes as a risk factor for periodontitis. However, only 17.8% of participants refer patients to dentists. Almost 90% of the practitioners showed their willingness to enrich their knowledge regarding the prevention of oral complications in diabetic patients [44].

Sut Yee Tse, 2018 [46] conducted a study including family physicians in Hong Kong. The results of the study showed that 99% of the participants were aware of the relationship between DM and periodontal disease. 90% of the participants knew that poor DM control can be a predisposing factor for periodontal disease, but only 76% knew that there is a bidirectional relationship between the two conditions. Only 2/3 of the participants knew the effect of periodontal treatment on DM.

5.7% of the doctors were interested in the dental history of the patients, 7.1% examined their oral cavity and 12.1% recommended them to go to a regular dental consultation. Among those who recommended their patients to go to the dentist, only 38.6% referred them to the periodontist [46].

Results of specific therapies for periodontal disease and oral mucosal diseases in DM patients. Regarding the therapies used in periodontal disease, the study by Chandra S. et al, 2019 in which diabetic patients with chronic periodontitis were divided into two groups (group A (control): only SRP and group B (test): SRP followed by the application of the dental diode laser) highlighted the improvement of clinical, microbiological and glycemic parameters in both group A and group B. [48].

Favorable results were also obtained in the study conducted by Preshaw P.M. et al, 2020 where periodontal treatment resulted in significant improvements in clinical status and

reductions in crevicular fluid biomarkers from baseline to 12 months. There was a greater reduction in systemic inflammation after periodontal treatment in patients with diabetes and periodontitis compared to those with periodontitis but no DM [51].

Regarding xerostomia, Malickaa B. et al, 2014 observed on the basis of the study that the sensation of dry mouth was diagnosed much more frequently in type 1 diabetics than in patients in the control group [38]. Similar results were obtained and, in the study, conducted by Saes Busato I.M. et al, 2012[32]. On the other hand, Dalodom S. et al, 2016 highlighted the beneficial effects of moisturizing oral jelly in reducing xerostomia symptoms [41].

As for the presence of changes in the oral mucosa in DM patients, in the study conducted by Alves Silva M. F. et al, 2015, the prevalence of oral lesions was 78.4%. Traumatic ulcers and actinic cheilitis were the most common lesions, with the lips and tongue being the most frequent locations [39]. Also, the results of the study conducted by Bastos A.S. et al, 2011 highlighted that there was a higher prevalence of oral mucosal changes in patients with DM, especially regarding potentially malignant lesions and fungal infections [31].

DISCUSSIONS

The progressive increase rate of diabetes among patients is not only due to genetic factors, but also to environmental factors as a result of an unbalanced lifestyle [29]. The results of this systematic review confirm previous evidence supporting the bidirectional relationship between periodontal status and glycemic control of diabetes and reinforce the idea that successful periodontal treatment can improve glucose metabolism [34,48,51]. In this sense, it has been proven that periodontal health can be restored through different types of surgical or non-surgical therapies (SRP), associated or not with antibiotics, the result of which led to the reduction of probing depths and HbA1c values [33 ,34,36].

The interdisciplinary collaboration between the diabetologist and the dentist is essential because it contributes to the general good condition of the patient. It is important for healthcare professionals to have knowledge about the oral complications of DM in order to provide preventive information to patients. Normally, they should have an important role in diagnosing and referring patients to the dentist [44].

In the studies included in this paper, a very small percentage of participants received oral health advice from a health professional [29,30,40]. The sources of information were mostly TV and the Internet. However, in the study conducted by Bowyer V. et al, 2011, only 30.2% of respondents stated that they had discussed diabetes with their dentist.

Diabetic patients do not have sufficient knowledge about the oral complications of DM and, regarding oral hygiene, it has not been categorized as an important personal care task [30]. Patients' knowledge of oral health in relation to diabetes was also associated with time since diagnosis. Thus, those who had DM for several years were more informed than those who had not received the diagnosis for a long time [35,40, 43, 45]. On the other hand, patients with uncontrolled DM were not concerned about their oral health [50].

Participants who had not been diagnosed with periodontal disease in the past had less knowledge about the correlation between periodontal disease and diabetes and how to prevent this oral complication. Also, they did not attend regular check-ups at the dentist [49].

The limitations of the systematic review assumed the fact that most of the studies were carried out only in certain medical units and regarding risk factors such as smoking, alcohol consumption or the administration of certain drugs, many studies did not mention their presence or absence.

CONCLUSIONS

The review concludes that diabetes significantly impacts all body tissues, including those in the oral cavity. Diabetic patients generally have less knowledge about the oral complications of diabetes compared to other systemic complications. To address this, interdisciplinary collaboration between health specialists, dentists, and diabetologists is essential for developing educational programs about these oral complications and their prevention. Maintaining oral hygiene and regular dental consultations are crucial for preventing periodontal disease and diseases of the oral mucosa. Additionally, there is a bidirectional relationship between diabetes mellitus (DM) and periodontal disease, where periodontal treatment can help reduce biomarkers in crevicular fluid and HbA1c values, thereby improving glucose metabolism.

REFERENCES

1.   Chen L., Magliano D.J., Zimmet P.Z. The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nature Reviews Endocrinology. 2012; 8: 228–236.
2.   https://www.idf.org/aboutdiabetes/what-is-diabetes.html
3.   Holt R. I. G., Cockram C., Flyvbjerg A., et al. Textbook of diabetes. 4th Edition. UK: Blackwell Publishing Ltd; 2010. p 25-29.
4.   American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2014; 37(Supplement 1): S81-S90.
5.   Șerban V., Albai A., Albai. O., et.al. Tratat român de boli metabolice(vol.1). Timișoara: Brumar;2010. p.69-71.
6.   American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diabetes Care.2020; 43(Supplement 1): S14-S31.
7.   Goyal R., Jialal I. Diabetes Mellitus Type 2. StatPearls Publishing, Treasure Island (FL).2018.
8.   John W. G. Expert Position Statement Use of HbA1c in the diagnosis of diabetes mellitus in the UK. The implementation of World Health Organization guidance 2011. Diabet. Med. 2012; 29: 1350–1357.
9.   Chris Florkowski. HbA1c as a Diagnostic Test for Diabetes Mellitus – Reviewing the Evidence. Clin Biochem Rev. 2013; 34(2): 75-83
10.   Verhulst M. J. L., Loos B. G., Gerdes V. E. A., et al. Evaluating All Potential Oral Complications of Diabetes Mellitus Front. Endocrinol.2019;
11.   Newman M.G., Carranza F.A, Takei H., et al. Carranza's Clinical Periodontology, 12th Edition. Saunders; 2015. p.50-51; 187; 401.
12.   Yamagishi Sho-ichi. Diabetes and Aging-related Complications. Singapore: Springer Nature; 2018. p. 186.
13.   Bissett S.M., Preshaw P.M., Presseau J., et al. A qualitative study exploring strategies to improve the inter-professional management of diabetes and periodontitis. Primary Care Diabetes. 2020; 14: 126–132.
14.   Yamamoto S.L. Periodontal disease: symptoms,treatment and prevention. New York: Nova Biomedical Books; 2011. p. 227-228.
15.   Craig R.G., Kamer A. R. A clinian's guide to systemic effects of periodontal diseases. Berlin: Springer; 2016. p.27.
16.   Malicka B., Kaczmarek U., Skośkiewicz-Malinowska K. Prevalence of xerostomia and the salivary flow rate in diabetic patients. Adv Clin Exp Med. 2014; 23(2):225–233.
17.   López-Pintor R.M., Casañas E., González-Serrano J., et al. Xerostomia, Hyposalivation, and Salivary Flow in Diabetes Patients. J Diabetes Res. 2016; doi: 10.1155/2016/4372852.
18.   Molania T., Alimohammadi M., Akha O.,et al. The effect of xerostomia and hyposalivation on the quality of life of patients with type II diabetes mellitus. Electronic Physician. 2017; 9(11): 5814-5819. DOI: http://dx.doi.org/10.19082/5814

19. Ambaldhage V. K., Puttabuddi J.H., Nunsavath P.N. Burning mouth syndrome:An update. Indian Journal of Pain. 2015; 29(1): 2-8.
20. Mahmoud A., Moneim W. A., Fakhr M.et al. Prevalence of Burning Mouth Syndrome in A sample of Egyptian Patients with Diabetic Neuropathy: A Cross Sectional Hospital- Based Study. Advanced Dental Journal. 2020; 2(2): 34- 42.
21. Mohammadi F., Javaheri M.R., Nekoeian S.,et al. Identification of Candida species in the oral cavity of diabetic patients. Curr Med Mycol,. 2016; 2(2): 1-7.
22. Rodrigues C.F., Rodrigues M.E., Henriques M. Candida sp. Infections in Patients with Diabetes Mellitus. Journal of Clinical Medicine. 2019; 8(1): 76.
23. Vila T., Sultan A.S., Montelongo-Jauregui D., et al. Oral Candidiasis: A Disease of Opportunity. Journal of Fungi. 2020; 6(1):15.
24. Al-Maskari A.Y., Al-Maskari M.Y., Al-Sudairy S. Oral Manifestations and Complications of Diabetes Mellitus. SQU Med J. 2011; 11(2): 179-186.
25. Mozaffari H.R., Sharifi R, Sadeghi M. Prevalence of Oral Lichen Planus in Diabetes Mellitus: a Meta-Analysis Study. ACTA INFORM MED. 2016; 24(6): 390-393.
26. Otero Rey E.M., Yáñez-Busto A., Henriques I.F.R., et al. Lichen planus and diabetes mellitus: systematic review and meta-analysis. Oral Diseases. 2019;25(5):1253-1264.
27. Mekala M.R., Bangi B.B., Jayalatha N., et al. Association of Diabetes with Oral Cancer- an Enigmatic Correlation. Asian Pac J Cancer Prev. 2020; 21(3): 809–814.
28. Shamseer L., Moher D., Clarke M., et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015; 349. doi: https://doi.org/10.1136/bmj.g7647
29. Eldarrat A.H. Diabetic patients: their knowledge and perception of oral health. Libyan J Med.2011; 6(1). https://doi.org/10.3402/ljm.v6i0.5691
30. Bowyer V., Sutcliffe P., Ireland R. et al. Oral health awareness in adult patients with diabetes: a questionnaire study. British Dental Journal. 2011; 211: E12.
31. Bastos A.S., Leite A.R.P., Spin-Neto R., et al. Diabetes mellitus and oral mucosa alterations:Prevalence and risk factors. Diabetes Res Clin Pract. 2011; 92(1):100-5. doi: 10.1016/j.diabres.2011.01.011.
32. Saes Busato I.M., Ignacio S.A., Brancher J. A. Impact of clinical status and salivary conditions on xerostomia and oral healthrelated quality of life of adolescents with type 1 diabetes mellitus. Community Dent Oral Epidemiol. 2012; 40: 62–69.
33. Mendonça A.C., Santos V.R., Ribeiro F. V., et al. Surgical and non-surgical therapy with systemic antimicrobials for residual pockets in type 2 diabetics with chronic periodontitis: a pilot study. J Clin Periodontol. 2012; 39: 368–376 doi: 10.1111/j.1600- 051X.2012.01860.x
34. Moeintaghavi A., Arab H.R., Bozorgnia Y., et al. Non-surgical periodontal therapy affects metabolic control in diabetics: a randomized controlled clinical trial. Australian Dental Journal. 2012; 57: 31–37. doi: 10.1111/j.1834-7819.2011.01652.x
35. Ahmed I., Nasreen S., Jehangir U., et al. Frequency of oral lichen planus in patients with noninsulin dependent diabetes mellitus. Journal of Pakistan Association of Dermatologists. 2012;22:30-34.
36. Pradeep A. R, Sharma A., Rao N. S., et al. Local Drug Delivery of Alendronate Gel for the Treatment of Patients With Chronic Periodontitis With Diabetes Mellitus: A Double- Masked Controlled Clinical Trial. J Periodontol. 2012; 83(10):1322-8.
37. Ahmed H. S. Trace Elements Levels and Oral Manifestations in Type 2 Diabetic Patients. The Iraqi Postgraduate Medical Journal. 2014; 13(2): 161-164.
38. Malickaa B., Kaczmareka U., Skośkiewicz-Malinowska K. Prevalence of Xerostomia and the Salivary Flow Rate in Diabetic Patients. Adv Clin Exp Med. 2014; 23(2):225–233.
39. Alves Silva M.F., Pereira J. V, Godoy G.P., et al. Prevalence of oral mucosal lesions among patients with diabetes mellitus types 1 and 2. An Bras Dermatol.Jan-Feb 2015;90(1):49-53. doi: 10.1590/abd1806-4841.20153089.
40. Bahammam M.A. Periodontal health and diabetes awareness among Saudi diabetes patients. Patient Prefer Adherence. 2015; 9: 225–233. doi: 10.2147/PPA.S79543.

41. Dalodom S., Lam-Ubol A., Jeanmaneechotechai S. Influence of oral moisturizing jelly as a saliva substitute for the relief of xerostomia in elderly patients with hypertension and diabetes mellitus. Geriatr Nurs. 2016;37(2):101-9.

42. Al Amassi B. Y., Al Dakheel R.S. Oral hygiene practice of adult diabetic patients and their awareness about oral health problems related to diabetes. Journal of Dentistry and Oral Hygiene. 2017; 9(2): 8-14.

43. Elsayed M. H. A., Awooda E.M. Knowledge and Attitude of Diabetic Patients towards the Oral Complications of Diabetes Mellitus and Factors Associated with Their Knowledge in Khartoum State, Sudan. British Journal of Medicine & Medical Research.2017; 21(4): 1- 13.

44. Obulareddy V. T., Nagarakanti S., Chava V.K. Knowledge, attitudes, and practice behaviors of medical specialists for the relationship between diabetes and periodontal disease: A questionnaire survey. J Family Med Prim Care. 2018;7(1):175-178. doi: 10.4103/jfmpc.jfmpc_425_16.

45. Çankaya H., Güneri1 P., Epstein J.B., et al. Awareness of Oral Complications and Oral Hygiene Habits of Subjects with Diagnosed Diabetes Mellitus. Balkan Journal of Dental Medicine. 2018; 22(3):138-145.

46. Sut Yee Tse. Diabetes mellitus and periodontal disease: awareness and practice among doctors working in public general out-patient clinics in Kowloon West Cluster of Hong Kong. BMC Fam Pract. 2018;19(1):199. doi:10.1186/s12875-018-0887-2.

47. Khera S., Saigal A. Assessment and Evaluation of Gustatory Functions in Patients with Diabetes Mellitus Type II: A study.

48. Chandra S., Shashikumar P. Diode Laser - A Novel Therapeutic Approach in the Treatment of Chronic Periodontitis in Type 2 Diabetes Mellitus Patients: A Prospective Randomized Controlled Clinical Trial. J Lasers Med Sci. 2019; 10(1):56-63.

49. Kudoh R., Shibayama T., Hidaka K. The role of knowledge and self-efficacy on dental consultation behavior of patients with type 2 diabetes. Jpn J Nurs Sci. 2020;18(1):e12378. doi: 10.1111/jjns.12378.

50. Kakooei S., Afzali S., Parirokh M., et al. The Knowledge and Attitude of Diabetic Patients Regarding Oral and Dental Disorders in Kerman Diabetes Clinics. J Dent Shiraz Univ Med Sci. 2020; 21(3): 195-201.

51. Preshaw P.M., Taylor J.J., Jaedicke K.M, et al. Treatment of periodontitis reduces systemic inflammation in type 2 diabetes. J Clin Periodontol. 2020 Jun;47(6):737-746. doi: 10.1111/jcpe.13274. 207. doi: 10.4103/ijem.IJEM_555_17 Indian J Endocrinol Metab. 2018 Mar-Apr; 22(2): 204–