The burden of Diabetes, Its Oral Complications and Their Prevention and Management

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Abstract

BACKGROUND: Diabetes mellitus (DM), chronic disease, is a public health problem that affects 8.5% adult population worldwide. The number of adults with DM has risen sharply from 108 million in 1980 to 422 million in 2014. In 2012, 1.5 million individuals died because of DM and an additional 2.2 million deaths occurred because of high blood glucose level resulting in cardiovascular and other systemic diseases. DM brings huge economic loss to patients, their families, and healthcare systems. Globally, the cost of DM was US$1•31 trillion in 2015.

AIM: This review article utilised the prevalence data of diabetes mellitus from the World Health Organization and International Diabetes Federation to provide a comprehensive picture of the disease in different parts of the world.

METHODS: Electronic databases such as Google Scholar, Medline via PubMed, Scopus, and Web of Science were used to search the literature. The library resources of Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia were used to retrieve studies on the topics of the present review.

RESULTS: Systemic complications of DM include heart attack, kidney disease, limb loss, blindness, and peripheral nerve damage. More than 90% of diabetic patients were found to have oral manifestations. It is known that DM severely damages oral tissues causing periodontal disease, tooth loss, xerostomia, caries, burning mouth disorder, taste and salivary gland dysfunction, delayed wound healing, lichen planus, geographic tongue, and candidiasis. The evidence is mounting about a strong bidirectional relationship between DM and periodontal disease. Unfortunately, many diabetic patients are unaware of the association between DM and oral health, and only a small percentage of them visit the dentist for routine dental check-ups. Changes in lifestyles (control of blood glucose levels and self-care practices), regular dental check-ups with emphasis on periodontal assessment, and reinforcement of oral health instructions can effectively prevent oral complications of DM. Scaling and root planning are effective in improving glycemic control among diabetic patients.

CONCLUSION: Dental professionals should be part of the multidisciplinary team that helps individuals with diabetes.

Introduction

Diabetes mellitus (DM) is a heterogeneous group of clinical and genetic metabolic disorders recognised by abnormally high levels of glucose in the blood. It is classified broadly into two types – diabetes mellitus type 1 (DM I) and diabetes mellitus type 2 (DM II). There is an absolute reduction in insulin secretion due to β-cell destruction in DM I. DM II, also known as non-insulin dependent, is the most common form of DM that results from a progressive defect in the secretion of insulin and or resistance to the effects of insulin [1]. Separate global estimates of prevalence for DM I and II do not exist, because sophisticated laboratory tests are usually required to distinguish between both conditions [2]. There were 30.3 million people with DM (about 9.4% of the total population), out of which 23.1 million were diagnosed, and 7.2 million were still undiagnosed in the U.S. [3].

Damage and failure of various organs of the body such as the heart, blood vessels, kidneys, eyes, and nerves are caused by chronic hyperglycemia. Hence, cardiovascular diseases, chronic kidney disease, acquired blindness, and non-traumatic limb loss are complications of DM [4]. Diabetic patients manifest a high prevalence of oral problems such as dental caries, xerostomia, periodontal disease, sensory disorders, taste problems, salivary gland dysfunction, and oral infections [5]. Periodontal disease is one of the most common chronic inflammatory conditions which is characterised by the destruction of connective tissue surrounding the teeth,

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and the condition gradually leads to tooth loss. Furthermore, the periodontal infection can predispose individuals to the complications of DM [5]. Increasingly, younger populations are now suffering from DM due to westernised lifestyles, poor eating habits, and the increased prevalence of obesity [4].

This review article utilised the prevalence data of diabetes mellitus from the World Health Organization and International Diabetes Federation to provide a comprehensive picture of the disease in different parts of the world. Also, the original studies and reports were used to describe the burden of diabetes, its oral manifestations and complications, and prevention and management.

Methods

Electronic databases such as Google Scholar, Medline via PubMed, Scopus, and Web of Science were used to search the literature. The library resources of Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia were used to retrieve studies on the topics of the present review. Various combinations of following keywords were used to search the studies. Keywords included "diabetes mellitus", "oral", "dental", "epidemiology", "prevalence", "incidence", "burden", "costs", "clinical", "manifestations" "signs", "symptoms", "complications", "xerostomia", "Burning mouth syndrome", "periodontal disease", "dental caries", "infections", "lichen planus", "healing" "halitosis", "bad breath" "candidiasis", "salivary", "dysfunction", "malfunction", "prevention", "control", "treatment", and "management". Also, the reference lists of retrieved articles were also searched to find more relevant articles.

For the present review, recent studies were used to synthesise the latest information to update the healthcare professionals on the topic.

Results

Burden of Diabetes

DM is one of the most common metabolic disorders as it affects about 2-5% of the European and 20% of world populations [6]. Globally, the number of diabetic adults has increased to 422 million in 2014 from 108 million since 1980 [2]. The standardised age prevalence of DM was 9.8% for men and 9.2% for women in 2008 which increased from 8.3% and 7.5% respectively in 1980 in the world [7]. A recent study reported that the rate of diabetic death increased by 60.7%, from 12.1 per 100,000 population

in 1990 to 19.5 per 100,000 population in 2013 [8]. By the year 2035, an estimated 592 million people will be diagnosed with DM [9].

Recent data were collected from World Health Organization and International Diabetes Federation (IDF) to provide a comprehensive picture of the prevalence of DM among selected high, middle and low-income countries [10] [11]. It can be seen from Figure 1 that Saudi Arabia has the highest prevalence of DM whereas Australia has the lowest prevalence rate among high-income countries. The average prevalence of DM in these countries is 8.61 (Figure 1).
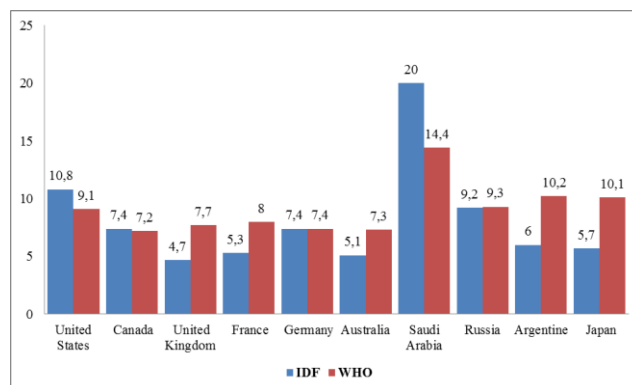

Figure 1: Prevalence of diabetes in high-income countries [10] [11]

Figure 2 shows the highest estimates of DM prevalence of Egyptians followed by Turks and Mexicans. Among the selected middle-income countries, Nigeria has the lowest prevalence of DM.
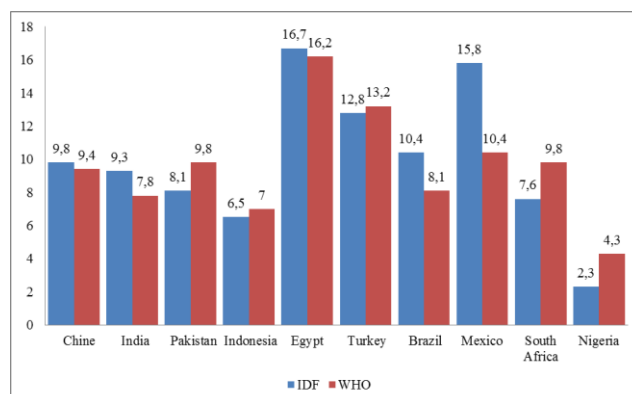
Figure 2: Prevalence of diabetes in middle-income countries [10] [11]

The average prevalence was 9.76 among these middle-income countries. Afghanistan has the highest prevalence of DM, and the average prevalence among these low-income countries was 5.3 (Figure 3).

There is no drastic difference in the average prevalence of DM in high and middle-income countries. However, the average prevalence of DM is considerably lower in low-income countries compared with high and middle-income nations. According to WHO, the Eastern Mediterranean Region has the

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highest prevalence of DM (13.7%) in the world [2]. Based on WHO estimates, the countries with the highest prevalence rates in this region include Egypt (16.2%), Kuwait (14.7%) and Saudi Arabia (14.4%). While according to IDF data, Kuwait (20%), Qatar (20%), Saudi Arabia (20%), Bahrain (19.6%), and United Arab Emirates (19.3%) have highest DM prevalence in the region (Figure 4).
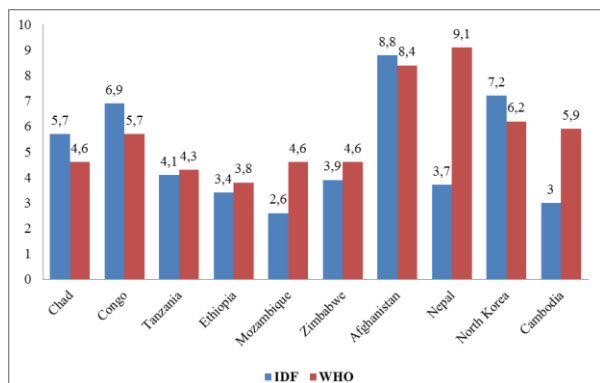

Figure 3: Prevalence of diabetes among low-income countries [10] [11]

DM is considered one of the principal causes of premature illness and deaths in most countries [12]. The patients with DM have increased the risk of cancers of the pancreas, liver, breast, urinary tract and colon [13]. Similarly, smokers are at greater risk (30%-40%) of developing DM than non-smokers [14]. It was also reported that HIV patients had a higher prevalence of DM than the adults from the general population [15]. DM is a major risk factor for coronary artery disease, and 75% of patients with DM die because of cardiovascular disease [16].
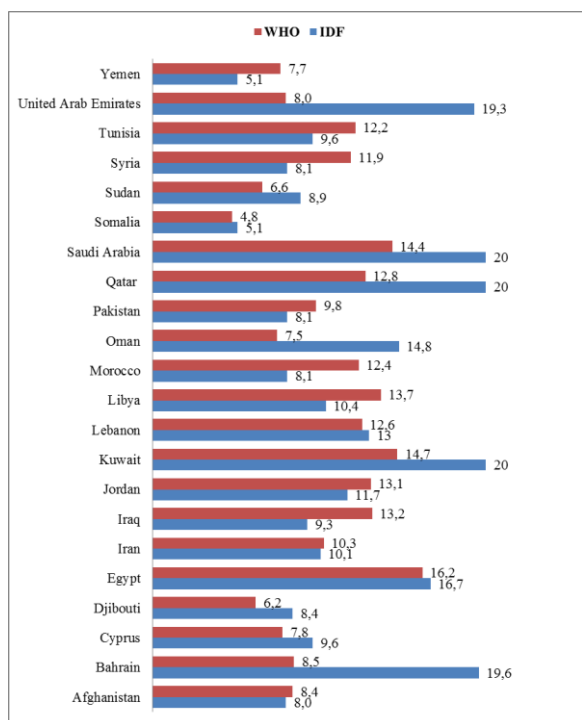

Figure 4: Prevalence of diabetes in the Eastern Mediterranean Region [10]

DM brings huge economic loss to patients, their families, and healthcare systems including loss of productivity and pressure on national economies [2]. In the U.S., an estimated cost of diagnosed DM was US$ 245 billion in 2012 out of which US$ 176 billion was spent for direct cost and US$ 69 billion was attributed to a reduction in productivity. There was an increase of 41% in the cost from the previous estimates of US$ 174 billion in 2007 [17]. Globally, the economic burden of DM was US$ 1·31 trillion in 2015, and indirect cost accounted for 34·7% of the total cost of the disease [18].

Oral manifestations and complications

Numerous oral complications are observed in both types of DM, which include periodontal diseases, oral candidiasis, tooth loss, xerostomia, halitosis, delay wound healing, burning mouth syndrome, salivary and taste dysfunction, tooth decay, lichen planus, geographic tongue, and complications associated with dental implants [19] [20].

DM is a risk factor for periodontal disease that affects its prevalence and incidence, and the degree of periodontal tissue destruction is determined by the level of metabolic control and the duration of DM [21] [22]. The prevalence of periodontitis is high (34%-68%) in diabetic patients, and deep pockets and attachment loss are common in patients with poorly controlled diabetes [21] [23]. The risk of alveolar bone loss is 11 times higher among patients with poorly controlled diabetes compared to healthy individuals [5].

The production of antibodies in response to microorganisms in periodontal tissues, and the presence of natural killer T cells, autoreactive B-cells, heat shock proteins, autoantibodies, and predisposing genetic factors provide the basis for an autoimmune role in the pathogenesis of the periodontal disease [24]. In diabetic patients, autoimmunity occurs in response to some defect in the usual self-control process resulting from chronic infection or tissue breakdown. The autoimmune process can target and destroy insulin-producing cells (β-cell), causing their destruction and impairing the production of insulin and promoting hyperglycemia. β-cell destruction occurs due to the production of autoantibodies by lymphocyte (B cell), and a T-cell mediated autoimmune response [25]. Epidemiologically, the link between periodontal disease and diabetes (DM I) is also attributed to the existence of autoimmune components in both these conditions [26].

There is a bidirectional relationship between periodontal disease and DM, and appropriate periodontal care can produce beneficial effects on metabolic outcomes among DM patients [27]. A meta-analysis of 9 randomised clinical trials found a moderate reduction in Haemoglobin A1c among DM patients after non-surgical periodontal treatment [28].

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Another meta-analysis demonstrated that there was 0.29% reduction in Haemoglobin A1c with periodontal care at 3-4 months [29]. Moreover, a meta-analysis of 9 clinical trials observed that periodontal treatment resulted in the reduction of inflammatory biomarkers such as tumour necrosis factor alpha and C-reactive protein in diabetic patients [22]. However, robust evidence is lacking about the long-term positive effects of periodontal therapy on diabetes and a reduction in the prevalence of its complications [30].

One-quarter of diabetic patients were shown to have oral candidiasis which is one of the early and non-specific signs of uncontrolled DM [23]. Although, Candida is a normal commensal of the oral cavity, however, hyperglycemia, immune dysfunction, and acid production promote candidal infection among people with diabetes [31]. Also, increased salivary glucose levels in diabetic patients can enhance candidal proliferation and increase the possibility of acquiring oral candidiasis [31]. Dental plaque contains predominantly Candida albicans species that give rise to infection in the mouth [32]. It has been shown that diabetic patients have higher candidal colony-forming units in saliva than non-diabetic subjects which are associated with increased salivary glucose [31]. It was found that increased salivary glucose was significantly related to increased serum glucose levels. Therefore, it was suggested that salivary glucose levels could be used to evaluate the diabetic status of the patients and to monitor their glycemic control [33].

Tooth loss is highly prevalent among diabetic patients. A recent cross-sectional study identified that 15.3% of diabetic patients lost all their teeth and only 6.4% retained all natural teeth, and tooth loss was associated with older age and diabetic retinopathy [34]. It was reported that the diabetic patients had 1.46 times higher odds of having one tooth removed compared with individuals without DM [35]. Diabetic patients were found to underutilise dental care services although it is known that regular dental visits are beneficial for them [36]. The increased tooth loss among diabetic patients is related to the severity of periodontal disease that leads to alveolar bone destruction consequently resulting in tooth removal [34] [37]. Smoking and bruxism are significantly associated with tooth loss related to periodontal disease [37].

Xerostomia can affect oral functions and compromise patient's wellbeing, and its aetiology has been linked, among other factors, to the existence of systemic diseases, including DM [38] [39]. A recent study of diabetic patients (65-91 years) found that 92.5% had reduced salivary flow [40]. In a meta-analysis of 32 studies, it reported that the prevalence of xerostomia was 46.09% among diabetic patients and salivary flow rates were lower in DM patients than in non-DM population [38]. Salivary secretions are vital to oral health, as they assist in mechanical cleaning and aid in protective functions through physiological and biochemical mechanisms [40].

Hyposalivation can negatively affect the quality of life of the patient by compromising their eating habits, nutritional state, speech, and tolerance to dental prostheses. It can also enhance the risk of oral infection such as candidiasis, and increase patient's susceptibility to dental caries, periodontal disease, and tooth loss [38] [39]. Because of the complex aetiology of xerostomia, its treatment entails an interdisciplinary approach that should focus on reducing possible complications and improving quality of life [38].

It was found that 52% of patients suffered from halitosis which was the second most common oral complications among people with diabetes and even higher prevalence (76%) was observed among patients with uncontrolled diabetic [41]. On the other hand, a study identified 16% of diabetic patients with halitosis [23]. Diabetic patients with chronic periodontitis were found to have a significantly higher concentration of odoriferous microorganisms in tongue coating and subgingival plaque than non-diabetic patients. These odoriferous microorganisms produce volatile sulfur compounds which are responsible for oral malodor in diabetic patients [42].

Burning mouth syndrome affects 1.3 million Americans. Burning painful sensation in the mouth is often linked with dysgeusia and xerostomia. Classically, its symptoms improve in the morning, worsen during the day, and diminish at night [43]. The condition is characterised by a burning sensation in the tongue or other oral sites. Depression, various nutritional deficiencies, and DM increase the risk of burning mouth syndrome [44]. Though oral mucosal conditions such as candida infections, lichen planus, and dryness can cause burning sensations in diabetic patients, however, a neuropathic basis explains the burning sensations often accompanied by an alteration in taste (dysgeusia) or other sensory distortions. Therefore, the patients with peripheral diabetic neuropathy are susceptible to have burning sensations in the oral tissues [45] [46].

DM disturbs the hemostasis of the oral cavity by altering salivary function and composition even in well-controlled patients [47]. Dysfunction of salivary glands is a common phenomenon in DM [48] [49]. It has been reported that saliva of diabetic patients contains the higher concentration of proteins than controls [50]. Similarly, significantly high glucose and potassium concentrations are found in people with diabetes. Salivary dysfunction alters the taste sensation, and its effect is pronounced especially in poorly controlled diabetic patients [49].

A high prevalence of dental caries is found in diabetic patients compared to non-diabetics. Accumulation of microbial plaque flora causes demineralisation and dental caries. In diabetic patients, decreased flow of saliva reduces cleansing and buffer capacity besides diminishing levels of calcium that promotes tooth decay [51]. The reduction

of saliva also decreases the resistance to caries producing bacteria [52]. Moreover, saliva contains high glucose levels in diabetic patients that increase the amounts of fermentable carbohydrates for oral bacteria. The available current evidence on the association between DM and dental caries are mainly from studies conducted on DM I patients; however, there is a higher prevalence of caries in DM II patients compared with non-diabetic patients [47] [53].

It's a disorder that occurs due to the inflammation of mucous membrane and skin and is characterised by the chronic recurrent rash [49]. It was found that 62%- 85% of lichen planus patients had diabetes and they had an abnormal glucose tolerance test [54]. It was reported that oral lichen planus was found in 5.76% of type I and 2.83% of type II diabetic patients [55]. Similarly, higher prevalence of oral lichen planus was reported in diabetic patients compared to controls [56]. Oral lichen planus has been shown to have an autoimmune mechanism and frequently occurs in DM I which is also an autoimmune disorder [49].

Geographic tongue is an inflammatory disease associated with DM [57]. The lesion, found on the dorsum and margins of the tongue, causes pain, discomfort, and burning sensations, and is more common in male than female subjects. There is atrophy of the filiform papillae that leaves an erythematous area with a white, yellow or faintly grey elevated peripheral zone, and ill-defined spiky pattern of the tongue [58].

DM is associated with poor bone healing, increased risk of bone fracture, osteoporosis and diminished bone regeneration [59]. However, the patients who have controlled DM or are on hypoglycemic medication may not be at risk of increased of delayed wound healing after tooth extraction [60]. Delayed wound healing among diabetic patients is attributed to reduced cellular response including diminished macrophage functions, impaired production of growth factors, decreased angiogenesis and insufficient blood supply [61]. Also, impaired response to injury in DM can occur due to reduced substance P (nerve-derived mediator) [62].
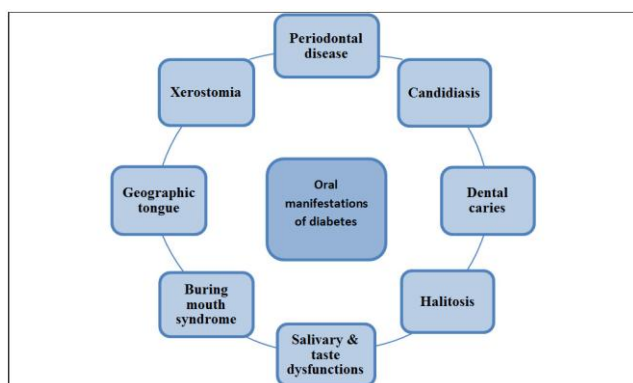

Figure 5: Oral manifestations among diabetic patients [23] [41]

Prevention of oral manifestations

The current body of evidence is not enough to prevent type 1 DM [2]. Oral manifestations of type 2 DM can be prevented through several approaches that are aimed at ensuring proper brushing and flossing behaviours, encouraging patients to visit the dentist for a routine check-up and controlling blood glucose levels [63].

Many DM patients are unaware of the relationship between DM and oral health [64]. There is a lack of awareness about the importance of maintaining oral health among patients with DM [65]. Additionally, the only a small percentage of patients diagnosed with DM visit their dentists for periodontal check-ups [66]. Every diabetic patient is assumed to be at risk for periodontal disease and should be referred for periodontal screening and educated on the importance of oral health and regular dental visits [67]. It was reported that more than 90% of DM patients had oral manifestations due to lack of periodic dental check-ups [68]. It has been suggested that individuals with high educational levels were more concerned about preventing and controlling the disease [69]. Therefore, providing education will raise awareness that will help prevent oral complications of DM.

The involvement of oral health care professionals in strategies to recognise individuals at risk for DM will strengthen preventive and screening efforts required to prevent oral diseases. Better treatment outcomes can be achieved if the dental practitioners are aware of dental implications and risk factors of DM [70] [71]. DM patients should be encouraged to visit the dentist for reinforcement and instruction on oral health information through diabetic and dental care centres. Systemic health is related to oral health particularly in diabetic individuals, which increases the need for dental and medical management of the patient. For improving the general and oral health of diabetic patients, collaborative relationship between patients, physicians, and dentists should be developed.

Dentists should provide advice about the use of fluoride mouthwash to prevent caries and antiplaque mouthwash to prevent periodontal problems. Tooth brushing with fluoride toothpaste twice a day and dental floss once a day should be emphasised to ensure plaque control. The patients with dentures should be advised to remove dentures at night and keep them properly cleaned [63]. Giving oral health education to relatives and friends could be beneficial as well because more than 55% of DM patients could be influenced by them [64]. The Internet can be used to educating DM patients because of its growing use among people [72]. Oral health educational material having accurate and updated information needs to be available to DM patients through different channels of communications. Dental practitioners should

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participate in educational activities at an organisational level to raise awareness about oral health matters with diabetic people. Preventing harmful complications by raising awareness through different campaigns is the responsibility of dental professionals as well as government agencies.

Several programs could be designed to prevent or reduce oral manifestations of DM. The program such as lifestyle Change Plus Dental Care (LCDC) was developed based on the Health Belief Model, Social Cognitive Theory, and Cognitive Behavioral Theory [73]. In the program, lifestyle changes and periodontal care were given particular attention to avoid dental complications. The program significantly improved glycemic control and periodontal health by improving periodontal status parameters such as plaque index, gingival index, pocket depth, clinical attachment loss, and bleeding on probing. LCDC program was effective in increasing awareness and modifying DM patients' attitudes about oral health care [74].

Having increased physical activity, eating healthy food, reducing body weight, and managing blood pressure, cholesterol levels, and emotional issues can prevent complications of DM. Also, high-risk individuals who have impaired glucose tolerance or fasting glucose are susceptible to developing DM; however, standard lifestyle changes, proper diet, regular exercise and use of antidiabetic drugs can help prevent DM in them [75]. It was reported that prediabetic patients were found to have deteriorated periodontal health as demonstrated by worse periodontal parameters, and glycemic control was shown to reduce the severity of these parameters [76]. Thus, an oral assessment should be part of routine measures and dentist should be a part of the multidisciplinary team that helps diabetic patients.

To sum up, the oral manifestations of DM could be reduced by several preventive measures that include blood glucose control, self-care practice about DM, and maintenance of proper oral health. These measures can also minimise health-care spending for diabetic patients.

Early identification, assessment, and management of patients who at risk of developing DM require a dentist's active role in diagnosing the condition in previously undiagnosed individuals. Diabetic patients should visit the dentist regularly, every 3 months [67]. Oral cavity examination and detailed history taking are necessary before undertaking any dental procedure [77]. The dentist should be familiar with the medical management of DM and the recognition of signs and symptoms of the undiagnosed or uncontrolled disease.

The regular self and professional periodontal care can benefit patients with periodontitis and DM [78]. Poor glycaemic control over a prolonged time can lead to impaired healing, and severe periodontal disease, as high levels of postprandial plasma glucose (PPg) and HbA1c are the leading cause of oral complications [79]. Appointments timing should be scheduled in the early morning, to reduce the disturbances in patients' medical regimens [71]. Vasoconstrictors such as adrenaline present in dental local anaesthetic cartridge could deregulate the blood glucose level. Therefore, adrenaline should be reduced in poorly controlled insulin-dependent diabetic patients [80]. The patients on insulin or other antidiabetic medications should take these with drugs as usual before visiting a dentist. These medications along with some snack or meal should be brought to the dental office [63].

It has been reported that diabetic patient's periodontal health status can be improved by scaling and root planning, with or without antibiotics [20]. Scaling and root planning is effective in reducing haemoglobin A1c (a marker of average blood sugar level) by 0.29% (3-4mmol/l) for up to three months [81]. Poorly controlled DM is considered a relative contraindication for implant therapy [27]. However, maintaining the blood glucose level of implant patients can help suppress the progression of periodontal destruction, bone loss and improve osteoblastic function [82] [83]. Dental clinicians should provide 6 months of peri-implant and periodontal maintenance phase which includes the provision of oral health instructions and full mouth scaling and root planning around natural teeth and implant [81].

Conclusion

In conclusion, DM is a public health crisis and health care professionals should play their roles to prevent and control the disease and its oral and other systemic complications. There is a high prevalence of DM, especially in high and middle-income countries. Eastern Mediterranean region has the highest prevalence of DM in the world. In addition to millions of people diagnosed with DM, a considerable proportion of the population is undiagnosed. The condition causes huge economic and financial burden to the healthcare systems in addition to increased morbidity and mortality. Oral complications of DM are numerous and include periodontal disease, hyposalivation, dental caries, halitosis, delayed wound healing, taste and salivary dysfunctions, candidiasis, and burning mouth syndrome.

Increasing awareness and knowledge about the DM, its association with oral health including oral complications among patients can help prevent DM and improve their quality of life. Diabetic patients should be emphasised to take good care of their oral hygiene and control DM by maintaining appropriate glucose levels to prevent oral complications. Health care providers can develop certain programs to help patients control DM and its oral complications. The patients should be encouraged to regularly visit dentists, and they should be part of an

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interdisciplinary team of health providers. Routine periodontal assessment and provision of scaling and root planning are necessary to maintain optimal periodontal health among diabetic patients. Health care providers should update their knowledge about the oral manifestations of DM and work collaboratively to control DM and prevent its complications.

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