REVIEW

Diabetes Mellitus and Its Influence on Oral Health: Review

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Abstract: Diabetes mellitus (DM) is one of the most common diseases all over the world. The effect of this endocrine disease on body systems cannot be ignored, where its oral side effects are well distinguished. As this disease incident is increasing dramatically, it is essential for the health care providers to be fully aware of the disease diagnosis, management and to deal with it in a full confident. This review discusses the disease itself, its complications, methods of diagnosis as well as its management. Furthermore, oral manifestations and dental considerations that should be followed when treating patients with diabetes mellitus have been discussed in this review.

Keywords: dental, diabetes mellitus, oral manifestation

Introduction

Diabetes mellitus (DM) is a group of metabolic multisystem diseases characterized by hyperglycemia as caused by the relative or absolute deficiency of insulin.[1] The high blood sugar causes an osmotic diuresis leading to the typical symptoms of thirst, polyuria, nocturia, weakness, and weight loss.[2] Three main types of diabetes include type 1, type 2, and gestational diabetes. Type 1 is caused by an autoimmune process with a sudden onset and requires insulin therapy.[3] Type 2 can be undiagnosed and unnoticed for years and may not warrant treatment with insulin. Gestational diabetes arises in pregnancy and can lead to serious risks to the infant and the mother and, later in life, it may also increase the risk of developing type 2 DM.[3] Types 1 and 2 DM can have common features including excessive urination (polyuria), excessive thirst (polydipsia), and excessive hunger (polyphagia).[4]

DM is considered the most common cause of hospital admission.[5] Despite DM affecting less than 10% of the general population in some countries, 30% of primary healthcare visits are due to DM.[5]

In 2017, the International Diabetes Federation Atlas reported that 451 million people (age between 18 and 99 years) were living with diabetes and around 49.7% were undiagnosed.[6] It has been stated that there is a chance of increasing the prevalence of DM by 55% in 2023.[6] Type 1 DM is less common than type 2 DM. Still, it is increasing each year in both poor and rich countries. In rich countries, most young, diabetic individuals or children have type 1 DM.[3,6] Due to worldwide economic development, increased urbanization, people living longer, changes in diet, low level of physical activities, unhealthy behaviors, and other changes in lifestyle patterns, the number of people with type 2 DM is increasing rapidly.[3,6] Diabetes is a chronic metabolic disorder that is of significant public health concern.[7–9] This review discusses the disease itself, its complications, methods of diagnosis as well as its management. Furthermore, oral manifestations and dental considerations that should be followed when treating patients with diabetes mellitus have been discussed in this review.

Classification

In 2010 and 2013, Wilson et al and Aguirre et al have classified DM into four main categories. They include Type 1 DM, type 2 DM, gestational DM and other causes. Firstly, a total destruction of B-cell which leads to severe deficiency in insulin secretion is referred to type 1. Secondly, type 2 could be as a result of deficiency in the amount of insulin secreted or the cells are poorly responding to this hormone. Thirdly, pregnant women can be affected by diabetes

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during second and third trimester. Finally, there are varieties of diabetes due to other causes. They represent themselves as monogenic diabetes syndromes and genetic defects, disease of exocrine pancreas and drug, eg, cyclosporine or chemical diabetes.

In addition, according to the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1998 DM was classified based on its aetiology. DM is divided into primary and secondary. Primary DM involves type 1 and type 2. Primary diabetes includes type 1 and type 2 where type 1 can involve type A immune mediated or type B idiopathic DM. Type 2 DM includes insulin resistance and an insulin secretory defect.[10] Secondary diabetes can take place as a result of multiple reasons such as pancreatic disease, hormonal abnormalities, severe illness, or other disorders such as gestational diabetes. Moreover, genetic syndromes, drug therapy, autoimmune endocrinopathies, and insulin resistance can lead to secondary diabetes.[10]

Prevalence and Incidence

According to national diabetes statistics report in 2020, around 10.5% of US population with all ages was diagnosed with DM in 2018. However, adults who are aged 18 years and above showed 13% of US population with DM. Moreover, undiagnosed DM was noticed in 21.4% among adults.[11] Table 1 gives statistics of adults (40 years and above) with diagnosed, undiagnosed DM in US in 2018. Figure 1 shows distribution of people who are affected by DM according to age and race in 2017–2018.

Incidence of DM

Incidence means number of new cases of DM that take place at specific time. According to National Health Interview Survey and 2018 US Census Bureau data, people who are aged 45 years old to 64 years old registered the highest incidence of DM and males were more than females. Regardind the race, White, non hispanic had the lowest incidence by 5.4 compared to Hispanic in which they had the highest incidence 9. Table 2 exhibits the incidence of people who are diagnosed with DM among adults (18 years and above) in 2017–2018 in US population.[11] These data were delivered from the National Health Interview Survey and 2018 US Census Bureau data.

Epidemiology

It has been reported that DM is the most common reason behind hospital admission. It was mentioned that even though DM can affect less than 10% of general population, 30% of people visiting healthcare centers is due to DM.[5] The International Diabetes Federation Atlas in 2013 reported that 382 million people were living with diabetes and around 46% were undiagnosed. The number of people with diabetes varies according to the region.[13] Table 3 shows the number of people with DM in 2013 and the percentage of increase in disease by 2035 according to the region.

Table 1 Total Numbers Were Calculated from 2013–2016 to July 2018 of All US Residents

Category	Diagnosed DM	Undiagnosed DM	Total DM
Total	26.8 million (24.4–29.1%)	7.3 million (6.3–8.4)	34.1 (31.6–36.6)
Age			
- 18–44	3.6 (3.0–4.1)	1.4 (0.8–1.9)	4.9 (4–5.8)
- 45–64	11.7 (10.3–13.1)	3.1 (2.3–3.9)	14.8 (13.4–16.3)
- >65	11.5 (10.1–12.8)	2.9 (2.1–3.6)	14.3 (12.7–15.9)
Gender			
- Male	14.0 (12.4–15.6)	3.9 (2.8–5)	17.9 (16.2–19.6)
- Female	12.8 (11.4–14.1)	3.4 (2.7–4.1)	16.2 (14.8–17.6)
Race			
- White, non-Hispanic	15.4 (13.8–17)	4.1 (3.1–5.2)	19.5 (17.9–21.2)
- Black, non-Hispanic	4.2 (3.8–4.7)	0.9 (0.6–1.3)	5.2 (4.7–5.7)
- Asian, non-Hispanic	1.6 (1.3–2)	0.7 (0.4–1)	2.3 (1.9–2.8)
- Hispanic	4.9 (4.1–5.6)	1.5 (1–1.9)	6.4 (5.4–7.3)

Note: Data from Centers for Disease Control and Prevention.[11]

Age-adjusted
Percentage
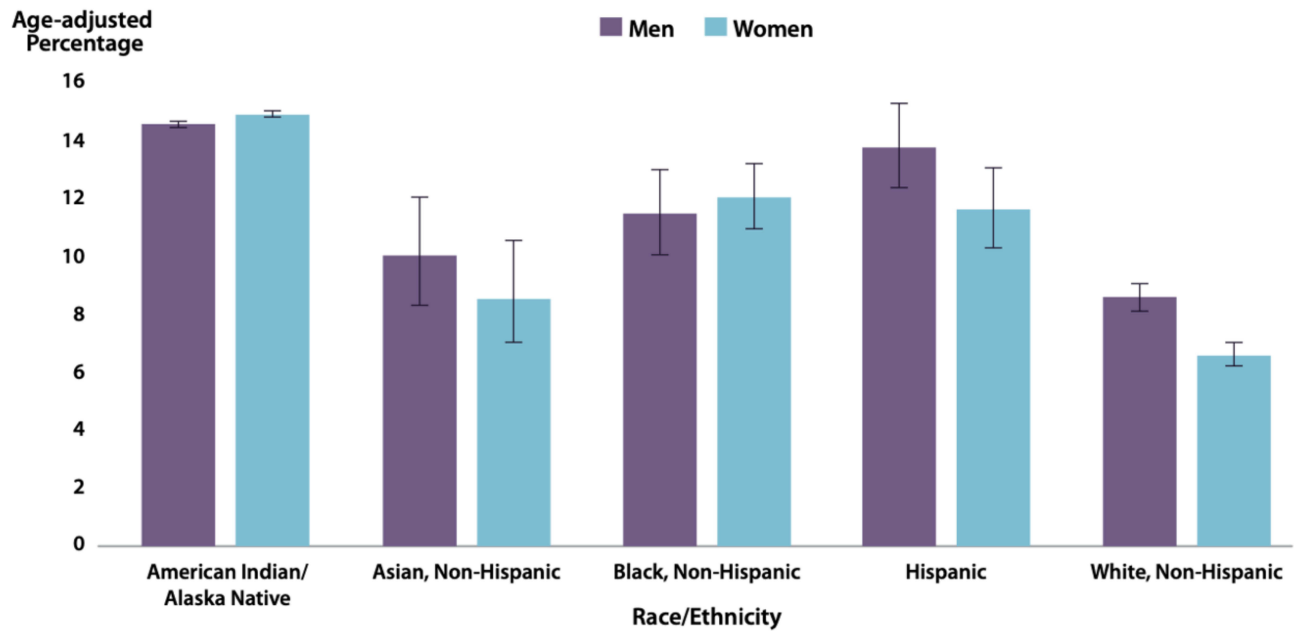
Figure 1 Prevalence of adults 18 years and above who are diagnosed with DM and their distribution according to age and ethnicity in 2017–2018.
Note: Data from Centers for Disease Control and Preventionand Indian Health Service National Data Warehouse (for American Indian and Alaska Native group only).[11]

Type 1

It has been stated that type 1 DM is less than type 2. According to NHS report in 2014, type 1 DM represents around 10% of total number of this disease. Internationally, there is increasing in type 1 DM by 2–5% per year. Scandinavia revealed the highest prevalence of DM, which is approximately 20%. In contrast, the lowest prevalence of DM type 1 is in Japan and China with less than 1% of the total number of people with diabetes type 1.[14]

Type 1 DM is less common than type 2 DM. Still, it is increasing each year in both poor and rich countries. In fact, in rich countries, most of young diabetic individuals or children have type 2 DM.[3] In the UK, type 1 accounts for 10% of the total number of DM (NHS, 2014). According to Imkampe in 2011, internationally the rates of type 1 DM are

Table 2 Distribution of US Population According to Demographic Data

Category	Population Estimates Rate per 1000
Total	6.9 (5.8–8.3)
Age	
- 18–44	4.3 (3.2–5.9)
- 45–64	9.9 (7.6–12.8)
- >65	8.8 (6.5–11.9)
Gender	
- Male	7.3 (5.8–8.3)
- Female	6.6 (5.1–8.4)
Race	
- White, non-Hispanic	5.4 (4.6–6.3)
- Black, non-Hispanic	7.9 (5.9–10.8)
- Asian, non-Hispanic	7.2 (4.8–10.8)
- Hispanic	9 (6.1–13.3)

Note: Data from Centers for Disease Control and Prevention.[11]

Table 3 Shows the Number of People with DM in 2013 and the Percentage of Increase in Disease by 2035 According to the Region

The Region	Number of People with Diabetes in 2013	The Percentage of Increase in Diabetes by 2035
Western pacific	138 million	46%
South east Asia	72 million	70.6%
Europe	56 million	22.4%
North America and Caribbean	37 million	37.3%
Middle east and north Africa	35 million	96.2%
South and central America	24 million	59.8%
Africa	20 million	109.1%

increasing by 2–5% per year. The highest prevalence is in Scandinavia, which is approximately 20% of the total number of people with DM. On the other hand, the lowest prevalence of DM type 1 is in Japan and China, accounting for less than 1% of the total number of people with diabetes type 1.[10]

Males are more affected with DM than females with a ratio 1.5:1. Non-Hispanic whites, Hispanic Americans and African Americans are more commonly affected, respectively. Although DM type 1 is increasing all over the world, the reason is still unknown. It could be due to environmental risks, diet, intra-uterine disturbances or viral infection.[3]

Type 2

Type 2 DM is more common than type 1 DM and it accounts for around 85–95% of patients with DM (NHS, 2014). Age plays an essential role in developing DM type 2. It can be seen in adults who are 40 years and older.[15]

There are several reasons behind this increasing percentage. They include economic development, aging, inactive lifestyle, low physical activities and unhealthy behaviors.[3] Moreover, women who are diagnosed with gestational DM are more commonly affected with DM type 2, individuals with high blood pressure or dyslipidemia. Certain ethnic groups such as African American, Hispanic/Latino, Native American, and Asian American.[16]

With regard to prediabetes, it becomes a major global concern since glycemic levels are increasing in both developed and developing countries. A rise in prediabetes percentage can take place as a result of increase in glycaemia levels. Fasting plasma glucose (FPG) exhibited its highest mean in Oceania (6.1 mmol/L for men and women). Moreover, some other areas showed also high FPG such as South and Central Asia, Latin America, the Caribbean, North Africa, and the Middle East.[17]

According to Centers for Disease Control and Prevention, the statistics of prediabetes among US population from 2017 to 2020 were as the followings; 38% of adults (18 years and above) had prediabetes, and this result was based on their fasting glucose or A1C level. Nineteen percent of people with prediabetes have informed by their healthcare professional that they have this condition. With regard to the gender, fasting glucose or A1C revealed higher percentages among males (41%) than females (32%). Race/ethnicity and education level did not have any significant difference in the prevalence of prediabetes. Likewise, age did not have a considerable influence on the prevalence of prediabetes. Only one-third of US adults had prediabetes during the period 2005–2008 to 2017–2020.[18]

Pathogenesis

Diabetes Mellitus can be a result of two main pathophysiologic processes. A deficiency in insulin secretion is considered the most common one. The second process is that the mechanism of insulin action does not work properly; therefore,

there is increase in insulin secretion as a compensatory mechanism. Genetic defects or environmental reasons or both can lead to insulin resistance.[19]

It is important to have glucose level in the normal range, thus a reverse relationship between insulin secretion and insulin sensitivity. For normal glucose tolerant people, if insulin level drops below the fifth percentile, hyperglycemia will be developed. For individuals who are having a regular insulin sensitivity, DM will be developed if there is a total absence in insulin production (type 1). In contrast, insulin resistance can result in DM even if there is insulin secretion.[19]

It has been observed that a direct relationship between high blood glucose level and physiological and behavioural reactions. Hyper-glycemia triggers the brain to release signals to pancreas and other involved organs to reduce their effect.[19]

Type 1 DM

The pathogenesis of type 1 DM represents itself as destruction of insulin producing cells as a result of autoimmune disease. Macrophages, CD4+ and CDB+ T cells are the main cells that are involved in this mechanism.[20]

The majority of patients who are diagnosed with type 1 DM have circulating anti-insulin antibodies that can be detected even before receiving insulin therapy. The glutamic acid decarboxylase that is located within pancreatic B cells is targeted by islet cell antibodies.[21]

As a result of pancreatic β-cells destruction, insulin production is affected which leads to metabolic derangement. Moreover, pancreatic α-cells have also disturbed and show aberrant behaviour in which excessive secretion of glucagon takes place. Physiologically, there is a reverse relationship between hyperglycemia and glucagon production. However, this process is disturbed in patients with type 1 DM in which glucagon level is elevated with hyperglycemia.[22]

Furthermore, insufficient insulin secretion has a direct effect on metabolism of lipid. This is represented as uncontrolled lipolysis and increased amount of free fatty acids in the plasma, which lead to destruction of glucose metabolism in peripheral tissues such as skeletal muscles.[23]

Insulin deficiency can cause genetic defect and affect the expression of a number of genes that are essential to help body tissues to respond normally to insulin. Glucokinase in liver and the GLUT 4 class of glucose transporters in adipose tissue are examples which give a sign that insufficient insulin secretion in type 1 DM impairs the metabolism of glucose, lipid and protein.[23]

Type 2 DM

There are two main pathological mechanisms in type 2 DM. They include disturbances in insulin production and disturbances in insulin work through tissue resistance.[10] In case of insulin resistance, alteration on insulin producing cells takes place and thus increase its production to compensate for this resistance.[24]

Glucose tolerance discrepancy is the outcome of insulin resistance and hyperinsulinemia.[25] The situation is different in the case of maturity onset diabetes of the young (MODY) in which the mode of inheritance for type 2 diabetes mellitus is still unclear. MODY is known as "hyper-glycemia diagnosed before the age of twenty-five years and treatable for over five years without insulin in cases where islet cell antibodies (ICA) are negative".[26] It has been mentioned that the reason behind it could be a mutation in glucokinase gene on chromosome 7p.[25]

Clinical Features and Complications of Diabetes Mellitus

Clinical features of DM vary according to the type and the associated complications. Hyperglycemia manifests as polydipsia, polyuria, weight loss, blurred vision, headache, fatigue, and occasionally polyphagia.[27] In addition, impaired growth and liability to infections can be associated with high blood sugar.[2,28] Type 1 DM can have sudden onset, and hyperglycemia can progress into ketoacidosis. In essence, long-lasting DM gives rise to an increased risk of atherosclerosis that ultimately affects many key body systems and, in particular, increases the risk of cardiovascular, retinal, and renal disease[3,6]. The complications of DM can provoke damages to multiple organs and systems such as the kidneys, feet, eyes, and heart and can unfortunately lead to early death if not treated[3,6] (Figure 2). The complications of DM can be classified as acute or chronic.[2]
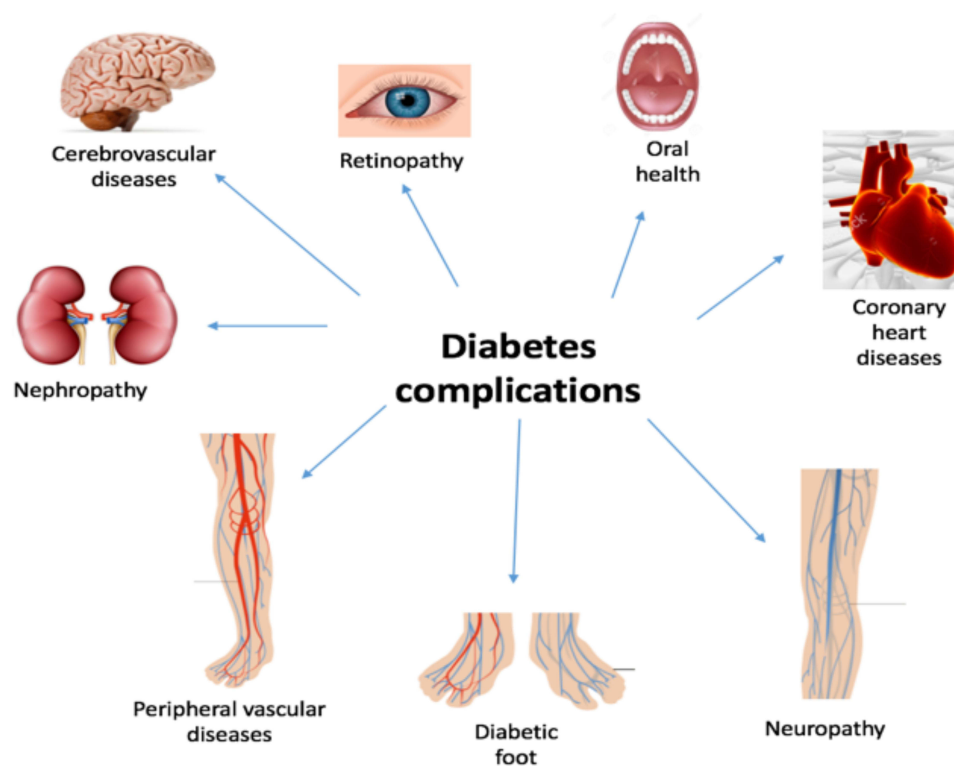
Figure 2 Shows major clinical complications of DM on different organs.

Acute and Chronic Complications

DM can cause hypoglycemic or hyperglycemia comas. Hypoglycemia is more common due to a loss of metabolic control in DM related to excess insulin or hypoglycemic drugs, missed meals, unaccustomed exercise, or alcohol consumption.[29] DM patients who are treated with insulin are more liable to hypoglycemic coma due to an imbalance between insulin therapy and food intake.[4] In hypoglycemia, rapid consciousness is lost and requires rapid treatment to avoid central nervous system (CNS) damage.[4,5,29] Hyperglycemia coma is less common than a hypoglycemic episode and has a slower onset not usually associated with loss of consciousness. This type of coma manifests as dehydration, dry skin, weak pulse, hypotension, and hyperventilation of ketosis breath.[29,30]

Chronic complications of DM are due to microvascular and macrovascular diseases that can affect multiple systems in the body.[4] The microvascular damages can include retinopathy, neuropathy, and nephropathy. Macrovascular complications can include strokes, peripheral vascular disease, and ischemic heart disease.[4]

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is one of the diabetes complications that can lead to death every year. It happens when the plasma glucose level is more than 250 mg per dl or even more. There are several reasons behind this side effect. They represent themselves as decreased insulin levels, reduced glucose use, and increased gluconeo-genesis from elevated counter regulatory hormones, including catecholamines, glucagon, and cortisol.[31] It has an influence mainly on patients who are diagnosed with type 1 DM, however individuals with type 2 diabetes can be affected too. Following a standard protocol can give a reliable result in managing DKA. It has been stated that patients with DKA can reveal polyuria, polydipsia, polyphagia, and weakness. In addition, 50–80% of them represent nausea and vomiting. Cerebral edema is a serious but uncommon feature that might be observed.

The first step in treating such a complication is diagnosis and management of precipitating factors. They include infection, noncompliance with insulin therapy, myocardial infarction, new-onset diabetes and others.[32]

Diagnostic Tools

Plasma glucose is used to diagnose diabetes, either by the fasting plasma glucose (FPG) or the 2-hours plasma glucose (2-PG) value after 75 g of an oral glucose tolerance test (OGTT).[33] The glycosylated hemoglobin (HbA1C) can also be used to monitor the long-term control of blood glucose level at least for 3 months.[33,34] The fructos-amine test is another assay. This gives estimation of a hyperglycemia state over the previous 12–21 days. Table 4 summarizes the different tests used to diagnose diabetes.[35]

Diagnosis Using Hba1c Test

The HbA1C is used to monitor the long-term control of blood glucose level. The haemoglobin is glycosylated in which the glucose binds to the erythrocytes in a stable process. This haemoglobin remains glycosylated for the full lifespan of the erythrocyte (123 days).[23] Therefore, this can give a reflection of the blood glucose level within the last 1–3 months.[27]

There are several advantages of using the HbA1C in measuring the level of glucose in the blood. They involve no fasting is required and does not alter significantly during illness and stress. On the other hand, it is less sensitive, costly compared to estimated plasma glucose and the relation between the average glucose and the HbA1C is poor.

A survey done by the National Health and Nutrition Examination (NHANES) indicated that one-third fewer cases are diagnosed with a HbA1C cut-off point of ≥48 mmol/L than a fasting glucose cut-off point of ≥7.0 mmol/L.[37] Moreover, when the HbA1C is used, features such as age, race, and haemoglobinopathies require to be considered.[35]

Management of Diabetes Mellitus

The aim of DM management is to prevent DM complications.[9,30,38] The optimum control is to keep the glucose levels between 4 and 7 mmol/l (72 −126 mg/dL) before meals and not higher than 10 mmol/l (180 mg/dL) 2 hours after meals.[39] The strategy now toward prevention is to obtain effective management. This management can be achieved by both medications and lifestyle modifications.[27] Obvious lifestyle changes that are encouraged include avoidance of tobacco, sensible alcohol consumption, weight loss, regular exercise, and diet modification.[36] The drugs required for the treatment of DM principally comprise oral hypoglycemic agents and insulin.

Insulin Therapy

A number of different preparations are available for insulin treatment of type 1 DM. Regular basal and bolus dosing plans or continuous pump delivery are commonly employed in a type 1 diabetic patient.[5] The different insulin preparations are according to the duration of action as noted in Table 5.

Table 4 Different Tests and Criteria Used for the Diagnosis of DM[36,38]

Test Used	Definition	Measurement
Fasting blood glucose (FBG)	Measures the blood glucose after not having anything to eat or drink (except water) for at least 8 hours	≥ 7.0 mmol/L (126 mg/dL)
2 h plasma glucose	Measures the blood glucose level after 2 hours of a meal	≥ 11.1 mmol/L (200 mg/dL) during an OGTT
Random (casual) plasma glucose level	Measures the blood glucose level at any time during the day	≥ 11.1 mmol/L (200 mg/dL)
HbA1C (glycated haemoglobin test)	Measures and monitors the blood glucose level over the past 2–3 months	≥ 48 mmol/mol (6.5%)
Fructosamine test (glycated protein)	Measures the average level of blood glucose control over the past 2–3 weeks.	Random plasma glucose ≥ 11.1 mmol/L (200 mg/dL)

Table 5 Types of Insulin and Their Duration of Action

Type of Insulin	Duration of Action
Rapid-acting insulin	4–5 hours
Short-acting insulin	6–8 hours
Intermediate-acting insulin	6–8 hours
Long-acting insulin	14–24 hours

Oral Hypoglycemic Agents

In type 2 DM, oral hypoglycemic agents (OHA) are considered as the first-line treatment. Their mode of action is to either to enhance the action of insulin at target cells or to increase the insulin secretion from the pancreas.[5,40] Table 6 lists the OHA mode of actions.[5]

Oral Manifestations

There are no specific oral manifestations of DM, although affected individuals may be more prone to infections and have more severe periodontal diseases. A broad spectrum of oral symptoms has been reported in the literature.[41,42] DM can give rise to immunological and salivary dysfunction that will increase the risk of common oral diseases such as caries and periodontitis.[42] Table 7 summarizes the oral manifestations of DM.

Salivary Dysfunction

Salivary dysfunction that changes in the quantity or quality of the salivary protection can consequently affect oral health. Xerostomia has been massively reported in the literature due to the impaired function of the gland as a result of the dehydration because of hyperglycemia and peripheral autonomic neuropathy.[9,29,41] Xerostomia is a common complaint of patients with DM, but the exact reason is not completely known.[27] Symptoms of dry mouth may reflect an increased glucose level that leads to a more viscous consistency of saliva.[27] Unrelated to the symptoms of xerostomia, sialosis can arise in which there is enlargement of the glands due to acinar cell enlargement.[43]

In DM, thirst, dehydration, oral sensory dysfunction, altered saliva composition, and reduced salivary flow can cause xerostomia.[42] In literature, studies have showed that as HbA1c values increase, there is a trend toward decreased salivary flow rate.[15] As a consequence of xerostomia, irritation of the oral soft tissue may occur leading to inflammation and pain. In addition, chronic complications of DM such as endothelial dysfunction, microvascular complication, and neuropathy can affect the microcirculation and deteriorate the salivary flow and composition.[44]

Dental Caries

The association between diabetes and dental caries is complex. No specific connection has been identified, and data are conflicted in this issue. There is no evidence that DM does increase the risk of dental caries.[12] Dentists should be aware that salivary dysfunction can reduce the salivary output in conjunction with a high content of glucose in saliva, which can subjectively increase the incidence of caries.[4,27] Research has shown that in the presence of standard oral health

Table 6 Commonly Prescribed Oral Hypoglycemic Agents and Their Mode of Actions

Mode of Action	Agent
Insulin secretagogues	Sulfonylureas (ie, Gliclazide®)
	Meglitinides
Insulin sensitizers	Biguanides (ie, Metformin®)
	Thiazolidinediones
Decreased intestinal absorption and breakdown of carbohydrates	α- Glucosidase inhibitors
Incretin pathway	Dipeptidyl peptidase IV inhibitors

Table 7 Oral Manifestations of DM and Their Etiology and Associated Risks

Manifestation	Etiology	Risks
Salivary dysfunction (xerostomia)	• Polyuria • High salivary glucose	• Caries • Periodontal diseases • Candida infections
Dental caries	• High salivary glucose • Xerostomia	• Cervical and root caries
Oral infections	• Xerostomia • Immune-compromised	• Angular cheilitis • Pseudomembranous candidiasis
Periodontal disease	• High levels of pro-inflammatory mediators • High crevicular glucose	• Poor glycemic control • High risk of periodontal diseases
Wound healing	• High levels of matrix metallo-proteinases	• Delayed wound healing
Neurosensory disorders	• Unclear	• Taste disturbances • Compromised oral hygiene
Trigeminal neuropathy	• Progressive dystrophy in trigeminal nerve	• Pain and discomfort

prevention with a good diabetic control, patients with diabetes are not a higher risk of developing caries in comparison to the general population.[27] Diabetic patients might have more dental caries due to poor oral hygiene or a higher number of meals a day.[12] In addition, type 2 DM children are exposed to a diet higher in carcinogens compared to type 1 DM children. This is due to the association between obesity and type 2 DM. This can increase the prevalence of caries amongst children with type 2 DM. Neuropathy can diminish the salivary flow rate and increase the risk of developing caries because of dry mouth, but this is not consistent in literature.[12] Also, the buffering capacity of saliva in patients with DM is diminished, leading to a higher risk of developing dental caries.[44]

Oral Infections and Other Oral Mucosal Diseases

A number of different oral mucosal disorders can arise in patients with DM, but the frequency of such lesions in DM is low. Oral lichen planus can arise as a consequence of sulfonylurea therapy, while candida infection manifests as pseudomembranous candidiasis or median rhomboid glossitis can occasionally occur.[4] The former may reflect impaired phagocytic function due to a lack of compliance with, or inappropriate insulin therapy.[4,27,44] There have been a number of reports of geographic tongue (erythema migrans) in patients with DM, but the vast majority of individuals with this oral disorder do not have DM.[12]

Periodontal Disease

Gingival and periodontal diseases are more common in patients with DM. It is considered the main oral problem as observed by dental professionals. Based on a literature review of 17 cross-sectional studies that evaluated the relationship between periodontal diseases and diabetes, it was reported that there is increased risk, prevalence, severity, extent, or progression of periodontal diseases. Besides, poor control of DM is associated with severe periodontitis compared to those without diabetes.[45,46] Periodontal diseases are a well-documented and well-recognized complication of DM.[47] This evidence base is supported by epidemiological data and studies on animal models. This also helped explaining the pathophysiology of periodontal diseases in DM.[12,48]

In the presence of periodontal diseases, bacteremia can cause an elevated and chronic systemic inflammatory response. This can be associated with increased serum C-reactive protein, cytokine levels, and interleukin-6.[27] Diabetic and non-diabetic patients with periodontitis have differences in their subgingival microflora that can alter the inflammatory response.[1,27] In addition, reduced collagen metabolism and high levels of local pro-inflammatory mediators can be found in diabetic patients.[27] The higher response of macrophage phenotype and compromised neutrophil function can be found in DM patients with periodontitis in comparison with a healthy individual with periodontitis.[1,27] Also, high levels of glucose in the crevicular fluid can increase the bacterial existence in the periodontal pocket.[1] These two conditions, the inflammatory response and bacterial existence, are reciprocal and are part of periodontitis in DM.[27,46] When DM is poor, there is a greater

risk of acquiring periodontal disease.[5] It was reported that periodontal diseases might lead to poor metabolic control.[12,47–49] In addition, periodontal diseases are the sixth complication type associated with DM after retinopathy, nephropathy, neuropathy, peripheral diseases, and cardiovascular diseases.[5,46] It is well described that poorly controlled diabetes can increase the incidence of gingival inflammation and alveolar bone loss.[1,50] The pathophysiology of this mechanism is similar to the microvascular and macrovascular pathophysiological complications of DM.[15,27] The evidence of the effect of periodontal disease on the glycemic control is poor. However, compared to individuals with healthy periodontal tissues, people with periodontal diseases and type 1 or type 2 DM have a greater risk of DM-related complications.[51]

Impaired Wound Healing

The exact pathogenesis of delayed healing in diabetic patients is poorly understood.[1] Abnormal keratinocyte and fibroblast migration, proliferation, differentiation, and apoptosis can contribute to impaired wound healing. In addition, decreased vascularization, impaired function of endothelial progenitor cells (EPCs) and mesenchymal stem cells (MSCs), and abnormal polarization of macrophages can be part of the complex factors involved in delayed wound healing. Furthermore, it has been reported that patients with DM had a prolonged expression of TNF- $\alpha\alpha$ that cause impaired healing.[52] It is supposed that diabetic patients have altered homeostasis and impaired phagocyte/macrophage function due to high levels of matrix metallo-proteinases that can contribute to delayed wound healing.[27,44]

Taste and Other Neurosensory Disorders

Taste is a complex symptom, and it might be related to changes in diet and salivary flow alterations associated with the disease management.[46] One in three adults with DM can have hypogeusia. Consequently, it can affect 80% and 50% of individuals with uncontrolled and controlled type 2 DM.[53] Taste alteration can affect the salty, sweet, and sour flavors. In the literature, there is no relation between the severity of gustatory impairment and the HbA1c levels.[53] Other neurosurgery disorders reported by diabetic patients are burning mouth syndrome and dysphagia. However, the prevalence of this data is not available.[5,12]

Trigeminal Neuropathy

In literature, DM can affect the function of the trigeminal nerve. In a study of 40 patients with trigeminal neuralgia (TN), 48% had DM. Another study reviewed 30 patients with TN, and 10 out of these patients had an elevated blood glucose level. Therefore, DM can cause TN.[54]

Special Implications for Dentistry
Access

Patients with diabetic foot ulcers and retinopathy as chronic complications of DM can have compromised access. Such as in complications of advanced nephropathy, access can be compromised due to dialysis. In type 2 DM, increased body weight can compromise access.[35] Loss of pain in distal extremities in DM patients can affect the access of the patient. Thus, joint flexibility can impact dental treatment and, if any dental procedure requires prolonged treatment, breaks should be allowed so the patient can move the stiff joint.

Communication

Communication is mainly affected in the case of retinopathy that can lead to blindness. In addition, the association of other comorbidities can affect the function of the brain such as stroke or dementia and compromise communication. Therefore, if there are retinopathy associated complications, communication aids should be considered such as braille or large fonts for documents.[8]

Consent

In situations where a patient with DM is in a coma due to hyperglycemia or loss of consciousness in hypoglycemia, they can have altered capacity. This can affect a patient's capacity and complicate consent. Therefore, the national legal regulations should be considered when obtaining consent.[55]

Education

Good oral hygiene measures should be in place to reduce the risk of oral infections in diabetic patients.[56] The International Diabetes Federation Atlas recommends an annual review of the patients' compliance with daily dental care, the patients' regular checkups with the dental professional, and awareness of the patients' regarding the symptoms of gum diseases such as red, swollen, or bleeding gums.[44] It is also advisable to educate the patients of the implication of diabetes on oral health and gum disease in particular if the diabetes is poorly controlled.[46] If blood glucose levels are poorly controlled, infectious diseases are therefore more common and insulin sensitivity is reduced.[15,44,45]

Dentists can play an important role in the preventive aspects of DM. They can screen and diagnose periodontal disease in diabetic patients and assess the general population who are at risk of developing diabetes.[5,27]

Surgical and Operative Dentistry: Challenges and Solutions

Surgical intervention in patients with DM can include the risk of infection and delayed healing due to impaired immunity. This can be managed by performing any dental procedure as atraumatic as possible by using chlorhexidine mouthwash (0.2%) and ensuring that controlled blood sugar levels are in place pre-operatively.[28] Therefore, liaising with the diabetic team is necessary to ensure all precautions are in place. This can include obtaining the profile of the blood glucose level of the patient and discussing the planned dental procedure with the diabetic team to consider the need for any antibiotics pre- or post-operatively.[5,9]

Hypoglycemia is the major issue and risk that most dentists will confront when treating diabetic patients. This is particularly an issue if diabetic patients are asked to fast before any procedure such as general anesthesia or receiving insulin therapy.[28] In addition, long dental procedures that may disturb regular food regimes or any procedures that require sedation or systematic anesthesia are associated with high-risk of hypoglycemia. All dental staff should be well trained to manage such an emergency.[57] A full awareness of the signs and symptoms of hypoglycemia such as unusual behavior should raise suspicion in staff, and proper management should be implemented before becoming unconscious.[5] Every practice should have a detailed and effective emergency management protocols, and all members of staff should be confident enough to treat any suspected emergency.[57]

Hyperglycemia or ketoacidosis is considered rare compared to hypoglycemia. It is sensible that if blood glucose levels are high enough that dental treatment should be postponed until reasonable blood glucose levels are achieved.[5,38]

Blood glucose levels should be monitored before any procedure.[5] Blood glucose levels should be as close as possible to normal. The blood glucose targets for non-diabetic, type 1 DM, type 2 DM, and pregnant women with diabetes are summarized in Table 8.

A multidisciplinary care pathway is essential to allow a professional and effective management with no associated risks that can alter the safety of treatment provided. Dental care providers should always have a clear appreciation of a patient's diabetic status, seek additional advice when necessary (eg, liaise with the patient's general medical practitioner), and modify clinical care procedures when necessary.[5,27,39] Postoperative instructions should necessitate the importance of well-controlled blood glucose levels during the healing period to allow infection free and healthy wound healing.

Delivering dental treatment under local anesthesia and conscious sedation can be safe and effective as long as the previous precautions are considered. The main challenge is providing dental treatment under general anesthesia as the patient should fast at least six hours and therefore increase the risk of hypoglycemia. Dental appointment length and time should not interfere with treatment and the control regime of diabetes. Consideration should be reflected to have a stress-free appointment to reduce the incidence of diabetic emergencies. Early morning or early afternoon appointments not interfering with the routine of food and drugs should be considered to reduce the risk of a hypoglycemia emergency.[27]

Table 8 Targeted Blood Glucose levels[36,58]

Type of DM	Targeted Blood Glucose Levels
Non-diabetic	3.5–5.5 mmol/l before meals Less than 8 mmol/l, two hours after meals.
Type 1 DM	On waking: 5–7 mmol/l
	Before meals at other times of the day: 4–7 mmol/l
	90 minutes after meals: 5–9mmol/l.
Type 2 DM	Before meals: 4–7 mmol/l
	Two hours after meals: less than 8.5 mmol/l.
Pregnant with DM	Fasting: below 5.3 mmol/l
	And
	1 hour after meals: below 7.8 mmol/l or
	2 hours after meals: below 6.4 mmol/l

Abbreviations: DM, diabetes mellitus; FPG, fasting plasma glucose; 2-PG, 2-hours plasma glucose; OGTT, oral glucose tolerance test; HbA1C, glycosylated hemoglobin; OHA, oral hypoglycemic agents; EPCs, endothelial progenitor cells; MSCs, mesenchymal stem cells; TN, trigeminal neuralgia.

Spread

Patients with DM are not at any increased risk of acquisition or carriage of bloodborne viruses (eg, HIV, HCV, or HBV), mycobacteria (eg, mycobacterium tuberculosis), or prion disease. Normal methods of infection control should be employed for the dental management of patients with DM.[28]

Conclusion

DM is a disease that all members of the dental team should be aware of. It can affect oral health in several ways, and there is a bidirectional relation between glycemic control and oral health status.[27] The long-term maintenance of the oral health of patients with DM may ensure better glycemic control as well as delay the painful symptoms that may require clinical invasive care.[5,59] As long as dental healthcare providers are aware of the key aspects of how DM may affect oral health and dentistry and take the necessary appropriate actions, it is unlikely that oral health care will increase the morbidity of patients. Central to the care of patients with DM, and indeed individuals with good health, it must be the prevention of commonly acquired oral diseases (eg, caries and periodontitis) that may cause pain, interfere in oral function, lessen quality of life, and require perhaps avoidable invasive dental procedures.[1]

Dental care providers should always give attention to diabetic patients, seek additional advice if required (eg, liaise with the patient's general medical practitioner) and modify clinical care procedures when necessary.[27,38]

As long as dental healthcare providers are aware of the key aspects of how DM may affect oral health and take the necessary appropriate actions – it is unlikely that oral health care will increase the morbidity of patients. Central to the care of patients with DM, and indeed individuals with good health, it must be the prevention of commonly acquired oral diseases (eg, caries and periodontitis) that may cause pain, interfere in oral function, lessen quality of life, and require perhaps avoidable invasive dental procedures.

Ethical Approval

There is no ethical issue.

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