ORIGINAL RESEARCH PAPER

Volume-8 | Issue-4 | April-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

UNDERLINING ROLE OF ORAL PHYSICIAN IN DIABETIC CAPITAL OF WORLD

Dental Science

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ABSTRACT

Diabetes mellitus is reaching potentially epidemic proportions in India. The level of morbidity and mortality due to diabetes and its potential complications are enormous, and pose significant healthcare burdens on both families and society. Worryingly, diabetes is now being shown to be associated with a spectrum of complications and to be occurring at a relatively younger age within the country. This article explores the associations between oral health and diabetes in the hope of providing the oral physician with the knowledge to support the diabetic patient with the best possible dental care and advice. It is necessary to be aware of the various oral manifestations of diabetes in order to make an early diagnosis and to provide best oral health care to the affected population.

KEYWORDS

diabetes mellitus, taste, candidiasis, oral physician

INTRODUCTION

Diabetes mellitus (DM) is a clinically and genetically heterogeneous metabolic disease characterized by abnormally elevated blood glucose levels (hyperglycemia) and dysregulation of carbohydrate, protein, and lipid metabolism.[1] Diabetes mellitus is the most common endocrine disorder, characterized by an inability of the body's cells to utilize glucose. The cardinal feature of this condition the presence of chronic hyperglycemia accompanied by greater or lesser impairment in the metabolism of carbohydrates, lipids and proteins. DM is probably one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago. In 1936, the distinction between type 1 and type 2 DM was clearly made. Type 2 DM was first described as a component of metabolic syndrome in 1988. [2]

The origin and etiology of DM can vary greatly but always include defects in either insulin secretion or response or in both at some point in the course of disease. Mostly patients with diabetes mellitus have either type 1 diabetes (which is immune-mediated or idiopathic) Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. [1,2]

Type 2 DM results from interaction between genetic, environmental and behavioral risk factors. Diabetes also can be related to the gestational hormonal environment, genetic defects, other infections, and certain drugs.[1]

Sustained hyperglycemia has been shown to affect almost all tissues in the body and is associated with significant complications of multiple organ systems, including the eyes, nerves, kidneys, and blood vessels. These complications are responsible for the high degree of morbidity and mortality seen in the diabetic population.

EPIDEMIOLOGY

The application of epidemiology to the study of DM has provided valuable information on several aspects of this disease such as its natural history, prevalence, incidence, morbidity and mortality in diverse populations around the world. Identification of the cause of the disease and the possible preventive measures that could be instituted to arrest or delay the onset of this disease which has reached epidemic proportions in both the developed and the developing nations.[7]

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India. India currently faces an uncertain future in relation to the potential burden that diabetes may impose upon the country.[8]

CLASSIFICATION

The American Diabetes Association suggests the use of the terms Type 1 and 2 when classifying diabetes and further suggests the dropping of the terms 'insulindependent diabetes mellitus' and 'non insulin-dependent\ diabetes mellitus' and their acronyms IDDM and NIDDM as these terms may cause confusion and lead to the classification of patients based on treatment rather than aetiology.[9]

I. **Type 1** (destruction of pancreatic b-cells, usually leading to absolute insulin deficiency)
a) Autoimmune
b) Idiopathic

II. **Type 2** (ranging from predominantly insulin secretory defect, to predominantly insulin resistance with varying degrees of insulin secretory defect)
III. Due to other specific mechanisms or diseases
A. Those in which specific mutations have been identified as a cause of genetic susceptibility
a) Genetic abnormalities of pancreatic b-cell function
b) Genetic abnormalities of insulin action
B. Those associated with other diseases or conditions
c) Diseases of exocrine pancreas
d) Endocrine diseases
e) Liver disease
f) Drug- or chemical-induced
g) Infections
h) Rare forms of immune-mediated diabetes
i) Various genetic syndromes often associated with diabetes
IV. Gestational diabetes mellitus

Table1: Etiological classification of diabetes mellitus and glucose metabolism disorders [10]

DIAGNOSTIC CRITERIA

Table 2: Criteria of fasting plasma glucose levels and 75 g oral glucose tolerance test 2-h value [1]

	Normal	Impaired Fasting Glucose	Diabetes Mellitus
Fasting Glucose *	<110 mg/dl	110-126 mg/dl	> 126 mg/dl
2h postprandial plasma glucose	<140 mg/dl	140-200 mg/dl	> 200 mg/dl
OGTT‡ (not recommended for routine clinical use)			Plasma glucose at 2 h > 200 mg/dl

*These criteria should be confirmed by repeat testing on a different day.
†Fasting = no caloric intake for at least 8 hours.
‡OGTT = oral glucose tolerance test performed using an oral load of 75 g anhydrous glucose dissolved in water.

PATHOGENESIS

Type 1 diabetes mellitus

Type 1 Diabetes is characterized by autoimmune destruction of insulin producing cells in the pancreas by CD4+ and CD8+ T cells and macrophages infiltrating the islets.[11] The autoimmune destruction of pancreatic β-cells, leads to a deficiency of insulin secretion which results in the metabolic derangements associated with it. In addition to the loss of insulin secretion, the function of pancreatic α-cells is also abnormal and there is excessive secretion of glucagons in Type 1 DM patients. Normally, hyperglycemia leads to reduced glucagons secretion, however, in patients with Type 1 DM, glucagons secretion is not suppressed by hyperglycemia. The resultant inappropriately elevated glucagons levels exacerbate the metabolic defects due to insulin deficiency.[12]

Although insulin deficiency is the primary defect in Type 1 DM, there is also a defect in the administration of insulin. Deficiency in insulin leads to uncontrolled lipolysis and elevated levels of free fatty acids in the plasma, which suppresses glucose metabolism in peripheral tissues such as skeletal muscle. [12] This impairs glucose utilization and insulin deficiency also decreases the expression of a number of genes necessary for target tissues to respond normally to insulin such as glucokinase in liver and the GLUT 4 class of glucose transporters in adipose tissue explained that the major metabolic derangements, which result from insulin deficiency in Type 1DM are impaired glucose, lipid and protein metabolism.[3]

Type 2 diabetes mellitus

In type 2 diabetes these mechanisms break down, with consequence that the two main pathological defects in type 2 diabetes are impaired insulin secretion through a dysfunction of the pancreatic β-cell, and impaired insulin action through insulin resistance.[13]

Impaired Insulin Secretion: In situations where resistance to insulin predominates, the mass of β-cells undergoes a transformation capable of increasing the insulin supply and compensating for the excessive and anomalous demand. In absolute terms, the plasma insulin concentration (both fasting and meal stimulated) usually is increased, although "relative" to the severity of insulin resistance, the plasma insulin concentration is insufficient to maintain normal glucose homeostasis.[3]

Insulin resistance: The primary events are believed to be an initial deficit in insulin secretion and in many patients relative insulin deficiency in association with peripheral insulin resistance. Resistance to the action of insulin will result in impaired insulin mediated glucose uptake in the periphery (by muscle and fat), incomplete suppression of hepatic glucose output and impaired triglyceride uptake by fat.[4]

COMPLICATIONS OF DIABETES MELLITUS

1. Acute complications

a. Hypoglycemia
b. Hyperglycemic crises
c. Diabetes Ketoacidosis (DKA)
d. Hyperglycemic hyperosmolar state (HHS)

2. Chronic complications:

a. Micro vascular complications
i. Diabetic retinopathy
ii. Diabetic nephropathy
iii. Diabetic neuropathy
b. Macrovascular disease

3. Other complications and associated conditions

a. Impaired growth and development
b. Associated autoimmune conditions
I. Hypothyroidism
ii. Hyperthyroidism
iii. Celiac disease
iv. Vitiligo
v. Primary adrenal insufficiency (Addison's disease)
c. Lipodystrophy (lipoatrophy and lipohypertrophy)
d. Necrobiosis lipoidica diabeticorum
e. Non-alcoholic fatty liver disease
f. Infections seen in patients with diabetes
g. Limited joint mobility
h. Edema

PATHOPHYSIOLOGY OF ORAL MANIFESTATIONS

Two mechanisms involved are involved in the pathogenesis of diabetic complications. Firstly, the polyol pathway converts glucose into the enzyme sorbitol byaldose reductase that causes tissue damage and numerous other diabetic complications. Secondly, the formation of advanced glycosylation end products (AGE), whose formation is due to binding of glucose to proteins, lipids and nucleic acids, results in the alteration of structures and functions, in addition to its deposition in specific organs that causes various complications. Atheroma deposits are formed in cells, which accumulate in the basal membrane and lumen causing decreased cellular defense capacity and impaired polymorphonuclear leukocyte response. This makes diabetic patients more susceptible to infection processes especially when these are caused by anaerobic bacteria due to the reduction of oxygen diffusion through the capillary wall. [15]

Figure 1 summarizes the most significant aspects of the pathophysiological relationship between diabetes and dental disease; the figure is based on a diagram proposed by Kudiyirickal MG et al. [16]

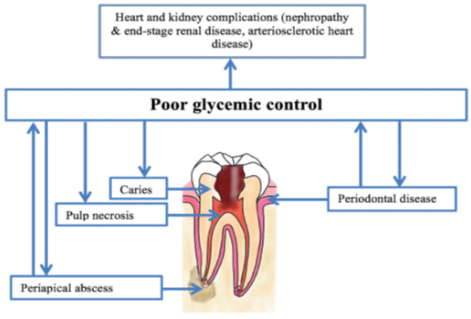

Figure 1: Pathophysiological relationship between diabetes and dental disease. Kudiyirickal adaptation of Kudiyirickal & Pappachan

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.

Periodontal diseases

Periodontitis is a chronic progressive disease affecting the gingivae and the periodontal tissues initiated by bacteria. Periodontal disease has been reported with increased incidence and prevalence in patients with Type 1 & Type 2 diabetes.[17]

The literature for Type 1 diabetes is less clear than for Type 2. Susceptibility to and severity of, periodontitis in the diabetic patient increases with the duration of diabetes. Diabetics with poor metabolic control have a higher prevalence of, and more severe, periodontal destruction and individuals with longer duration diabetes have a greater degree of periodontal destruction.[18]

The main mechanisms by which diabetes and periodontitis are related are via alterations in host responses and collagen metabolism. The primary factor responsible for the development of diabetic complications is prolonged tissue exposure to hyperglycaemia, which results in the production of advanced glycation end products (AGEs). This leads to an increase in collagen cross-linking and the generation of reactive oxygen intermediates, such as free radicals. The modified collagen fibres accumulate in the tissues, resulting in thickening of the basement membrane. This impairs oxygen diffusion, waste elimination, leukocyte migration and the diffusion of immune factors and may thereby contribute to the pathogenesis of periodontitis.[19]

There may be an increase in the local production of cytokines that enhance the inflammatory response, leading to connective tissue damage, bone resorption and delayed wound repair. Significantly higher cytokine levels have been found in the gingival crevicular fluid of diabetics when compared with non-diabetics, with both groups demonstrating periodontitis.[19]

Increased plasma glucose levels are also reflected in elevated gingival crevicular fluid (GCF) glucose levels in individuals with diabetes.

High GCF glucose levels directly hinder the wound-healing capacity of the fibroblasts in periodontium by inhibiting the attachment and spreading of these cells that is crucial for wound-healing and normal tissue turnover. The function of immune cells, including neutrophils, monocytes, and macrophages, is altered in diabetes. Neutrophil adherence, chemotaxis, and phagocytosis are often impaired, which may inhibit bacterial killing in the periodontal pocket and significantly increase periodontal destruction.[20]

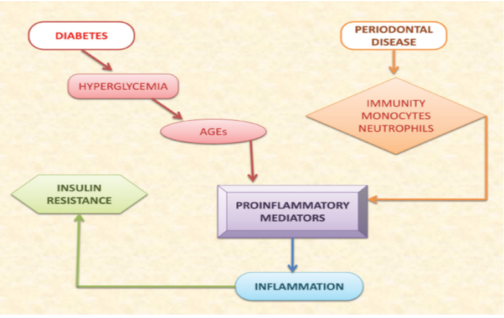

FIGURE 2. A schematic presentation of the two-way relationship between diabetes and periodontitis.

Salivary dysfunction

People with diabetes usually complain of xerostomia, i.e. dry mouth and experience salivary gland dysfunction. This may be resulting due to either excessive loss of water via urination or from alterations in basement membranes of salivary glands, or from medications. Furthermore, urea and glucose levels in saliva were significantly higher in diabetics than healthy subjects. In addition, increased salivary glucose promotes the proliferation and colonization of various microbes in oral cavity. [21]

Dental caries

It could be said that dental caries occurs as a sequelae to other oral manifestations in diabetics. Patients having complaints of xerostomia are more susceptible to caries because of reduced salivary flow. Patients with periodontal problems also are more prone to develop caries. Other factors responsible are increased levels of streptococcus mutans and poor metabolic control of diabetes.

Diabetes and Periapical Pathology

The scientific literature shows a higher prevalence of periapical lesions in patients with poorly controlled diabetes. A recent clinical study showed that patients with Type 2 DM presented a significant association with an increased incidence of periapical lesions and endodontic treatments. Regarding the success rate of endodontic treatment, an article published in 2011 states that patients with DM had a lower success rate in primary root canal treatment in comparison with non-diabetic patients, while both groups presented the same success rate in secondary root canal treatment. Another study found that patients with diabetes are at increased risk of the need for tooth extraction following endodontic treatment. This risk increases in patients with hypertension as well as DM and /or coronary artery disease.[22,23]

The dental pulp of diabetic patients may have limited dental collateral circulation, impaired immune response, and an increased risk of infection or pulp necrosis. Regarding molecular pathology, hyperglycemia is a stimulus for bone resorption, inhibition of osteoblast differentiation, and a reduced capacity for bone recovery.[23] It has been observed that the removal of periodontal inflammation can reduce the dose of insulin required for the patient's glycemic control. For this reason, it is essential to remove all dental pulp infections. The special characteristics of periapical lesions in patients with diabetes provide evidence that the treatment objectives and definition of success should be different for these patients. A recent review concluded that current knowledge about the microbiology of endodontic infections and inflammatory reactions is limited, and that such knowledge could help implement new forms of treatment for these patients. Further research is needed to better understand the issue and so increase the success rates of endodontic treatment among these patients.[22]

Taste disturbances

Taste is an essential component of oral health. It is adversely affected in patients with diabetes. According to a report, more than one-third of all adults suffering from diabetes had hypogeusia, i.e. diminished taste perception. Because of this, patients tend to eat more, leading to obesity. This symptom, known as hyperphagia, would prevent the patient from maintaining a proper diet and this would subsequently result in poor glycemic regulation.[21]

Neuro-Sensory Oral Disorder

Oral dysesthesia or burning mouth syndrome (BMS) is a painful condition affecting the oral cavity. Tingling, numbness, dryness or sore mouth may also be seen. Diabetic neuropathy could be the underlying cause of BMS in patients with diabetes.[17]

Oral Infections

Oral candidiasis is an opportunistic infection frequently caused by Candida albicans species. Candidal infection is more prevalent in patients with diabetes especially in those who smoke, wear dentures, have poor glycaemic control and use steroids and broad spectrum antibiotics. Salivary dysfunction in diabetics can also contribute to higher risk of oral candidal infection.[21]

Oral bacterial infections are more likely to develop in patients with diabetes. Diabetics with diabetic complications and poor metabolic control are more prone to spreading and recurrent bacterial infection. Several studies have reported that patients with diabetes are more prone to deep neck bacterial infections. [21]

Poor Oral Wound Healing

Poor soft tissue regeneration and delayed osseous healing in patients with diabetes are known complications during oral surgery. Therefore, the management of patients with diabetes undergoing oral surgical procedures is more difficult.[17]

Non-Candidal Oral Soft Tissue Lesions

Fissured tongue, irritation fibroma and traumatic ulcer have been reported in patients with diabetes. Altered or delayed wound healing may play a role in traumatic ulcer. [21]

Oral Mucosal Diseases

Lichen planus and recurrent apthous stomatitis have been reported to

Table 3: The pathophysiology, treatment and prevention aspects of orofacial diseases related to diabetes

Oral pathology related to DM	Pathogenesis	Treatment and Prevention
Periodontal disease	Accumulation of AGEs in periodontal tissues, decreased periodontal regenerative capacity and defective immune regulation	Assessment of risk of disease progression, periodic reviews, dietary advice and periodontal therapy
Dry mouth	Reduced salivary flow as a result of polyuria and dehydration	Proper control diabetes and dental hygiene
Root Caries	As a result of gingival resorption and decreased salivary flow	Use of fluoridated pastes, restorative treatments. The optimal glycemic control prevents progression
Oral Candidiasis	Because salivary dysfunction, hyperglycemia and impaired immune system	Antifungal nystatin or miconazole treatment. Good glycemic control and prevention
Pulp necrosis and periodontal abscess	Ischemic tissue damage related pulp own vascular damage from diabetes	Endodontic treatment and control of diabetes
Delayed wound healing and increased incidence of infections following surgery	Caused by vascular dysfunction and decreased immune on diabetes	Preventive administration of antibiotics and good glycemic control

occur in diabetics. Oral lichen planus is reported to occur more frequently in patients with type 1 diabetes compared to type 2 diabetes.[17]

PREVENTION OF ORAL MANIFESTATIONS

It was reported that more than 90% of DM patients had oral manifestations due to lack of periodic dental check-ups. 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.[24,25]

Many DM patients are unaware of the relationship between DM and oral health [64]. Only a small percentage of patients diagnosed with DM visit their dentists for periodontal check-ups. 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. It has been suggested that individuals with high educational levels were more concerned about preventing and controlling the disease. Therefore, providing education will raise awareness that will help prevent oral complications of DM.[24]

Oral cavity examination and detailed history taking are necessary before undertaking any dental procedure. 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. 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. The Internet can be used to educating DM patients because of its growing use among people. Oral health educational material having accurate and updated information needs to be available to DM patients through different channels of communications. Dental practitioners should 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. [25]

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 . 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.[24,25]

The dentist should be familiar with the medical management of DM and the recognition of signs and symptoms of the undiagnosed or uncontrolled disease.

Future Challenges

Given that the prevalence of diabetes is high at the population level, it imposes a financial burden on both our healthcare system and the individuals living with the disease. An attempt continues to be discussed; yet as the number of undiagnosed patients continues to grow, the prevalence and impact of the disease on patient quality of life and the overall cost of diabetes to healthcare is also important.

Full understanding and awareness of the pathophysiology, manifestations, and management of different types of diabetes-related orofacial infection by the endocrinologist and the dentist are essential to optimizing the care of diabetic patients.

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