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Review Article

Mouth is the Mirror of the Human Body- Diabetes mellitus & the oral cavity

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Abstract

Diabetes mellitus represents a syndrome of deranged carbohydrate, fat and protein metabolism that leads to acute and chronic complications owing to absolute or relative lack of insulin. An array of oral manifestations have been reported in the diabetic population. Oral physicians can play a pivotal role in diagnosing the undiagnosed cases of this most common and debilitating endocrine disease on the basis of the oral signs and symptoms. This article attempts to review the myriad orodental effects of this systemic disorder to facilitate the recognition of the afflicted and to necessitate appropriate referral of the untreated cases thereby reducing the mortality and morbidity associated with this condition.

Introduction

Diabetes mellitus represents the most common endocrine disorder affecting approximately 2% of the population although about 50% of the cases remain undiagnosed^{1, 2}. Diabetes mellitus adversely affects almost all organs and tissues of the body including the oral cavity. Of greater concern is the ability of oral infections to profoundly affect metabolic control of the diabetic state³. Knowledge of the wide spectrum of the oral markers of diabetes mellitus is imperative for the oral health care providers as they frequently encounter individuals with undetected, untreated or poorly controlled disease who present more often with oral manifestations that may indicate the underlying undiagnosed disease⁴. In addition, untoward complications could be avoided during or after the dental therapy by employing appropriate precautionary measures to balance the underlying metabolic deficiency.

Review

Malamed S F among others, defines diabetes mellitus as a syndrome of disordered glucose metabolism and inappropriate hyperglycemia resulting from an absolute deficiency in insulin secretion, a reduction in the biological effectiveness of insulin, or

both⁵. Diabetes mellitus has been traditionally classified as type 1 (previously, insulin-dependent diabetes) and type 2 (previously, noninsulin-dependent diabetes)^{1,3,6}. Increased blood glucose levels that do not fulfill the definition for type-1 or type-2 diabetes mellitus are categorized as impaired glucose tolerance or impaired fasting glucose⁶. Abrupt onset of symptoms, reduced serum insulin, dependence on exogenous insulin and likelihood of ketosis characterize type-1 diabetes mellitus⁷. On the contrary, patients with type-2 diabetes mellitus present with minimal to no symptoms resulting from the metabolic imbalances⁷. These individuals are not susceptible to ketosis unless perpetuated by stress, infection or trauma⁷. Classically type-1 diabetes mellitus has been attributed to absolute deficiency of insulin while type-2 diabetes mellitus has often been associated with insulin resistance related to an obese state^{1,3,7}. The archetypal signs and symptoms of diabetes mellitus include the classic triad of frequent urination (polyuria), increased thirst (polydipsia), and increased hunger (polyphagia)⁴. In addition to this pruritis of the skin, vagina or rectum, weight loss, weakness, fatigue, irritability, restlessness, apathy, peripheral neuropathy, blurred vision, opportunistic infections, mental confusion, acetone/‘fruity’ breath, delayed wound healing, numbness of extremities and a spectrum of oral manifestations may become apparent in the diabetic patient^{4,8}.

According to the American Diabetes Association, a fasting blood glucose level of 126 mg/dL or more is diagnostic for diabetes⁸. Individuals with diabetes have a significantly greater risk of mortality than those unaffected⁸. They are vulnerable to numerous long-term microvascular and macrovascular complications that can affect almost every part of the body¹. These may include retinopathy leading to blindness, neuropathy, nephropathy leading to renal failure, ischaemic heart disease, peripheral vascular disease and hypertension^{1,7}. It has been estimated that diabetics have a 25-fold increased risk of blindness, 17-fold higher risk of renal disease and five times greater susceptibility to gangrene than their non-diabetic counterparts⁷.

The oral attributes of diabetes have been reported as early as 1862 and have been extensively reviewed and researched upon since then⁴. Oral manifestations are frequently apparent in undiagnosed, poorly controlled diabetes mellitus. They are thought to manifest more severely and rapidly in uncontrolled type-1 diabetics compared to uncontrolled type-2 diabetics⁴. The oral findings in the diabetic patients result from the microvascular changes, decreased resistance to infection, dehydration and excess glucose concentrations in saliva.

The oral manifestations of diabetes mellitus may be broadly categorized into two types: those affecting the hard tissues and those afflicting the soft tissues of the oral cavity. The hard tissue manifestations include variations in tooth development and prevalence of dental caries, unexplained odontalgia, and periodontal manifestations. The soft tissue attributes include an increased prevalence oral mucosal lesions, infections, burning mouth syndrome, taste disorders and oral changes resulting from salivary gland abnormalities.

Tooth development

An accelerated tooth development in diabetic children up to age 10.5 years has been reported^{1,7}. Following this initial acceleration, steady retardation of dental development with advancing age is eminent^{1,7}. Such a dual influence on tooth development has been credited to stimulation of the pituitary gland in the initial stage of diabetes that gradually becomes ‘exhausted’ over time in type-1 diabetics⁷.

Dental caries

There has been considerable research regarding the prevalence of dental caries in diabetic patients⁹. An increased, a decreased and a similar occurrence of dental caries have all been documented in diabetics in comparison to their non-diabetic peers⁹. According to several studies increased glucose levels in saliva and gingival crevicular fluids, altered plaque microflora, reduced salivary flow, greater number of *Streptococcus mutans* and lactobacilli as well as poor metabolic control of diabetes predispose this group of the population to dental caries^{4,7,8,9,10,11}. It has also been suggested that salivary yeasts incline the geriatric diabetic population to dental decay⁹. Current evidence however is suggestive of decreased caries incidence in the well-controlled diabetic than in age-matched healthy controls due to dietary restrictions especially an elimination of dietary sucrose, adequate metabolic control, observance of meticulous oral hygiene procedures and regular dental follow-up appointments^{4,7,10}.

The higher frequency of untimely extractions owing to pulpal and subsequent periapical involvement from deep caries or advanced loss of periodontal bone in diabetic children has been attributed to a greater edentulous interval between the premature loss of a deciduous tooth and eruption of the permanent successor⁷.

Gingivitis and periodontitis

Diabetes mellitus has been associated with advanced periodontal disease since 1892⁷. Several pathophysiologic changes have been proposed as plausible explanations for such an association. These mechanisms are very similar to those responsible for the long-term sequelae of diabetes¹². This has led to the proposal that periodontitis be listed amongst the 'classic' complications of diabetes¹². Halitosis can be apparent in diabetic patients owing to periodontal diseases. In addition, acetone breath odor may be perceived in cases of diabetic ketoacidosis¹.

Distinct gingival hyperplasia may represent the first sign of disease onset⁴. Enlarged velvety-red gingivae that bleed readily, a typical bluish-purple hue of the gingivae, proliferation of tissue at the gingival margin, putrescent exudates from periodontal pockets, multiple lateral periodontal abscesses as well as advanced loss of supporting alveolar bone leading to mobility of teeth in areas where this cannot be attributed to local factors and the patient's age are considered the characteristic signs of gingivitis and periodontitis in diabetic patients^{2,7}. Numerous contributing factors are responsible for increased susceptibility of diabetics to periodontal diseases. Compromised polymorphonuclear leukocyte function resulting from impaired neutrophil adherence, chemotaxis and phagocytosis prevent destruction of bacteria in the periodontal pocket and markedly enhance periodontal destruction¹². Abnormalities of collagen metabolism, impaired proliferation of osteoblasts and weakened mechanical properties of newly formed bone have been documented in hyperglycemic patients^{8,10,12}. Formation of advanced glycation end products (AGE) is relatively common in sustained diabetes^{10,12}. AGEs enhance collagen cross-linking making them resistant to normal enzyme degradation and facilitate its accumulation in the walls of larger blood vessels resulting in atherosclerotic changes¹². AGE-modified arterial collagen immobilizes circulating low-density lipoprotein leading to atheroma formation³. Production of AGE also leads to greater basement membrane thickness of the microvasculature hampering normal homeostatic transport across

the membrane and result in higher production of vascular endothelial growth factor, either which add to microvascular complications of diabetes¹². Binding of AGE to macrophage and monocytes receptors (RAGE: Receptor for AGE), results in increased production of interleukin-1 and tumor necrosis factor- α that enhances vulnerability to tissue destruction^{10,12}. High levels of glucose in the gingival crevicular fluid diminish wound-healing capacity of fibroblasts in the periodontium by hindering their attachment and spreading¹². Studies have also implicated that tobacco-use and smoking enhance the risk of periodontal disease manifold in diabetics^{8,10}.

Interestingly, accumulating evidence suggests that periodontal infections and periodontal treatment possess the potential to affect glycemic control^{8, 10,13}. The probable mechanisms for such an association are presently under investigation⁸. It has been proposed that chronic gram-negative periodontal infections lead to greater insulin resistance and poor glycemic control¹². It has also been hypothesized that periodontitis-induced bacteremia causes rise in serum proinflammatory cytokines resulting in hyperlipidemia that eventually leads to an insulin-resistance syndrome contributing to destruction of pancreatic beta cells⁸. An improvement in glycemic control following complete extraction of all periodontally compromised teeth in patients with type 2 diabetes mellitus has been recently reported¹⁴.

Salivary gland abnormalities

Asymptomatic bilateral parotid gland enlargement in diabetics had been reported in the early 1900's⁷. Seifert termed such non-neoplastic and non-inflammatory type of glandular enlargement as 'sialadenosis'⁷. The exact cause for such enlargement of the glands has not been determined^{7,10}. A compensatory hyperplasia resulting from reduced insulin level and xerostomia has been hypothesized as a probable cause⁷. A hyperglycemic state leads to inhibition of UDPG-pyrophosphorylase enzyme that produces components of salivary mucoproteins⁷. Accumulation of the substrate of this enzyme has also been linked to parotid acinar hypertrophy⁷. It has been reported that with control of the diabetic state one half of the cases show slight reduction in glandular size⁷.

Dryness of the mouth or xerostomia is frequently reported by diabetics^{4,7,8}. Poorly-controlled disease has been associated with lower stimulated parotid flow rate¹⁰. This phenomenon appears to be related to parotid gland basement membrane variations¹⁵. Polyuria, polydypsia and the resulting dehydration may significantly contribute to oral dryness⁸. Further, consumption of drugs used in the management of diabetes and its complications may also induce oral dryness^{3,4}. Salivary gland hypofunction in older adults has also been attributed to undesirable hormonal, microvascular, and neuronal changes in poorly-controlled diabetes¹⁶. Xerostomia causes increased accumulation of food debris and plaque providing significant etiologic factors for periodontitis and dental caries⁴. Dry and desiccated oral mucosa predisposes diabetics to opportunistic infections such as candidiasis⁴. Xerostomia may lead to impaired taste perception and stomatopyrosis (burning mouth and tongue)^{4,8}. However, some authors report the occurrence of sialorrhoea (increased salivation) in diabetics subsequent to diabetic neuropathy¹¹.

Increased concentrations of calcium in stimulated parotid and submandibular saliva of type-1 diabetics has been reported⁷. This contributes to increased plaque and calculus formation thus enhancing periodontal problems in the affected⁷.

Oral mucosal diseases

Clinical observation of diabetics indicates their likelihood for the development of some mucosal disorders^{17,18}. A higher prevalence of oral lichen planus especially the erosive type, oral fungal infections and recurrent aphthous stomatitis has been reported^{4,8,10}. Although these findings have not been consistently reported in various studies, a majority attribute them to a state of chronic immunosuppression^{8,17}. It has also been postulated that immunologic defects resulting from endocrine dysfunction in the diabetic population may lead to the development of lichen planus¹⁷.

Diabetes mellitus has been linked to oral lichen planus and hypertension, a triad referred to as the Grinspan's syndrome¹⁷. Presently the reported associations between oral lichen planus and systemic diseases remain controversial¹⁷. A 10% - 85% prevalence of diabetes mellitus in patients with oral lichen planus has been documented in the past¹⁷. According to a recent study however, no association between oral precancerous lesions such as lichen planus and diabetes mellitus has been found¹⁸.

Lichenoid reactions may be encountered in diabetics resulting from the use of non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, chlorpropamide and other oral hypoglycemic or antihypertensive medications, which resolve once the drug is withdrawn^{1,10,17,19}.

Albrecht M et al have reported an increased prevalence of oral leukoplakia in diabetics (6.2%) as compared to non-diabetic controls (2.2%) and a prevalence of 1% for oral lichen planus in 1600 patients with diabetes mellitus¹⁹. Both these conditions exhibited highest incidence in the second year of the disease and were interestingly higher among the insulin-treated diabetics¹⁹.

Oral colonization with candida species is often documented as being higher in the diabetic patient when compared to their healthy counterparts^{20,21}. Oral manifestations of candidiasis such as median rhomboid glossitis (central papillary atrophy), angular cheilitis, diffuse atrophy of tongue papillae, as well as denture stomatitis occur more frequently in type-1 diabetics and may result in a severe burning sensation of the mouth^{18,22}. An enhanced adhesion of candida to oral epithelium is eminent in patients with diabetes^{20,22}. Factors that favor increased candidal pseudohyphae carriage in diabetics include neutrophil dysfunction, altered host resistance due to smoking, denture-wear, hyperglycemia, increased salivary glucose levels, impaired antifungal immunoglobulins in the saliva, salivary hypofunction and use of immunosuppressant medications^{20,22}. According to a study, diabetic retinopathy was found to occur in association with median rhomboid glossitis and denture stomatitis, thereby reflecting the underlying poor glycemic control²².

Mucormycosis (phycomycosis), a potentially fatal infection caused by saprophytic fungus occurs in individuals with poorly controlled diabetes³. The most frequent oral sign of mucormycosis is ulceration of the palate caused by necrosis resulting from invasion of a palatal vessel³. The lesion is typically large and deep causing exposure of the underlying bone³. The affected individuals present with lethargy, fever, headache, nasal discharge, facial cellulitis and anesthesia¹⁰.

Fissured tongue, inclusive of a generalized plication in addition to a double fissure running longitudinally along the tongue dorsum has been more frequently documented in type-1 diabetics especially in association with dry mouth²³. This probably occurs due to alterations in the oral environment, a genetically determined developmental variation or may represent a feature of aging²³.

According to one study, a greater prevalence of oral traumatic ulcers and irritation fibromas has been reported in type-1 diabetics^{10,23}. Excessive consumption of alcohol, smoking, denture wear, neuropathy and slower wound healing time has been implicated as the possible risk factors for the same²³.

Taste disorders

Diminished taste sensation/hypogeusia is more common in individuals with poorly controlled diabetes¹⁰. This has been attributed to sensory dysfunction, xerostomia and disordered glucose receptors^{4,10}. Taste disturbances lead to hyperphagia and obesity that eventually hamper adequate glycemic control⁸.

Burning mouth syndrome (BMS)

Burning mouth syndrome refers to a dysesthesia characteristically described by the patient as a burning sensation of the oral mucosa in the absence of clinically apparent mucosal alterations²⁴. BMS in the diabetic has been attributed to peripheral neuropathies associated with diabetes²⁵. BMS appears to be slightly more common in type-1 diabetic population particularly in women with peripheral neuropathy¹¹.

Oral infections and delayed wound healing

An increased risk of infection and impaired wound healing is eminent in the hyperglycemic patient owing to compromised neutrophil adherence, chemotaxis, phagocytosis, bactericidal activity and cell-mediated immunity^{6,11}. This results in an increased incidence of dry sockets (alveolar osteitis) and osteomyelitis, frequently after mandibular extractions due to a decreased vascular supply to the mandible as a consequence of atherosclerosis in the diabetic⁸.

Ueta E et al found statistically significant elevation of C-reactive protein levels in odontogenic bacterial infections in the diabetics²⁶. Suppression of neutrophil superoxide production by C-reactive protein derived degradation products may be ascribed to an increased severity of inflammatory changes and odontogenic infections in the diabetic patients²⁶. Fascial space involvement resulting from severe dentoalveolar abscesses in apparently healthy individuals may be indicative of diabetes¹. Recurrent periodontal abscesses are characteristic of diabetes¹¹. As described earlier, an increased prevalence of opportunistic infections such as candidiasis and mucormycosis may be eminent in poorly-controlled diabetes.

Miscellaneous manifestations

Diabetics may experience persistent distressing oral dysesthesias which can adversely affect adequate oral hygiene maintenance^{8,26}. Diabetic retinopathy can produce visual disturbances and peripheral neuropathies that hamper appropriate use of oral hygiene devices compromise maintenance of daily oral and prosthesis hygiene^{8,26}. Altered strength, speed and/or coordination of the cranial nerve musculature and decreased muscle tone of tongue may lead to dysphagia in the affected individual^{8,26}. Inexplicable dental pulpitis, Bell's palsy, temporary lingual and labial paraesthesias following removal of mandibular molar teeth may arise as a consequence of diabetic neuropathy^{1,26}. When severe, diabetic pulpitis may lead to

necrosis of the dental pulp^{27,28}. Extensive gangrenous or necrotic lesions may develop spontaneously in the uncontrolled diabetic, or follow oral surgical procedures in such patients^{3,24}. According to older literature, the filiform papillae of the tongue are hypertrophic in controlled diabetics while they are atrophic in non-controlled diabetics^{27,28}. Glossitis, macroglossia and crenated tongue borders, benign migratory glossitis (geographic tongue), xanthomatous nodules as well as hyperemia of the fungiform papillae have also been reported in literature^{27, 28}.

Conclusion

The oral signs and symptoms of diabetes mellitus empower an oral physician with the ability to predict the systemic status of the patients examined thus enabling identification of the underlying undiagnosed disease. In addition, oral physicians may play a dynamic role in improving the overall quality of life of diabetic patients as insulin resistance and glycemic control may be affected by the oral diseases and their management. It is absolutely vital for oral physicians to be acquainted with the oral manifestations of diabetes mellitus owing to the strong association between the oral and systemic status of the diabetic patient. It has thus been rightly stated:

"Mouth is the mirror of the human body"

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

COMPETING INTERESTS

The author(s) declare that they have no competing interests'.

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