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Review

Diabetes mellitus and oral manifestations – An overview

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Abstract

The global pandemic of diabetes mellitus is leaving a huge proportion of the population debilitated. The hyperglycemic state along with the inflammatory and immune-mediated changes result in long-term complications of diabetes. The quality of life of affected individuals is drastically reduced if metabolic control is not achieved. The rate of progression of oral diseases is faster in a diabetic individual and this, in turn, can adversely affect the metabolic control of the disease. This review elaborates the oral manifestations of diabetes mellitus and mandates the need to educate non-dental health care professionals involved in diabetic care about the complications.

Keywords: diabetes mellitus, caries, periodontitis, mucosa, dental pulp.

Introduction

Diabetes mellitus (DM) is a metabolic syndrome either due to defective secretion of insulin or due to insulin resistance or both. The global prevalence of DM was 463 million in 2019 and is expected to be around 700 million by 2045 [1]. With the alarmingly increased incidence of this disease which is a public health concern, the morbidities and mortalities associated also are at the spike. The sequel of DM includes both micro- and macrovascular complications like neuropathy, nephropathy, retinopathy, coronary artery diseases, stroke, and peripheral vascular diseases along with various oral complications [2]. Many oral diseases like periodontitis, caries, neurosensory changes, impaired salivary gland function, altered taste, oral mucosal lesions, and infections coexist with DM. The severity of the oral signs depends on the extent of metabolic control and duration of disease [3].

The detection of oral diseases in diabetic patients can help in the early identification of DM and achieving better glycemic control as the disease advances. Oral care should be integrated into the diabetic treatment regimen and dentists should work in close collaboration with the physicians. Awareness should be created in diabetic patients about their increased risk for oral diseases and motivate them to have control of oral diseases through self-care and professional monitoring. This review elaborates the various oral complications of DM and pathways involved in the same.

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Periodontal diseases

Periodontitis is a chronic inflammatory disease and is the sixth major complication of diabetes. Various cross-sectional and longitudinal studies have confirmed that the risk of developing periodontitis is 3–4 times more in diabetic individuals than in non-diabetic subjects. There has been an increased prevalence of gingival and periodontal diseases associated with both type 1 and 2 diabetes. Studies have found a difference in the composition of subgingival plaque in diabetics and non-diabetics with a higher composition of Prevotella intermedia and Porphyromonas gingivalis in diabetic periodontal patients. An increased glucose content and a decreased cAMP in the crevicular fluid may contribute towards this [4]. Patients with severe periodontitis and uncontrolled diabetes have a higher risk for cardiorenal mortality [5]. It was seen that the odds ratio for developing periodontal destruction in individuals with mild, moderate and severe diabetes is 1.97, 2.10, and 2.42, respectively compared to non-diabetics [6].

Both periodontitis and diabetes are characterized by an increased level of systemic markers of inflammation. The hyperglycemic state accelerates the pathways of inflammation, apoptosis, and oxidative stress. In type1 diabetics with gingivitis or periodontitis, there is an elevated level of Prostaglandin E2 (PGE2) and interleukin 1 beta (IL -1 beta) [5]. Type 2 diabetic patients with HbA_{1c} >8% had higher levels of IL1B compared to patients with HbA_{1c} <8% [7]. This dysregulated synthesis of host-derived mediators of inflammation is greater in periodontitis patients with diabetes than controls.

An altered neutrophil response marked by decreased chemotaxis, phagocytosis, and microbial functions is a feature of DM. The decreased polymorphonuclear apoptosis results in increased retention of neutrophils in the periodontal pocket and an increased release of matrix metalloproteinases and reactive oxygen species. Diabetes enhances the alveolar bone loss that would otherwise take place in a periodontitis patient. The bacterial and host cell interactions in a periodontal patient release the local inflammatory mediators. This response is heightened in a diabetic patient with the elaboration of tumour necrosis factor, IL-1beta and IL-6. There is a release of advanced glycation end products, reactive oxygen species, and chemical mediators of inflammation resulting in enhanced PDL and osteoblast apoptosis and osteoclast genesis culminating in accelerated alveolar bone resorption [8].

The bidirectional relationship between periodontal diseases and diabetes mellitus is well-known. Professional mechanical tooth cleaning accompanied by chemical methods followed by a proper oral care regimen can prevent periodontal diseases. Patient compliance is much needed for maintaining the health of periodontal tissues. It is the duty of the clinician to ensure that patients follow a thorough oral care regimen. This can be achieved by educating the patients about the formation of plaque and demonstrating plaque control mechanisms, assisting and assessing the patient oral hygiene performance and reinforcing these at each visit. When periodontitis patients are delivered oral hygiene instructions followed by supragingival plaque removal, it resulted in an improved glycemic control indicated by the HbA_{1c} levels as well as fasting blood sugar levels. There is also a significant decrease in the level of inflammatory cytokines/ biomarkers indicated by the levels of C reactive protein, lactoferrin, and aspartate transaminase. A significant association is found between twice-daily tooth brushing and glycemic control among diabetic adults [9].

Dental caries

Dental caries results when the balance between demineralization and remineralization of dental hard tissues is affected. In diabetic patients, there is an increase in glucose content in both blood, saliva, and gingival crevicular fluid. The increase in oral glucose content favors the growth *Streptococcus mutans*. The salivary flow, pH, mineral content is altered in this condition which predisposes an individual for dental caries. Most of the studies showing the effect of diabetes on dental caries are cross-sectional. A five-year longitudinal study showed that patients with good metabolic control have a significantly

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lower rate of caries progression than patients with poorly controlled diabetes [10].

The normal resting saliva flow rate is 0.3–0.5 ml/min. Hyposalivation in diabetics is characterized by a flow rate of 0.1–0.01 ml/min salivary secretion is under the control of the autonomic nervous system. A decreased salivary flow can be due to diabetic neuropathy. While the pH of resting saliva in normal individuals is between 5.5 and 7.9, in diabetic individuals, it is found to be lower. The decrease in pH can be attributed to the microbial activity or a decrease in bicarbonate content [11]. An increased level of total salivary proteins has been noted in diabetics in some studies. It can be due to the periodontal proteins or due to increased microbial activity. An increased basement membrane permeability is noted in diabetics which can cause increased passage of protein from exocrine glands to the secretions. The serum originating proteins which are elevated in saliva are albumin, hemoglobin, alpha 2 macroglobulin, serum amyloid A, serotransferrin, hemopexin, haptoglobin, and complement C3. The elevated salivary gland originating proteins are amylase, carbonic anhydrase 6, cystatin, prolactin inducible protein, and uteroglobin. An elevated level of GAPDH, a mucosal originating protein and increased levels of IgG was found [12]. The amount of salivary calcium is decreased in diabetics, which favors demineralization of the hard structures and less remineralization.

Oral mucosal lesions

Studies exploring the association between oral mucosal lesions and diabetes mellitus are controversial and not conclusive. Candida infection is the most common oral mucosal lesion identified. Denture stomatitis is the most common form of candidiasis in DM patients. The mucosa under the maxillary dentures will be reddened as a result of contact hypersensitivity to Candida which infects the porous acrylic dentures. Angular cheilitis characterized by fissures or redness of corners of the mouth at the junction of oral mucosa and skin is also a form of candidiasis [13]. Hyperglycemia favors the growth of candida, causing increased retention to the oral epithelium. Denture wearers are at increased risk of candidiasis. Low pH, hyposalivation, and oral habits make the condition more complex.

The prevalence of lichen planus in DM patients ranged from 1.6% to 85% [14]. Oral lichen planus prevalence was more in type 1 diabetes than type 2 diabetes. It can be substantiated on the grounds that both diseases have an autoimmune mechanism [15]. Lingual varicosity, erythematous candidiasis, cheilitis, traumatic ulcer, gingivitis, gingival hyperplasia, fissured tongue, atrophy of lingual papilla, hyperkeratosis, migratory glossitis, coated tongue, potentially malignant lesions like oral lichen planus, actinic cheilitis, and mucor mycosis was seen in various studies on diabetic patients [16].

The dorsum of the tongue in a healthy individual is smooth and light pinkish with an even distribution of fungiform and filiform papillae. With the changes in salivary flow, the oral environment changes, and the slow healing tissues of the tongue are traumatized resulting in fissures along the length of the tongue. Diabetic patients can have a complete or patchy loss of papillae resulting in a “bald” tongue. Median rhomboid glossitis is common in diabetics which can be flat and smooth or elevated or depressed and is often associated with candida pseudo hyphae[13]. The tongue coating is the collection of exfoliated mucosal cells, debris, and microorganisms on the surface of the tongue. The thickness of tongue fur is increased in diabetics and the yellow tongue coating is linked to pre-diabetes [17]. Among diabetics, a significant association is present between the thickness of the tongue coating and the extent of diabetic control. Poorly controlled diabetics were found to have a thicker coating [18]. Taste disturbances are reported in patients with diabetes. It can be due to microangiopathy of taste buds or neuropathy involving nerve tracts [19]. DM is associated with an impaired sweet taste perception which is concentration-dependent as the sensory cells get adapted to the elevated glucose concentrations [20].

The use of oral hypoglycemics has resulted in lichenoid reactions in the oral mucosa of a few patients. An increased prevalence of geographic tongue which is an inflammatory

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condition is seen which can be due to a slower repair and delayed healing mechanisms caused by hypoxia and microangiopathy of oral vasculature. The lesion is characterized by regions of atrophy of papilla that migrate over time and are bordered by yellowish-white raised areas. Both traumatic and aphthous ulcers were found at a higher rate in type 2 than type 1 diabetes [21]. Chronic non-healing oral ulcers are seen in diabetic patients. The epidermal growth factors (EGF) help in maintaining mucosal integrity and wound healing by promoting epidermal growth and keratinization. In DM patients the levels of EGF are considerably low. DM is associated with vascular sclerosis which causes reduced tissue perfusion, tissue hypoxia, and impaired wound healing. Diabetics have decreased levels of glutathione and melatonin in saliva, which are scavengers of free radicals. The accumulation of advanced glycation end products (AGEs) results in impaired neutrophil function. The salivary gland becomes hypofunctional because of poor autonomic innervation and accumulation of AGEs. All these factors cumulatively contribute to impaired wound healing in diabetics [22].

Pulp and periapical tissues

Various studies have shown an increased prevalence of periapical pathosis, delay in periapical repair and osteolytic lesion in diabetic patients. Most of these lesions are associated with the metabolic control and duration of hyperglycemia [23]. High glucose levels can inhibit the proliferation and differentiation of human dental pulp cells. Impaired collateral circulation and thickening of basement membrane in the dental pulp in diabetics result in decreased oxygen supply and oxygen saturation favoring the growth of anaerobic organisms [24]. The peripheral nerve cells in diabetics undergo glycosylation and endo neural microangiopathy. The entry of increased levels of glucose into the cell causes the release of excess oxidants in mitochondria which decreases the conduction potential of nerves [23]. While many studies indicate that the response to stimuli of nerves in pulp is greatly reduced in diabetes there are few conflicting results too. Pulp stones occur at an increased rate with advancing age. In diabetic patients, the presence of sickle-shaped pulp stones is noted as compared to normal globular or spherical ones [25].

"Diabetic odontalgia" is a condition experienced by many uncontrolled or undetected DM patients. The condition is characterized by dental pain similar to pulpitis in the absence of caries. The teeth respond negatively to electric testing for pulp vitality which is due to the impaired sensory activity of sensory nerves in pulp and impaired microcirculation. The microorganisms and the toxins may reach the dental pulp in the absence of caries through systemic circulation resulting in "anchoress" causing asymptomatic pulpal and periapical infection. Following non-surgical endodontic therapy, the prognosis is poor in diabetics compared to healthy individuals leading to tooth extraction [26].

Public health significance

The bidirectional relationship between oral health and diabetes is gaining much importance. It is important for practitioners of both dentistry and medicine to apply this knowledge in the prevention of these diseases. Periodic screening of oral mucosa in susceptible individuals helps to identify the warning signs of diabetes. Early detection reduces the odds of a person being disabled and debilitated in the later stages of the disease. This can reduce the burden of these non-communicable diseases which is an emerging epidemic in both developed and developing countries.

Conclusions

Diabetes mellitus has a strong association with many oral diseases. Early detection of diabetes can help in the metabolic control of the disease. The oral cavity is an excellent indicator of the diabetic status of a patient. Control of oral diseases can help maintain the metabolic control of diabetes.

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Conflict of interest

The authors declare no conflict of interest.

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