



DIFFERENT ORAL MANIFESTATIONS OF DIABETES MELLITUS AND ITS COMPLICATIONS A REVIEW

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ABSTRACT

Aim: A review explaining different oral manifestations & complications of diabetes mellitus

Objective: To relate different oral manifestations and oral complications of diabetes mellitus

Background: Diabetes mellitus is a chronic lifestyle disease affecting all age groups. It is one of the leading causes of mortality and morbidity worldwide. The term “diabetes mellitus” describes a group of disorders characterised by elevated levels of glucose in the blood and abnormalities of carbohydrate, fat and protein metabolism. A number of oral diseases and disorders have been associated with diabetes mellitus, and periodontitis has been identified as a possible risk factor for poor metabolic control in subjects with diabetes. The article will speak in depth about the complications of diabetes mellitus. This article aims to review and increase the awareness of oral manifestations and complications of diabetes mellitus and to stimulate research on the subject.

Reason: It is important to know the different oral manifestations of diabetes mellitus to prevent its complications at the early stages.

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INTRODUCTION

Diabetes mellitus is a growing public health concern and a common chronic metabolic disease worldwide¹⁻⁴. Diabetes mellitus represents a group of metabolic diseases that are characterised by hyperglycaemia due to a total or relative lack of insulin secretion and insulin resistance or both. The metabolic abnormalities involve carbohydrate, protein and fat metabolism. Diabetes mellitus affects all age groups, but is more common in adults. The World Health Organization (WHO) has recently declared it to be a pandemic². Its prevalence has increased dramatically over the past few decades and it is expected to triple in the next decade. Diabetes mellitus is considered a leading cause of death due to its microvascular and macrovascular complications^{5,6}. The most common types of diabetes are type 1 (insulin dependent) and type 2 (non-insulin-dependent)^{7,8}. Type 2 is the more prevalent type. Countries with the highest rates of diabetes in the Eastern Mediterranean region and the Middle East are the United Arab Emirates, Saudi Arabia, Bahrain, Kuwait and Oman⁹. Oman is one of the countries that has a high prevalence of diabetes mellitus, especially type 2 diabetes, and its prevalence is expected to increase in the next twenty years^{10,11}.

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Various inflammatory diseases and soft tissue pathologies in oral cavities are associated with diabetes mellitus¹²⁻¹⁴. However, awareness of these complications is lacking worldwide¹⁵⁻¹⁸. Periodontal diseases have been proposed as the sixth most prevalent complication of diabetes mellitus following the other diabetic complications¹⁹. It has been reported as a more frequent oral complication of diabetes compared to other oral manifestations such as dry mouth and caries. Periodontitis is more frequent and severe in patients with diabetes with poor glycaemic control. Early identification and/or management of these oral manifestations may help in the early diagnosis of diabetes and in attaining better glycaemic control²⁰. Therefore, diabetic oral complications need to be identified and included in the ultimate care of diabetes in order to fight this chronic metabolic disease effectively.

Oral manifestations of diabetes mellitus

Several soft tissue abnormalities have been reported to be associated with diabetes mellitus in the oral cavity. These complications include periodontal diseases salivary dysfunction leading to a reduction in salivary flow and changes in saliva composition, and taste dysfunction. Oral fungal and bacterial infections have also been reported in patients with diabetes. There will be occurrence of oral mucosa lesions in the form of stomatitis, geographic tongue, benign migratory glossitis, fissured tongue, traumatic ulcer,

lichen planus, lichenoid reaction and angular cheilitis²¹⁻²⁵. In addition, delayed mucosal wound healing, mucosal neuro-sensory disorders, dental carries and tooth loss has been reported in patients with diabetes²⁶. The chance of developing oral mucosal lesions were found to be higher in patients with diabetes compared to healthy controls²⁷.

Diabetes mellitus and periodontitis

Periodontitis is one of the most widespread diseases in the world affecting the oral cavity, and is highly prevalent in both developed and developing countries²⁸. Periodontitis is a chronic inflammatory disorder affecting the gingivae and the periodontal tissue initiated by bacteria²⁹. The micro-flora in the dental plaque that forms daily adjacent to the teeth causes this inflammatory process. Eventually, the toxins that are released by the microorganisms in the dental plaque will start the gingival inflammation as a result of failure to remove the dental plaque on a daily basis. A periodontal pocket is formed as a result of the progression of the gingival inflammation causing the gingivae to detach from the tooth surface. This periodontal pocket is filled with bacteria and its toxins. As the disease worsens, the pocket will get deeper carrying the dental plaque until it reaches the alveolar bone that will eventually be destroyed with the periodontal attachment. This process is very common and causes destruction of periodontal tissues, loss of alveolar bone and, finally, tooth loss. There are many factors contributing to this type of inflammation beside the presence of bacteria in dental plaque; a susceptible host is one of them.

The link between diabetes mellitus and periodontal disease is not well recognised by the medical community. Periodontal disease has been reported with increased prevalence and severity in patients with type 1 and type 2 diabetes³⁰. The mechanism by which hyperglycaemia can induce periodontal destruction is not yet fully understood. However, there are many theories which propose factors such as advanced glycation end products, changes in collagen status, and altered immune function that causes impaired polymorphonuclear leukocyte function which may facilitate bacterial persistence in the tissue and the accumulation of advanced glycation end products, which results from prolonged and chronic hyperglycaemia and increased secretion of pro-inflammatory cytokines such as tumour necrosis factor- and prostaglandin^{31,32}. The increase in collagenase activity together with the reduction in collagen synthesis will adversely influence collagen metabolism. This would result in compromised wound healing as well as periodontal tissue destruction. Recent studies indicate that periodontitis has a bidirectional effect on glycemic control in patients with diabetes³³. There is a cluster of research studies, which support the hypothesis of periodontitis occurring more frequently in patients with diabetes with poor glycemic control³³⁻³⁸. In addition, there is enough evidence to support the hypothesis that poor periodontal conditions could worsen glycemic control as well. Many studies report that diabetes is a risk factor for gingivitis and periodontitis and it is more severe with poor glycemic control³⁹. The risk of developing periodontitis in patients with diabetes has been reported to be three times higher than the general population⁴⁰.

Numerous risk factors have been reported that make patients with diabetes more susceptible to periodontal disease, especially those with poor oral hygiene, poor

metabolic control, longer duration of diabetes and who are smokers⁴¹⁻⁴³. Smoking was identified in many studies as being a major preventable risk factor for periodontal disease and tooth loss in the general population and in patients with diabetes⁴⁴⁻⁴⁸. The dentist and the physician should play an important role in advising and supporting patients with diabetes regarding smoking cessation.

In a study carried out in Aurangabad a total of 1500 periodontitis patients were selected from Out Patient Department of multiple hospitals. The fasting and postprandial blood glucose levels were determined by autoanalyzer. Of the 1500 patients, 3.4% of patients had insulin-dependent diabetes mellitus (IDDM) and 96.6% had non-insulin-dependent diabetes mellitus (NIDDM).

The dentist should be engaged in counselling these patients and referring them to a specialist organisation which deals with smoking cessation⁴⁹. Several studies showed that the treatment of periodontal disease has an influence on glycemic control in both type 1 and type 2. A recent meta analysis of the efficacy of periodontal treatment on glycemic control in patients with diabetes suggested that such treatment could lead to a significant reduction in HbA1c⁵⁰. No However, they also recommended that the results need to be viewed with caution due to a lack of strength and limitations in the designs of some of the studies included. Periodontitis and diabetes are related to each other therefore further larger studies are required to determine the effect of periodontal treatment on glycemic control.

Xerostomia

Dryness of the mouth as a feature of uncontrolled diabetes was first described in 1942^{51,52}. The xerostomia may be a consequence of dehydration, although long-standing oral dryness may be due to microvascular disease and neuropathy affecting the major salivary glands⁵³. In addition the xerostomia may be due to concomitant drug therapy, (antihypertensives, diuretics, anxiolytics or antidepressants)^{54,55,56,57}.

Prolonged xerostomia predisposes to local accumulation of plaque and debris and may contribute to the development of opportunistic oral infections, altered taste^{57,58}, oral malodour and oral mucosal soreness.

In a study conducted with 100 diabetic patients, Xerostomia was diagnosed with the use of a specially prepared questionnaire and Fox's test & the salivary flow rate of resting mixed saliva was measured. Of 100 patients, 97% of patients had xerostomia.

Xerostomia in type 1 DM seems to be dependent up on glucose control^{59,60,61,62} where as in type 2 DM, salivary secretion seems to be particularly influenced by xerogenic drugs and autonomic neuropathy⁶³.

Taste impairment

Diabetes mellitus can cause a loss of the sweet taste sensation^{64,65} in deed this may be present at time of diagnosis. Although the taste impairment is usually not severe, and is generally tolerated without complaint, the undiagnosed diabetic patient may favour sweet, sugary food hence exacerbating any hyperglycaemia. Many patients with polydipsia with hyperglycaemia have a predilection for sweet drinks, which have a high content of refined carbohydrate⁶⁶.

Altered taste sensation of DM may reflect taste receptor anomalies⁶⁷. In addition, sulphanyl ureas may cause an alteration of the taste sensation⁶⁸.

Sialosis

It has been previously reported that almost 10–25% of patients with long-standing type 1 and 2 DM can develop asymptomatic, non-inflammatory, non-neoplastic enlargement of the salivary glands^{69,70,66,71} however recently, a low correlation between DM and parotid enlargement was reported, only 3% of 405 patients with DM type 1 being found to have such salivary gland enlargement⁷². Both parotid glands are usually affected, although the submandibular glands may be also involved^{69,71}. Histologically the enlargement, sometimes termed sialosis, comprises fatty infiltration of the interstitium⁷³ and enlargement of acinar cells⁷⁴. It is suggested that patients may be predisposed to calculus formation and obstruction, however in general salivary function is preserved and the sialosis does not influence the duration nor the severity of DM.

Oral infections

Fungal infection

Oral candidiasis is an opportunistic infection frequently caused by *Candida albicans* species. Many predisposing factors can lead to this infection; these include smoking, xerostomia and endocrine and metabolic diseases⁷⁴. Other factors were also implicated such as old age, medications, Cushing's syndrome, malignancies, and the use of dentures⁷⁵. Oral candidiasis has been classified into primary and secondary. Primary oral candidiasis is sub classified into acute (pseudomembranous and erythematous), chronic (pseudomembranous, erythematous and hyperplastic) and candida associated lesions.

Pseudo membrane candidosis is also known as oral thrush. It is characterised by the presence of a creamy white patch which, when wiped, reveals underlying erythematous and bleeding oral mucosa. The soft palate is the most commonly affected area followed by the cheek, tongue and gingivae. It could be chronic in immunocompromised patients⁷⁶. Erythematous candidiasis can present as acute or chronic infection. It is believed to result from the usage of steroid and broad spectrum antibiotics and mainly affects the tongue⁷⁶. Hyperplastic candidiasis is known as candidal leukoplakia. It appears as an irregular whitish raised plaque like lesion commonly seen in the buccal mucous membrane near the commissures.

Candida associated lesions include denture induced stomatitis, angular cheilitis and median rhomboid glossitis which have mixed bacterial and fungal etiology. Denture induced stomatitis is mainly seen in full denture wearers in the underlying surface of the upper denture. Angular cheilitis is seen in the lip commissures as an erythematous crusting lesion. The lesion has been reported to occur in diabetics with poor glycaemic control. Median rhomboid glossitis is seen on the dorsal surface of the tongue as a depopulated erythematous diamond-shaped patch at the midline.

The incidence of fungal infections in patients with diabetes mellitus has been recognised for many years⁷⁷. Candidal infection is reported to be more prevalent in patients with diabetes especially in those patients who smoke, wear

dentures, have poor glycaemic control and use steroids and broad spectrum antibiotics⁷⁸. In addition, salivary dysfunction in patients with diabetes can also contribute to higher carriage of fungi in this group of patients. It is clear from these studies that both local and systemic predisposing factors might increase candidal carriage rate and hence increase the risk of oral candidal infection in patients with diabetes⁷⁹⁻⁸¹.

Bacterial infection

Patients with diabetes are more susceptible to developing oral bacterial infections. They are well known to have an impaired defence mechanism hence considered to be immunocompromised. 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 infection compared to patient without diabetes^{82,83}. A four year prospective study by Rao *et al.* investigated the severity of maxillofacial space infection of odontogenic origin, the type of micro-organism, the sensitivity of the micro-organisms to antibiotics, and the length of hospital stay of patients with diabetes compared with patients without diabetes. They concluded that the spread of the bacterial infection to the submandibular space was more common in patients and controls and that the second commonest area was the buccal space. Streptococcus species was more commonly isolated in both groups. Patients with diabetes were found to stay longer in hospital due to more severe infection and required more time to control their blood glucose levels⁸⁴.

Geographical and fissured tongue

Geographical tongue (benign migratory glossitis; erythema migrans), is a common inflammatory disorder that typically affects the dorsum of the tongue. An association between geographical tongue and DM⁸⁵ has been suggested, as the former has been reported to be present in up to 8.0% of patients with DM⁸⁵. However, a recent study, which had investigated oral soft tissue pathologies in 405 type 1 DM patients⁷², did not report a statistically significant correlation between geographic tongue and DM. Fissuring in the tongue, can affect about 5% of the general population⁸⁶. The fissuring is probably genetically determined⁸⁷, although a higher prevalence (8% in comparison with 2% of no-diabetic population) has been reported in type 1 DM patients^{88,72} particularly patients who have type 1 DM of long duration.

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 and treatment of patients with diabetes undergoing oral surgery is more complex. It was reported that delayed vascularisation, reduced blood flow, a decline in innate immunity, decreased growth factor production, and psychological stress may be involved in the protracted wound healing of the oral cavity mucosa in patients with diabetes⁸⁹.

Oral mucosal disease

Both lichen planus and recurrent aphthous stomatitis have been reported to occur in patients with diabetes^{90,91}. Oral lichen planus (OLP) is a skin disorder that produces lesions in the mouth. OLP is reported to occur more frequently in patients

with type 1 diabetes compared to type 2 diabetes⁹⁰. The reason for this is that type 1 diabetes is considered an autoimmune disease, and OLP has been reported to have an underlying autoimmune mechanism. Patients with diabetes are subjected to a prolonged state of chronic immune suppression especially in type 1 diabetes. In addition, acute hyperglycaemia causes alteration in the immune responsiveness in diabetes mellitus. Atrophic erosive oral lesions are more common in patients with diabetes with OLP⁹¹.

Neuro-sensory oral disorder

Oral dysesthesia or burning mouth syndrome (BMS) is a painful condition affecting the oral cavity (palate, tongue, throat and gingiva)^{92,93}. Other abnormal oral sensations may co-exist with the burning mouth sensation such as tingling, numbness, dryness or sore mouth at the same time. The exact cause of BMS is unknown, but it has been attributed to several conditions such as dry mouth, menopause, candidal infection, diabetes mellitus, cancer therapy, psychological problems and acid reflux. BMS is classified into two types: primary idiopathic, and secondary as a result of a systemic process; secondary BMS has been reported to occur with diabetes mellitus. It could adversely affect the ability to maintain good oral hygiene in patients with diabetes. Diabetic neuropathy could be the underlying cause of BMS in patients with diabetes. The nerve damage in diabetic neuropathy has been reported to show an increase in the Langerhans cells that are associated with immune disturbance^{94,95}. Therefore, it is crucial to screen patients who have symptoms of BMS for diabetes mellitus.

Dental caries and tooth loss

It is well known that patients with diabetes are susceptible to oral infections that lead to tooth decay and loss⁹⁶. Salivary secretion dysfunction, periodontal and sensory disorders could increase the likelihood of developing new and recurrent dental caries and tooth loss. The relationship between diabetes and development of dental caries is still unclear. It is well-known that the cleansing and buffering capacity of the saliva is diminished in patients with diabetes mellitus resulting in increased incidence of dental caries, especially in those patients who suffer from xerostomia.

CONCLUSION

Diabetes mellitus is a chronic, non-communicable and endemic disease. Type 2 compared to type 1 diabetes mellitus is more prevalent worldwide. Oral manifestations and complications in patients with diabetes mellitus have been recognised and reported as a major complication of diabetes mellitus. The degree of metabolic control seems to influence the susceptibility of patients affected by DM to periodontal diseases, presence of fungal infections and taste alterations & other complications. There is increasing evidence that chronic oral complications in patients with diabetes adversely affect blood glucose control. Prevention and management of oral complications, especially periodontal disease, in patients with diabetes is important due to their possible adverse effect on glycaemic control. Promotion of a healthy oral cavity in patients with diabetes is paramount.

There are several clinical implications from this review.

These include: 1) an understanding of the way diabetes affects oral health is necessary for both clinicians and patients, therefore research in this field should be encouraged; 2) the need for regular follow-up of patients with diabetes mellitus by both dentist and physicians; 3) the major role that dentists should play in recognising the signs and symptoms of diabetes and their oral complications; 4) advice and counselling for diabetic smokers regarding smoking cessation, and 5) vigorous treatment of oral infection either bacterial or fungal in these patients, especially if they have poor glycaemic control.

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