The Association between Diabetes Mellitus and Oral Health: Implications and Management

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Abstract

Diabetes mellitus is a common metabolic condition that is associated with increased risk of inflammatory and infectious dental complications. Caries, gingival inflammation, plaque deposition, and alveolar bone loss can combine to make the oral cavity a prime target for diabetes-related problems. In general, the higher is the ambient glucose level, the greater the propensity to oral and dental issues. Critical aspects of management are patient education and the degree of resources available to the clinician and the patient. Improving glucose control is associated with better oral health and conversely, timely responsiveness to dental, periodontal, and gingival hygiene may alleviate hyperglycemia. Since both diabetes and oral disorders are highly prevalent, their bidirectional relationship has great significance from the public health perspective.

Keywords: Diabetes Mellitus; Hyperglycemia; Oral Health; Periodontal Disease; Dental Caries

Introduction

Diabetes mellitus (DM) is a common metabolic disorder that afflicts approximately 451 million individuals globally, a number that is projected to increase significantly in the future [1]. The adverse health impact of diabetes and its long-term complications is dependent on the level of chronic hyperglycemia, the management of its comorbidities, and the degree of resources available to the clinician and the patient. In addition to the classically described complications of the disease, attention has recently been paid to its dental and oral manifestations. Hyperglycemia predisposes to dental plaque and caries, periodontal disease, gingivitis, and tooth and alveolar bone loss. Improved glycemic control often contributes to better oral health; conversely, greater attention to oral and dental care may have a salubrious impact on diabetes itself. Data seem to suggest that the hyperglycemia and vascular compromise that may accompany diabetes are associated with relatively poor oral health, thereby having implications locally as well as systemically. On a community level, increased awareness of the vital role of adequate oral hygiene on the overall health of the individual suffering from diabetes is the essential first step in devising a collaborative plan by the diabetes specialist, the dentist, and the patient in order to combat the ravages of this metabolic condition on dental well-being.

Observations and Evidence

Cross-sectional and observational studies have revealed a close association between both type 1 diabetes (T1DM) and type 2 diabetes (T2DM) and oral health (Table 1). Statistics indicate a low awareness regarding general oral hygiene and relatively infrequent encounters with a dental specialist in patients with diabetes [2-5]. It is interesting to note that most dentists are aware of the link between systemic diseases and oral pathology and believe that patients’ access to oral care would improve if they were aware of this connection between oral and systemic health [6].

Periodontal disease (PD) is a pathological inflammatory condition of the gum and bone support structures (periodontal tissues) surrounding the teeth. The periodontal manifestations of DM have come into the limelight with recent reports highlighting the adverse impact of hyperglycemia on dental health [7,8]. Periodontal disease is a primary culprit for poor dentition among individuals with diabetes. The risk for both these noncommunicable, chronic conditions increased in older individuals [9]. A meta-analysis compared over 3500 diabetic and nondiabetic adults and found that the former had a two-fold higher risk of developing PD [10]. Racial disparities regarding the rates of PD in patients with diabetes are also evident, with the prevalence in blacks having been reported between 59.7% and 70.6% [11]. Although research in developed nations has highlighted associations between oral health and diabetes, the low- and middle-income countries appear to have a paucity of such data. A cross-sectional, nested part of the Cardiometabolic Risk Reduction in South Asia Surveillance Study consisting of participants residing in Delhi, India were evaluated with standardized questionnaires and underwent oral examination with determination of diabetes status [12]. Nearly 85% of 2045 participants suffered from at least one oral disease, and the adjusted prevalence of periodontitis was significantly higher among diabetic individuals (42.3%, compared to 31.3% in those without diabetes). The authors highlighted the need for public health strategies to integrate oral health within the existing disease control programs. Differences in oral health were also noticed in older persons with diabetes residing in France and Brazil; the former had better oral health and adherence to principles

Table 1: Oral and dental pathologic conditions commonly encountered in patients with diabetes.

- Increased risk of dental caries – tooth decay and cavities due to acid destruction of enamel, most commonly by streptococcus mutans and lactobacillus bacteria [15]
- Gingivitis – red, inflamed, and swollen gums that bleed easily and respond to improved oral hygiene [22,23]
- Periodontitis – bacterial plaque progression causing soft tissue, gum, and bone damage and tooth loosening or loss [7,8,10]
- Loose or missing teeth – resulting from untreated periodontitis and progressive alveolar bone loss [24,29]
- Aphthous stomatitis – painful, recurrent lesions (“canker sores”) that may interfere with eating, drinking, or talking [18]
- Oral candidiasis (“thrush”) – opportunistic infection that appears as creamy white lesions on the mucous membranes [19]
- Traumatic ulceration – local trauma due to physical agents or damaged teeth [16]
- Fissured tongue – deep grooves on the dorsum of the tongue [16]
- Lichen planus – inflammatory, whitish, lacy patches or open sores [17]
- Burning mouth syndrome – of unknown cause but usually accompanied by diabetic neuropathy [43]
of oral hygiene such as regular brushing and flossing of teeth [13].
A general caveat that should be kept in mind is the methodological
rigor of the meta-analyses looking at trials evaluating the connection
between PD and DM [14].

Of note, several studies have reported a greater prevalence of dental
caries in individuals with DM [15]. Diabetes is also associated with
an increased propensity for soft tissue abnormalities in the oral cavity,
such as traumatic ulcers, fissured tongue, irritation fibroma [16], lichen
planus [17], recurrent denture stomatitis [18], and oral fungal afflictions
such as thrush and candidiasis [19]. Decreased salivary flow is linked
to increasing glycosylated hemoglobin (Hemoglobin A1c, or HbA1c)
values in patients with DM, which may be a prominent underlying
reason for the high prevalence of dry mouth and gingival-dental
problems in this population [20,21]. Patients with T2DM also had
greater gingival inflammation and bleeding [22,23], as well as increased
risk of progressive loss of periodontal attachment and alveolar bone
[24], as compared to subjects without diabetes, notably in patients with
poor glycemic control [25]. Gingival inflammation and periodontitis
are also more prevalent in children with T1DM than in nondiabetic
children [26]. Younger subjects with type 1 diabetes seemed to be at
particular risk for periodontitis [27]. In general, it appears that the
presence of diabetes and hyperglycemia is associated with a high risk
of peri-implantitis [28]. Alveolar bone loss due to periodontitis in
diabetic patients can lead to proclination and spacing between the teeth,
resulting in pathological tooth migration and often requiring orthodontic
correction. Paradoxically, orthodontic treatment can worsen the bone
loss in such patients if glycemic control is suboptimal [29].

Although rigorous epidemiological data is lacking, a systematic
review provided evidence that diabetes was associated with increased
risk of periodontitis onset and progression in adults [30]. Finally, a
recent publication of consensus emphasized the close, bidirectional
relationship between diabetes and periodontal disorders, with the
former conferring an increased risk of oral pathology. A co-management
approach could lead to improved oral health as well as glycemic control
[31].

Although in its infancy, the association of less common types of
diabetes is worth mentioning. A meta-analysis pointed to a statistically
significant increased risk for gestational DM in the presence of
periodontitis [32]. Notably, a recent study not only showed a significant
association of periodontal disease with gestational DM, but also
an increased risk of developing pre-eclampsia [33]. In a setting of
prediabetes screening, the propensity for glucose intolerance and the
presence of progressively severe periodontitis was highly correlated
[34].

Pathologic Mechanisms

General Concepts – PD is a chronic inflammatory condition of the
tissues that support and attach the teeth to the maxilla and mandible.
It is characterized by gingival inflammation, loss of connective tissue
attachment, periodontal pocket formation, and alveolar bone resorption,
potentially resulting in ultimate tooth loss [35,36]. Controlled clinical
trials have confirmed that subjects diagnosed with diabetes have a
greater prevalence of PD compared to healthy individuals [3,37].
Diabetes and PD are both associated with a heightened inflammatory
state that initiates an immune response. Cytokines are released and cause
destruction of the connective tissue and alveolar bone responsible for
supporting the teeth while interfering with normal repair mechanisms.
Both conditions tend to coexist in the same individual in a multifactorial
manner. In addition, the severity of periodontitis is linked to worse
glycemic control [38]. The potential pathologic changes in the teeth
and gums in individuals with diabetes are portrayed diagrammatically
in Figure 1.

Pathophysiologic Mechanisms – The mechanisms of adverse
consequences of hyperglycemia on oral health may be both causal
and due to shared cofactors between the two conditions [39,40] (Table
2). Several pathways have been proposed to explain the increased
susceptibility to PD among patients with uncontrolled DM, including
alterations in host response, collagen metabolism and vascularity.
Individuals with poorly controlled T2DM present an exaggerated
inflammatory response to the bacterial challenge of periodontitis. A
brisk response coupled with impaired wound healing and repair may
enhance the inflammatory reaction and periodontal tissue destruction
for these patients [41]. The evidence suggests that the host inflammatory
response appears to be the critical determinant for susceptibility to,
and severity of, periodontitis in systemically compromised individuals
[23], such as patients with T2DM. Periodontitis-induced bacteremia
causes elevations in serum proinflammatory cytokines and reactive
oxygen species, leading to worsening of metabolic risk factors and
insulin resistance.

Contributing Factors – The higher incidence of dental caries
in DM is in part attributable to decreased salivary secretion; as
mentioned previously, the resultant dry mouth may contribute to
gingival complications [21], in addition to oral yeast proliferation

Figure 1: A diagrammatic representation of dental and gingival disease in persons with diabetes.
Table 2: Pathologic mechanisms that underlie oral complications in patients with diabetes.

<table>
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<td>• Accumulation of advanced glycation end-products (AGE) related to hyperglycemia [41]</td>
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<td>• Adverse effects of hyperglycemia on cell-to-matrix interactions [43]</td>
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<td>• Increased tissue oxidation stress [45]</td>
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<td>• Proinflammatory state and altered endothelial cell function [45]</td>
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<td>• Functional changes in immune cells: neutrophils, monocytes and macrophages [45]</td>
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<tr>
<td>• Impairment of neutrophil adherence, chemotaxis and phagocytosis [44]</td>
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<td>• Heightened proinflammatory state and cytokine release [41]</td>
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<th>Macro-structural and pathophysiologic changes of periodontal disease</th>
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<tr>
<td>• Increased chronic gingival inflammation [22]</td>
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<td>• Destruction of connective tissue attachments [23,41]</td>
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<td>• Periodontal pocket formation [43]</td>
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<tr>
<td>• Alveolar bone resorption and tooth loss [8,10]</td>
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<tr>
<td>• Abnormal or insufficient repair mechanisms [42]</td>
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<td>• Prolonged wound healing [42]</td>
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and increased infection with streptococci and lactobacilli. Chronic immunosuppression and delayed wound healing may predispose to oral mucosal diseases [42]. Neurosensory changes of unclear etiology lead to a disorder characterized by a burning sensation of the oral mucosa without any associated clinical or laboratory findings [43].

*Heightened Inflammation: a Vicious Cycle –* Diabetes adversely affects the health of the periodontium in a variety of ways, which in turn worsens glycemic control. The periodontium is highly vascularized and susceptible to the adverse effects of accumulating advanced glycation end-products (AGE) and their undesirable effects on cell-to-matrix interactions, increased tissue oxidant stress, and altered endothelial cell function. In this respect, inhibitors of proinflammatory cytokines appear to suppress alveolar bone loss [23]. Diabetes alters the function of immune cells including neutrophils, monocytes and macrophages. In the dysbiotic milieu of diabetes, the transcriptional activity of the periodontal pocket microbiota is increased, leading to impaired neutrophil chemotaxis and phagocytosis [44]. Bacteria are able to persist in the periodontal pockets and to significantly increase periodontal destruction and prolong wound healing. There is increased production of pro-inflammatory mediators of oxidative stress. Diabetic individuals with periodontitis exhibit high levels of circulating TNF-α, CRP IL1-β, TNF-α, IL-6 and other mediators of oxidative stress, and successful periodontal treatment leads to a reduction in these markers [45]. Thus, the relationship is bidirectional and promotes a vicious cycle.

**Impact of Periodontitis on Glycemic Course** – PD is also associated with an increased risk for diabetic complications. Thorstensson et al. demonstrated that, in subjects with diabetes, 82% of those with periodontitis experienced a cardiovascular, cerebrovascular or peripheral vascular event over a decade, compared to only 21% in those without periodontitis [46]. Additionally, the impact of PD on mortality was examined in 600 subjects with T2DM; in the presence of severe periodontitis, the death rate from ischemic heart disease and diabetic nephropathy was 2.3 and 8.5 times higher respectively [47]. In Indian patients, worsening periodontal inflamed surface area (PISA) scores correlated with significantly higher HbA1c levels, retinopathy and nephropathy (P < 0.05) [48].

**Population-based Findings** – The relationship between oral pathology and cardiovascular risk has been explored in more detail recently. Inflammation in the oral cavity is a result of a complex biologic alteration of the periodontal microenvironment and a subsequent shift in the distribution of oral pathogens. The metabolic syndrome, which comprises a clustering of cardiovascular risk factors, has been linked to PD [49]. Shrestha et al. [50] interviewed 7,848 adults who underwent a clinical oral-health examination and had serum immunoglobulin G titers measured against 19 periodontal bacteria as part of the third National Health and Nutritional Examination Survey (NHANES). The periodontal bacterial profile was not found to be associated with the metabolic syndrome or its individual components, including hypertension, hypertriglyceridemia, low high-density lipoprotein cholesterol, and central obesity – other than a very moderate association with elevated plasma glucose. In a cross-sectional analysis by Merchant and colleagues [51], little relationship was found between periodontitis and cardiovascular risk factors in youth with T1DM who had good oral health. However, in a sample consisted of 468 men aged 47-80 years who participated in the Health Professional Follow-up Study [45], self-reported periodontal disease was associated with significantly higher levels of C-reactive protein (30%), tissue-plasminogen activator (11%), and low-density lipoprotein (11%). The authors concluded that the associations between periodontal disease and biomarkers of endothelial dysfunction and dyslipidemia could potentially explain a possible relationship between oral health and cardiovascular disease.

In summary, it is important to keep in mind that elucidation of the underlying pathophysiologic links between hyperglycemia and clinical disorders commonly encountered in diabetic patients await further research. Nevertheless, the emerging scientific link between diabetes and periodontal disease was affirmed by a joint consensus report based on the proceedings of a workshop between the respective professional organizations [52].

**Management**

**General Approach** – There is increasing agreement that dental health professionals should be part of a multidisciplinary team caring for patients with diabetes [53]. Information from the patients’ health history and interview should include the time of their most recent dental visit and cleaning, complaints of tooth pain or loosening, gum swelling or bleeding (including when brushing), the occurrence of dry mouth, and any difficulty with swallowing. An integral part of the patient’s management of diabetes includes a basic oral evaluation that is performed by dental specialists as members of the health care team. Both the American Dental Association and the American Diabetes Association recommend that patients with diabetes visit a dentist on a regular basis for a comprehensive evaluation of the oral cavity and for a detailed assessment and management of pathology related to the teeth, gums, and alveolar bone [54,55].

**Management** – Inspecting a patient’s mouth for pathologic changes requires a keen eye and simple instruments such as a flashlight, a tongue depressor, and cotton gauze. Findings of concern include, but are not limited to, mucosal redness, broken or missing teeth, brown or black discoloration, cavity formation with root exposure, and tenderness or burning sensation in the mouth. Periodontal treatment usually consists of scaling and either surgical or nonsurgical debridement of...
root surfaces to remove bacterial biofilms, calculus, and mineralized plaque. The use of chlorhexidine mouthwash in diabetic patients has been demonstrated to result in a significant improvement in gingival inflammation and pocket depths [56].

Studies – In patients with type 2 DM, non-surgical periodontal treatment improved systemic oxidative stress measures and quality of life [57]. The benefits of a multifactorial approach with nonsurgical periodontal treatment have been demonstrated in a randomized, controlled setting [58]. In addition to oral hygiene instructions, patients with diabetes who received scaling and root planing using ultrasound and Gracey curettes had a statistically significant improvement in glycosylated hemoglobin at 6 months [59] (Table 3).

Use of Antibiotics – The general principles of antibiotic usage to counter the bacteremia associated with oral surgery apply to individuals with DM as well [60]. The tetracycline class, in particular the chemically modified derivatives, have bactericidal activity and are known to decrease production of matrix metalloproteinases such as collagenase [61]; the subsequent reduction of periodontal inflammation benefits the patient both locally and systemically. In diabetic subjects, the combination of amoxicillin and metronidazole also seems to be effective against the multitude and gram-negative and anaerobic organisms found in periodontitis [62]. The use of local antimicrobials as an adjunct to scaling and root planing may result in additional reductions in the degree of periodontitis reduction seen in otherwise well-controlled individuals with DM [63].

Ancillary Measures and Related Issues – Management of burning mouth syndrome can be challenging and is geared towards improving quality of life and reducing symptoms [64]. Avoidance of oral irritation and providing psychological support are important factors. The presence of diabetic neuropathy may also impair sensation and contribute to worsening of oral hygiene. Recommending an electric toothbrush and adherence to a dental maintenance schedule are important in maintaining the long-term oral health in these patients. Proper dentition is necessary to support facial structure and enunciation of speech, both of which can affect a patient’s self-image and self-consciousness. Of note, preserving the patient’s ability to masticate properly and thus be able to consume a high-fiber diet is critical for overall good health. A recent report revealed the advantages of supplementing the diet with high-molecular weight fucoidan, a seaweed derivative widely used in Japanese cuisine [65]. Among other gastrointestinal benefits, fucoidan intake led to enhanced taste sensitivity, which could potentially improve glycemic control in diabetes. Interestingly, the use of metformin has recently been shown to independently reduce experimentally-induced “diabetic periodontitis” by the suppression of kinase enzymes involved in its pathophysiology, thus cementing its position as a first-line oral glucose-lowering medication for therapy of type 2 diabetes [66].

Preventive Measures and Hygiene Maintenance – Prevention of periodontal disease is of paramount importance in maintaining oral health in the patient with diabetes. Fortunately, a variety measures can be taken for optimizing oral hygiene practices. Powered or manual brushing and flossing, diet modification with more fruits and vegetables, reduced consumption of sugary food, and a liberal intake of vitamin C and E have been shown to be helpful in this regard [67]. Use of fluoride (in the form of stannous fluoride) and zinc in toothpaste may confer anti-gingivitis, anti-cariogenic, and anti-plaque benefits [68], while antimicrobial actions can be enhanced by the regular use of chlorhexidine mouthwash [67]. A cornerstone of preventive care is the regular scaling and the surgical and non-surgical debridement of root surfaces [58]. Finally the critical importance of smoking cessation for dental as well as overall health cannot be overemphasized [69].

Promising Avenues – Certain therapeutic agents approved and in use for the management of hyperglycemia may have a salutary effect on oral health. For example, a novel metformin-containing resin achieved substantial enhancement of odontoblastic differentiation of dental pulp stem cells (HDPCs) and greater mineral synthesis [70]. It appears to be promising for deep, perforated cavities and tertiary dentin formation. It may have a role in root coatings for periodontal regeneration, and for root canal fillings with apical lesions to stimulate bone formation. In a recent study the agent saxagliptin, a potent inhibitor of dipeptidyl peptidase-4 (DPP-4) approved for the treatment of type 2 diabetes, significantly inhibited lipopolysaccharide-induced expression and secretion of proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β and IL-6 in HDPCs [71]. The authors speculated that saxagliptin might have a potential benefit in the treatment of dental conditions such as pulps. In addition, with the advent of electronic health records, detailed patient-level data with automated dental quality measures could be useful in evaluating and improving the quality of dental care provided to patients with diabetes [72].

Impact of Diabetes on Dental Procedures

Hypoglycemia is a feared but preventable complication that can occur in the dental office. Antidiabetic medications may be inappropriately dosed, exceed the recommended dosage, or peak insulin levels may overlap with the time of the appointment [73]. Mild hypoglycemia may manifest as irritability, lack of proper judgement, mood changes, decreased spontaneity, hunger and weakness. These may be followed by sweating, incoherence and tachycardia and untreated, can lead to unconsciousness, hypotension, and seizure activity. Morning dental appointments are preferred in diabetic patients since the cortisol levels are higher at that time, thus raising glucose and minimizing the risk for hypoglycemia. Advice to the patient about food intake prior to the appointment should be given and medications should be adjusted in consultation with the patient’s physician. Reduction in morning insulin amount may be necessary. The patient should be asked to bring their own blood glucose monitoring device as well as quick-acting snacks or glucose tablets to the dental appointment [74]. It is desirable to have dextrose (D50) and glucagon emergency kit available for parenteral administration in cases of severe hypoglycemia. It is expected that with close attention to the above-mentioned factors along with close vigilance, conscious sedation of the diabetic patient for dental procedures can be safely used [75].

Conversely, hyperglycemia reflected in extremely high glucose readings (>400 mg/dl) and a recent hemoglobin A1c that is elevated (>8%) could adversely impact the dental procedure. In fact, delayed wound healing is one of the major complications in diabetic patients. Age, obesity, malnutrition, macro- and microvascular disease may all contribute to impaired recovery. Dental procedures like extractions and implant placement should be avoided in patients with poorly controlled diabetic patients but can be performed in well controlled patients and moderately controlled diabetic patients in consultation with the

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Table 3: Prevention and management of periodontitis in individuals with diabetes.

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<tr>
<th>Establish regular schedule of preventive and diagnostic dental visits</th>
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<tbody>
<tr>
<td>• Comprehensive dental history and oral examination at each visit</td>
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<tr>
<td>• Scaling and debridement of bacterial biofilms and plaque</td>
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<td>• Targeted antibiotic therapy when clinically indicated</td>
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<td>• Prompt cavity filling and tooth preservation and restoration</td>
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<td>• Optimize glycemic control and glycosylated hemoglobin level</td>
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Table 4: A summary of important considerations regarding the relationship between oral health and diabetes mellitus.

- Diabetes mellitus appears to be a hitherto under-recognized risk factor for poor dental health and oral pathology. There is increasing awareness of the association between diabetes mellitus and suboptimal oral health.

- Hyperglycemia predisposes to dental plaque and caries, periodontal disease, gingivitis, and tooth and alveolar bone loss; these problems are more prevalent and worse in individuals with uncontrolled hyperglycemia. An intensely heightened inflammatory and immune response with plaque deposition leaves the oral cavity prone to yeast proliferation and bacterial infection.

- Improved glycemic control often contributes to better oral health; conversely, greater attention to oral and dental care may have a salubrious impact on diabetes itself.

- A careful and comprehensive oral examination by a dental specialist in order to promptly detect and treat oral problems should be an integral component of the standard of care in patients who suffer from diabetes mellitus; such care has shown to result in better glucose control and fewer pathologic complications in the oral cavity.

Concluding Points

DM is closely associated with periodontal disease and both are highly prevalent chronic conditions. DM appears to be a hitherto under-recognized risk factor for poor dental health and oral pathology. Periodontal disease, gingival inflammation, and alveolar bone problems are more prevalent and worse in individuals with uncontrolled hyperglycemia. Increased inflammation and the resultant immune response are critical underlying factors that contribute to plaque deposition and leave the oral cavity prone to yeast proliferation and bacterial infection. Diabetes and hyperglycemia thus place an individual at an increased risk of a myriad of dental and oral soft tissue problems. Preventive and therapeutic measures, when done proactively and on a regular basis, can go a long way in reducing the mutual burden of these interrelated conditions. A multidisciplinary approach to dental care can improve general well-being and limit the impact of the diabetic state on the patient’s health. A careful and comprehensive oral examination by a dental specialist in order to promptly detect and treat oral problems should be an integral component of the standard of care in patients who suffer from diabetes mellitus; such care has been shown to result in better glucose control and fewer pathologic complications in the oral cavity. In order to combat these challenges, the principles of management are important to adhere to, both at the individual as well as the community level (Table 4).

References


