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Review Article

Association between Diabetes and Periodontal Disease: A Literature Review

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Abstract

Diabetes is considered a global health issue among clinical society with an increasing incidence. Awareness of the disease etiologies, high-risk group, and the associated complications can provide a critical approach for disease prevention and management. We conducted an electronic database search for suitable studies and included all studies reporting the association between periodontal diseases and diabetes. There was a significant increase in periodontal disease among diabetic patients. Moreover, a mutual association between periodontal disease and glycemic control was reported by many studies. A good clinical collaboration between dentists and physicians is a must a successful detection and treatment of patients with diabetes. Large-scale studies are essential to get more solid results and to resolve the heterogeneous reporting in literature.

Keywords: *Diabetes; Periodontal Disease; Glycemic Control; Periodontitis*

Introduction

Diabetes is considered a global health issue among clinical society with an increasing incidence; 439 million individuals will experience the dangerous disease in 2030 [1]. Diabetes prevalence varies according to age, sex, racial disparities, educational level and geographical distribution [2,3]. Awareness of the disease etiologies, high-risk group, and the associated complications can provide a critical approach for disease prevention and management. Diabetes elicits several complications among affected patients including erectile dysfunction, neuropathy, retinopathy, and macroangiomyopathy in order [4]. Moreover, poor diabetic control is associated with severe adverse effects up to mortality [5]. Recently, diabetes constitutes a risk factor for periodontal disease affection [6]. Diabetes type is a significant moderator of pathological consequences involving the teeth and surrounding tissue. Type 2 diabetes but not type 1 is associated with more probing depth, attachment loss and missing teeth compared to controls. Moreover, type 1 is associated with more dentist regular visits rather than controls. However, after adjustment of all confounders, type 1 diabetes was associated with tooth loss [7]. Diabetic patients are associated with less number of teeth, periodontitis, bleeding, more pocket depth and plaque index [6].

Several hypotheses by which periodontitis occurs in diabetic individuals. The glycated metabolites in diabetic patients alternate with the blood supply of periodontal tissues [8]. The low associated-immunity in diabetic patients increases the susceptibility to infection [9]. Moreover, the impaired tissue healing and continuous bleeding due to high glucose levels increase the risk for periodontal tissue infection in those individuals [6,10].

Once periodontitis occurs in diabetic patients, treatment should be started to avoid negative consequences initiated by periodontitis on those individuals. The previously stimulated immune system with a high level of tumor necrosis factor α (TNF-α) plays an important role in increasing the response to other infections and consequently fastens the development of diabetic complications [11]. Furthermore, the circulating cytokines during periodontal disease increase insulin resistance in diabetic patients [12]. Treatment of periodontal in diabetic individuals constitutes a corner-stone in decreasing the level of glycated materials. In a preliminary report, glycated hemoglobin was significantly decreased after periodontal treatment supporting the evidence of the pathognomonic role of periodontitis in the regulation of diabetes levels [11]. Akin to that, treatment of periodontal disease is significantly associated with improvement of fasting insulin level, glycated hemoglobin and TNF-α [13].

The severity of periodontal disease possesses a significant effect in increasing mortality of diabetic patients. Patients affected with severe periodontal disease was significantly associated with all causes of death, ischemic heart disease and diabetic nephropathy mortality [14]. Derived from that thought, we aim to provide an insight towards the incidence of periodontal diseases in diabetic patients and to study the impact of periodontal diseases in diabetes control and progression.

Methods

We conducted an electronic database search for suitable studies till July 2019 in four databases including Google Scholar, Scopus, Web of Science (ISI) and PubMed. A manual search was conducted by searching for relevant publications from references of included articles, relevant papers in PubMed and Google Scholar and primary studies that had cited the included papers. All papers reporting the association between periodontal diseases and diabetes were considered for inclusion. After proper screening of the potential studies, we selected the better 61 studies to compose this review work.

Literature Review: Prevalence of periodontitis in diabetic patients

There are controversy data about the prevalence of periodontitis in the United States (US) [15]. The prevalence of periodontitis showed a 10% decline; however, other interpretations suggested that about 50% of US adult population suffers from different degrees of periodontitis [16,17]. Moreover, the prevalence of periodontitis was significantly higher in diabetic patients compared to their non-diabetic peers [18]. As reported per the National Health and Nutrition Examination Survey, a history of periodontal disease is associated with undiagnosed diabetes among 27% to 53% of the patients [19]. In the same context, a population-based study showed that periodontal disease was associated with both type 1 and type 2 diabetes [7].

Noteworthy, periodontitis is the sixth most common complication of diabetes [20]. Moreover, the duration of diabetes was a significant risk factor for increased severity of periodontal diseases [20]. Diabetic patients with a history of the disease for more than five years showed a higher severity of periodontal disease [20]. In contrast, Faulconbridge., *et al*. showed different result regarding this topic [21].

Effect of diabetes on the periodontium

Effect on microflora

Several studies have focused on the alteration of oral microflora in diabetics. Some of these studies have found a relation between glycemic control and alterations in microflora which may increase the susceptibility of diabetics to periodontal disease [22-23]. The counts of *Capnocytophaga* species were found to be significantly higher in periodontal pockets of diabetics compared to periodontal pockets in healthy individuals [26-28]. Nevertheless, Other studies did not find a significant difference in the oral microflora between diabetics and healthy individuals [29,30]. Thorstenseon., *et al.* studied several bacterial species in the subgingival microflora in long-term type 1 diabetics and non-diabetics [29]. They reported that *A. actinomycetemcomitans*, *C. rectus, Capnocytophaga* species, *E. corrodens, F. nucleatum, P. gingivalis,* and *P. intermedia* are recovered in diabetics a well as non-diabetics [29]. The same study observed that *P. gingivalis*

was detected both in shallow and deep pockets in diabetic subjects, whereas the pathogen was only found in deep pockets in non-diabetic individuals [29]. Local environmental changes in diabetics because of salivary alteration and high glucose levels in gingival crevicular fluid (GCF) may result in shifts of the microbial flora [31-33].

Advanced glycation end products (AGEs)

The sustained hyperglycemia in poorly controlled diabetics in combination with elevations of serum low density lipoproteins and triglycerides will induce an irreversible glycation of proteins like collagen and lipids to form the AGEs. AGEs will accumulate in tissues of diabetic patients and are thought to be a major link between the various diabetic complications. They may also be involved in tissue changes within the periodontium. Therefore, poorly controlled diabetics show higher AGEs levels and are more susceptible to periodontitis. The biologic effect of AGEs is mediated by the receptor for AGEs (RAGE) which is found on the surface of smooth muscle cells, endothelial cells, neurons, monocytes and macrophages [34-39].

Effect on host response

Polymorphonuclear leucocytes (PMNs) act as first-line-of-defence cells and the reduction of their function may explain the high susceptibility of diabetics to infection. Clinical investigations in diabetic patients and experimental studies in diabetic rats and mice have clearly demonstrated that the defects of PMNs include chemotactic, phagocytic and bactericidal activities. This defective PMNs function is highly related to poor glycemic control [40]. GCF collagenase concentration is higher in diabetics and it is primarily derived from PMNs [41].

In the same context, higher concentration of cytokines (IL-1β, PGE2, TNF-α) has been detected in GCF of diabetic patients with periodontitis compared to non-diabetic patients. The release of these cytokines in response to bacterial lipopolysaccharides (LPS) by monocytes was significantly higher in diabetics than in non-diabetics. This hyperinflammatory response is thought to be a result of AGE-RAGE interaction on monocytes and macrophages. This can result in the formation of a destructive cell phenotype with increased sensitivity to stimuli, resulting in excessive release of cytokines [42-45]. AGE-RAGE binding on macrophage surfaces may alter macrophage phenotype. This may be responsible for dysregulation of macrophages cytokine production and increased inflammatory tissue destruction and alveolar bone loss. It may alter the scavenging function of macrophages and delay the wound healing [46-49].

Effect of periodontal diseases on glycemic control

A Cochrane review showed an improvement in glycemic control of diabetics following control of periodontal diseases; however, it also concluded that this evidence is weak with lack of statistical power to support [50]. A meta-analysis showed that effective control of periodontal disease in type 2 diabetics was associated with better glycemic control [51]. Additionally, another meta-analysis, with a follow-up duration of three to nine months, showed a significant reduction in HBA1C up to 1.7% following periodontal therapy, when compared to the control group [52]. Moreover, non-controlled diabetics with Hemoglobin A1C (HbA1C) > 9.0% showed a reduction of 0.6% with the introduction of periodontal therapy only and by 1.4% with changes in diabetic medications [53].

In the same context, a decrease in HBA1C, C-reactive protein and TNF-α was identified following a good periodontal therapy [54,55]. Moreover, the use of systemic antimicrobial agents for periodontal therapy showed an associated reduction in HBA1C by 0.2% [56]. Multiple primary studies have showed a significant improvement in different parameters of glycemic control following good periodontal therapy [20,57-59]. Moreover, chronic periodontitis was associated with a higher risk of diabetic complications including neuropathy and retinopathy [58]. This association goes in both directions with better control of periodontitis with only good glycemic control and without the use of any periodontal therapy [59]. This can be explained by the subsequent elimination of inflammation at the gingival site of periodontal tissue as a result of good diabetic control [59].

The following biologic mechanisms have been proposed to explain how periodontitis may affect the systemic environment: entrance of bacteria or bacterial products, such as LPSs, from the ulcerated periodontal pocket into the systemic circulation and/or systemic effects of inflammatory mediators like TNF-α, IL-1β, and IL-6 produced locally in response to periodontal infection. These mediators potentially can increase low-grade inflammation and worsen insulin resistance (Figure 1) [60].

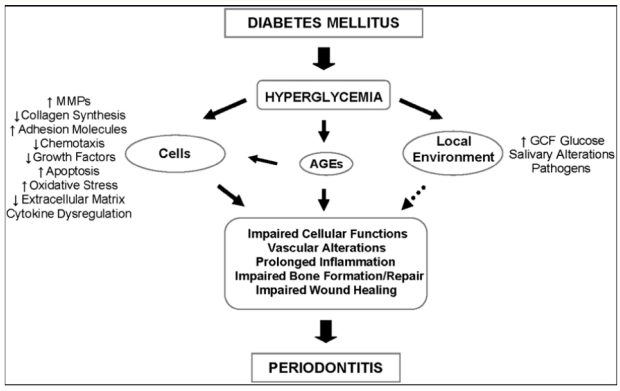

Figure 1: *Possible mechanisms for the increased susceptibility to periodontitis in diabetic patients.*

Medical periodontal therapy eliminates local and systemic inflammation and infection through a decrease in TNF-α. However, this is not sufficient alone to achieve a significant reduction in HBA1C levels without the strict glycemic control in diabetic patients. Thus, a good clinical collaboration between dentists and physicians is an important component for successful treatment of patients with diabetes.

Conclusion

Conjoint attention to oral health in addition to medical diseases by both medical and dental care providers will improve the ability to detect patients unaware of their diabetic status. Dentists should establish referral programs, communicate with physicians, and use dental examination as a screening tool for referral of patients with severe periodontal diseases. Noteworthy, large-scale studies are essential to get more solid results and to resolve the heterogeneous reporting in literature.

Conflict of Interest

None.

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