Periodontitis And Diabetes Mellitus-A Two Way Relationship

Dr. Sneha Kothari*, Dr. Viral Patel, Dr. Anita Panchal***, Dr. Hardik Mehta****, Dr. Bhaumik Nanavati*****

*Post Graduate Student, **Prof. & Head, ***Professor, ****Reader, *****Sr. Lecturer, Department of Periodontology, College Of Dental Sciences And Research Center, Manipur, Bopal. Ahmedabad, Gujarat, India.

Abstract : Periodontal disease (PD) and diabetes mellitus (DM) hold a consistent relationship. DM not only increases the risk of having PD and with that its prevalence, but it also augments the progression of more aggressive and quickly defining signs. There is a bidirectional relationship between DM and PD. The treatment of periodontitis in diabetic patients favors a reduction in mediators responsible for the destruction of periodontal tissue and decreases with it, resistance to insulin. PD is characterized by low grade chronic inflammation that may remain silent in diabetics causing damage that is not locally limited but may extend systemically. Our aim of this article is to make aware, both general dental and medical practioner about interrelationship between periodontal disease and diabetes with special emphasis on importance of mutual consultation between the two fraternity, which in turn significantly contributes to general well being of an individual. [Kothari S et al NJIRM 2013; 4(5) : 94-101]

Key Words: Periodontal Disease, Diabetes Mellitus, Poor Glycemic Control, AGE's, Inflammation

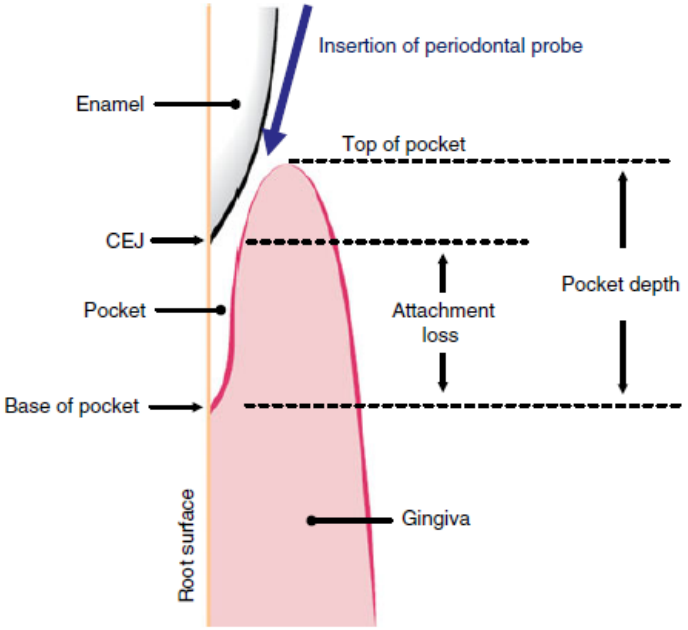
Author for correspondence: Dr. Sneha Kothari , 71/363, Saraswati Nagar. Opp. Himmatlal Park 2. Ambawadi. Ahmedabad - 15. 360007 e- mail: sneha_kothari1589@yahoo.co.in

Introduction: Over the past 30 years; diabetes mellitus has been recognized as a major disease associated with high morbidity and mortality. In India alone, the prevalence of diabetes is expected to increase from 31.7 million in 2000 to 79.4 million in 2030.[1] India has earned the dubious distinction of being the ''diabetes capital of the world''. Diabetes mellitus is a systemic disease with several major complication affecting both the quality and length of life. One of these complications is periodontal disease (periodontitis). Periodontitis is much more than a localized oral infection. Recent data indicate that periodontitis may cause changes in systemic physiology. The interrelationship between peridontitis and diabetes provide an example of systemic disease predisposing to oral infection, and once that infection is established, the oral infection exacerbates systemic disease. In case, it may also be possible for the oral infection to predispose to systemic disease[2].

Diabetes: Diabetes mellitus is a metabolic disorder characterized by hyperglycemia due to defective secretion (IDDM) or activity of insulin(NIDDM). This elevation is the result of a deficiency in insulin secretion or an increased cellular resistance to the actions of insulin, leading to a variety of metabolic abnormalities involving carbohydrates, fats and proteins. A number of pathological mechanisms related to elevated levels of glucose in the blood have been defined, including the activation of the sorbitol pathway, the formation of advanced glycation end products (AGEs)[3], the damaging effect of oxidative stress and altered lipid metabolism. . These mechanisms have been associated with classical clinical complications of diabetes mellitus such as retinopathy, nephropathy, neuropathy, macrovascular disease and poor wound healing. In 1993, Löe[4] proposed that periodontal disease was the sixth complication of diabetes mellitus. In a 2008 article, Taylor and Borgnakke[5] identified periodontal disease as a possible risk factor for poor metabolic control in people with diabetes mellitus. This bidirectional relationship between periodontal disease and diabetes mellitus makes diabetes a disorder of importance to dentists and dental hygienists and to patients seen in the dental office. Long-term complications may occur in both type 1 and type 2 diabetes. Macrovascular complications include coronary artery disease, cerebrovascular disease and peripheral vascular disease. Microvascular complications include retinopathy, nephropathy and neuropathy. Retinopathy may lead to blindness, whereas progressive renal disease can lead to kidney failure. Peripheral neuropathy may lead to loss of limbs and dyesthesias (burning sensations).[6] In terms of oral manifestations, the patient may experience delayed wound healing and xerostomia, as well as an increased susceptibility to periodontal disease.[4]

Periodontitis: Periodontal disease is a group of inflammatory disease that affects the periodontal attachment apparatus. Periodontitis is a chronic oral infection that results in loss of attachment, bone destruction and eventually the loss of teeth. The signs and symptoms of periodontitis include swollen gums, discolored gums, bleeding on brushing, increased spacing between the teeth, loose teeth, pus between the teeth and gums, a bad taste, and halitosis. Clinical examinations gauging the loss of attachment are performed using periodontal probes. A radiograph is essential to detect the degree of bone loss. The major etiology of periodontitis is bacterial plaque, which harbors a variety of pathogenic bacteria. Bacterial products, such as endotoxin or lipopolysaccharide (LPS), are responsible for inducing and propagating the inflammatory cascade. Periodontitis is a slowly progressing disease but the tissue destruction that occurs is largely irreversible. In the early stages, the condition is typically asymptomatic; it is not usually painful, and many patients are unaware until the condition has progressed enough to result in tooth mobility. The pockets deepens as a result of the further destruction of fibres of the periodontal ligament (referred to as attachment loss; Fig. I) and the resorption of the alveolar bone that occurs in parallel with the progressing attachment loss. Advanced periodontitis is characterised by gingival erythema and oedema, gingival bleeding, gingival recession, tooth mobility, drifting of teeth, suppuration from periodontal pockets, and tooth loss. Periodontitis is therefore a highly prevalent, but largely hidden, chronic inflammatory disease. Furthermore, it has negative and profound impacts on many aspects of daily living and quality of life, affecting confidence, social interactions and food choices.[7] Smoking is a major risk factor; it significantly increases risk for periodontitis and severity of the condition.[8,9] Other risk factors for periodontal diseases include diabetes, conditions associated with compromised immune responses (e.g. HIV), nutritional defects, osteoporosis, medications that cause drug induced gingival overgrowth (e.g. some calcium channel blockers, phenytoin, ciclosporin), genetic factors (as yet poorly defined), and local factors (e.g. anatomical deficiencies in the alveolar bone).[8]

Figure.I : Diagram of periodontal pocket in a patient with periodontitis.



The pocket is the space between the root surface and the gingiva. In healthy gums, the base of the pocket is coincident with the cementoenamel junction (CEJ, the boundary between the enamel crown and the root) and there is no attachment loss. In periodontitis, the base of the pocket migrates apically (i.e. away from the enamel crown towards the root tip), thereby creating a pocket. The base of the pocket is therefore apical to the CEJ, and attachment loss can be measured (in mm, using a periodontal probe) from the CEJ to the base of the pocket. Pocket depth (also called probing depth) is measured in mm from the top of the pocket (i.e. from the gingival margin) to the base of the pocket. In this example, the pocket depth might be 6 mm, with 4 mm loss of attachment (as indicated in this example, pocket depth is usually greater than attachment loss due to the inflammation-induced swelling of the gingiva). The direction of insertion of a periodontal probe is indicated.

Influence Of Diabetes Mellitus On Periodontal Infection: Both diabetes and periodontitis are chronic diseases. Diabetes has many adverse effects on the periodontium, including decreased collagen turnover, impaired neutrophil function,

and increased periodontal destruction. Diabetic complications result from micro- and macrovascular disturbances. With respect to the periodontal microflora, no appreciable differences in the sites of periodontal disease have been found between diabetic and non-diabetic subjects.[10]A great deal of attention has been directed to potential differences in the immunomodulatory responses to bacteria between diabetic and non-diabetic subjects. Neutrophil chemotaxis and phagocytic activities are compromised in diabetic patients, which can lead to reduced bacterial killing and enhanced periodontal destruction.[11,12] Inflammation is exaggerated in the presence of diabetes, insulin resistance, and hyperglycemia.[13]Various studies have revealed elevated production of inflammatory products in diabetic patients.[13] Levels of the acute-phase reactants fibrinogen and C-reactive protein (CRP) have been found to be higher in people with insulin resistance and obesity.[14]

Altered immune cell function in diabetes: The function of inflammatory cells, such as neutrophils, monocytes, and macrophages, is altered in diabetic patients. Chemotaxis, adherence, and phagocytosis of neutrophils is impaired.[15]The impairment in neutrophil function may disturb host defense activity, thereby leading to periodontal destruction. In the presence of periodontal pathogens, macrophages and monocytes exhibit elevated production of cytokines, such as tumor necrosis factor (TNF)-a, which may result in further host tissue destruction.[11,16] These findings were reproduced in an animal model of diabetes in which inoculation of mice with Porphyromonas gingivalis resulted in a prolonged inflammatory response.[17]

Effects of AGEs on Periodontium: AGEs accumulate twofold in human diabetic periodontium as compared to other tissues. This accumulation plays an important role in the pathogenesis of diabetes associated periodontitis. Increased accumulation of AGEs and their interaction with RAGE in diabetic gingiva leads to vascular dysfunction and hyperpermeability, loss of effective tissue integrity and barrier function, alteration, immobilization and activation of mononuclear phagocytes, critical mediators in generation of proinflammatory cytokines and matrix metalloproteinase's (MMP's) [18]. These AGEs act to "prime" endothelial cells and monocytes, making them more susceptible to stimuli that induce the cells to produce inflammatory mediators. Accumulation of AGEs in the plasma and tissues of diabetic patients has been linked to diabetic complications. There is some speculation that AGE-enriched gingival tissue has greater vascular permeability, experiences greater breakdown of collagen fibres and shows accelerated destruction of both nonmineralized connective tissue and bone.[6] If glucose mediated AGE accumulation altered the migration and phagocytic activity of mononuclear and polynuclear cells, a more pathogenic sub gingival flora would result[11]. With maturation and transformation, the subgingival flora would become more Gram –ve and in turn produce a source of chronic systemic challenge through the ulcerated pocket epithelium. This chronic infection further trigger cytokine upregulation especially TNF-α and IL-1 leading to further connective tissue degradation and destruction.

Periodontal Vasculature: Changes affecting renal, retinal vasculature, also affect periodontium in diabetes. Increase in thickening of gingival capillary endothelial cell basement membrane and wall of small blood vessels takes place. This impairs oxygen diffusion and nutrition provision across basement membrane which alters normal tissue homeostasis leading to increased severity and progression of periodontal disease [19,20,21].

Collagen Metabolism: Increased collagen breakdown through stimulation of collagenase activity has been observed in periodontium of diabetic individuals. Collagenase primarily degrades more newly formed and therefore more soluble collagen macromolecules. Sustained hyperglycemia results in AGE modification of existing collagen with increased cross linking. This results in rapid degradation of recently synthesized collagen by host collagenase and predominance of

older highly cross linked modified collagen. Since collagen production and degradation exist as a highly balanced homeostatic mechanism, change in collagen metabolism result in altered wound healing. Impaired wound healing is a well recognized complication of diabetes and may affect any tissues including periodontium [22]. The cytokines also effect the increased production of MMPs by major cell types of periodontium. MMPs are responsible for increased bone resorption and connective tissue breakdown[23].

Influence Of Periodontal Infection On Diabetes: Periodontitis can alter systemic physiology in diabetic patients. Periodontitis can have far-reaching effects, rather than just being a mere localized oral infection.[24,25] Severe periodontitis can elicit a systemic response, with bacteria and bacterial products entering the systemic circulation. Bacteria are the major etiologic factor for periodontitis. However, no significant differences in the microbial flora have been noted between diabetic and non-diabetic subjects,[26,27] although some studies have reported higher levels of Capnocytophaga spp. in diabetic patients[6]. Some culture studies have demonstrated similarities in the bacterial flora of diabetic and non-diabetic patients with periodontitis.[26,27] Bacterial products can also play an important role in the inflammatory cascade.

Studies have shown that diabetic patients with periodontal infection have a greater risk of worsening glycemic control overtime compared to diabetic subjects without periodontal disease [28]. Periodontal interventional trials have suggested a significant potential metabolic benefit of periodontal therapy in patients with diabetes[13]. Several studies of diabetic subjects with periodontitis have shown improvements in glycemic control following scaling and root planing combined with adjunctive systemic doxycycline therapy. The magnitude of change is often about 0.9 to 1.0% in HbA1c test(glycosylated hemoglobin)[9,29]. Studies have shown that systemic infections such as viral or bacterial infections increase insulin resistance and have adverse impact on glycemic control [30]. Recent evidence suggest that chronic infections like periodontitis may induce a chronic state of insulin resistance which would then result in poor glycemic control which would contribute to the cycle of hyperglycemia, non enzymatic irreversible glycation, AGEs of protein binding with further accumulation[13]. Blood levels of TNF-□, IL-6 and Creactive proteins (pro inflammatory cytokines) are increased in patients with diabetes especially in those with periodontal disease [31]. Monocytes from patients with diabetes produce 24 to 32 times increase level of TNF α, when stimulated by periodontal pathogen than do monocytes from subjects without diabetes [32].TNFα is an antagonist to the cell surface insulin receptor substrate (IRS-1), which inhibits phosphorylation and translocation of insulin receptor [33].Resulting inhibition of intracellular glucose transport and insulin action contributing to insulin resistance. This explains why periodontitis increases the risk of poor glycemic control in patients with type 2 diabetes[28], and may also explain why improvement in glycemic control has followed periodontal therapy in studies of diabetic subjects[29].Thus periodontal treatment may reduce inflammation locally and also decrease serum levels of the inflammatory mediators that may cause decreased insulin resistance thereby positively affecting glycemic control.

Thus relation between periodontal disease and diabetes may be a two way street, a dual highway of catabolic response and tissue destruction resulting in more severe periodontal disease and less glycemic control (Fig. II). Various mechanisms of diabetic influence on periodontium are explained in figure III.

Guidelines for Dentist And Periodontist: Prevention and control of periodontal disease must be considered as an integral part of diabetes control. The principles of treatment of periodontitis in diabetic patients are the same as those for non diabetic patients. Major efforts should be directed at preventing periodontitis in patients who are at risk of diabetes. Diabetic patients with poor metabolic control should be seen more frequently especially, if periodontal

Figure II - Mechanism by which periodontitis may influence Diabetes Mellitus

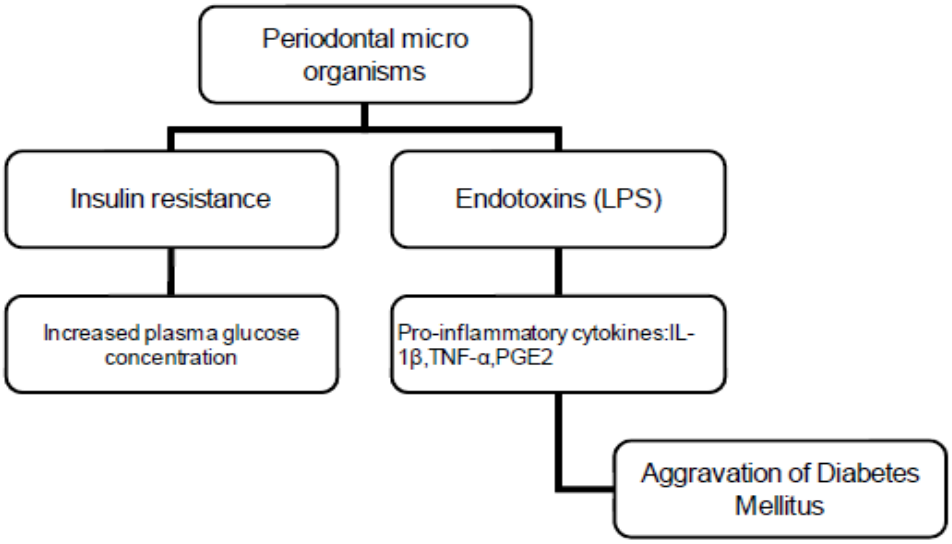
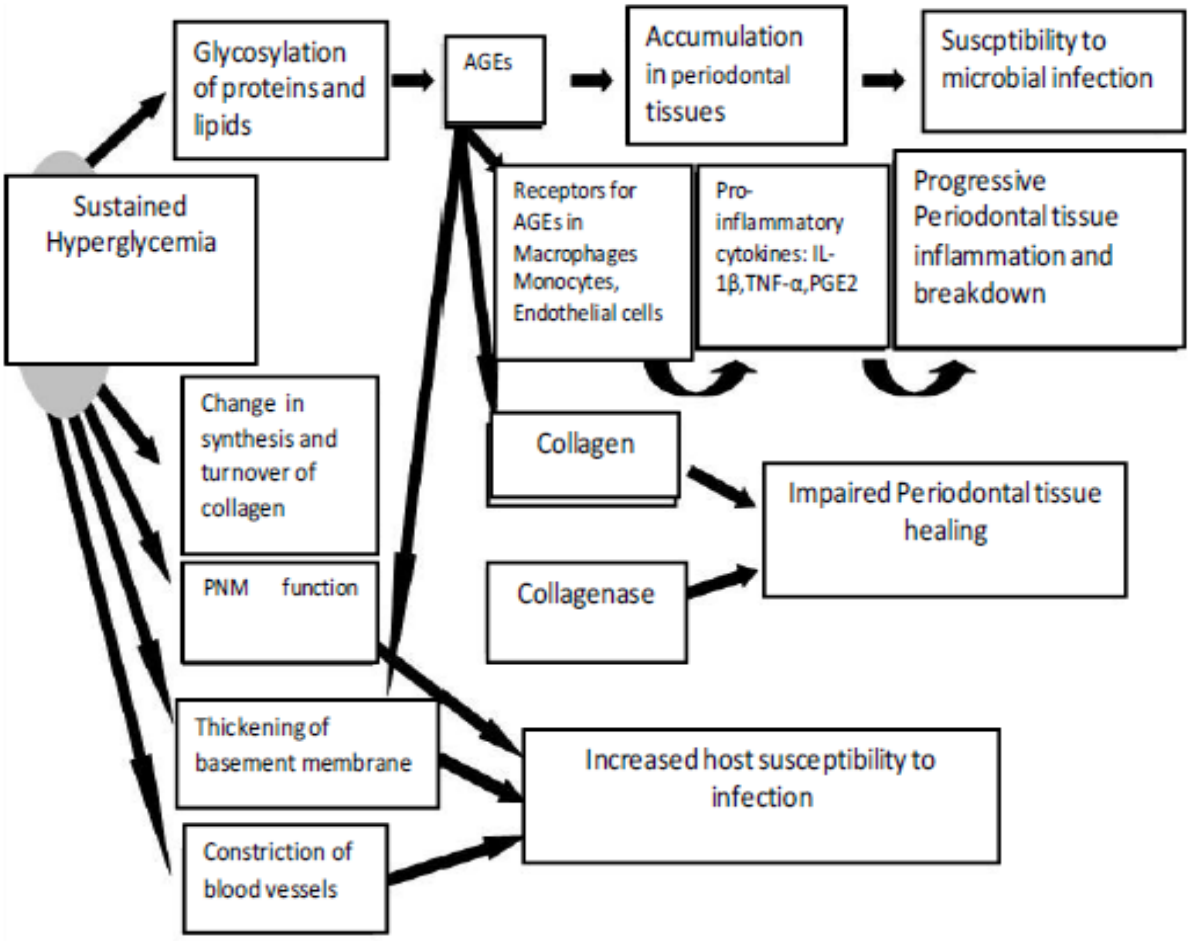


Figure III- mechanism by which diabetes can influence periodontal disease.



disease is already present. Periodontist should understand the diagnostic and therapeutic modalities used in diabetes care. They should thoroughly understand the pharmacological agents commonly used to treat diabetes and the risk they pose in the form of hypoglycemia and its treatment in dental clinic is a must. It is the duty of periodontist to educate both patient and physician about interrelationship between periodontal health and glycemic control with emphasis on inflammatory nature of periodontal disease and potential systemic effects of periodontal infection.

Conclusions: There is a two way relationship in which periodontal disease has adverse impact on glycemic control and in turn diabetes exaggerates periodontal infection, affecting the overall general health of an individual. Diabetes increases the risk of periodontal destruction, especially in patients having poor glycemic control. These patients are most likely to report to dental office with significant periodontal treatment needs. All diabetic patients should have routine periodontal evaluation and preventive therapy. The practioner, who understands the role of diabetes in etiology of oral diseases, the potential for oral infections to influence glycemic control, the current medical therapeutic approaches to diabetes and implications of diabetes on dental care provides patient with the best chances of successful treatment outcomes. The best treatment protocol includes referral of patients to respective specialists like diabetologist and periodontist for specific treatment concerns.

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