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### TWO WAY RELATION OF DIABETES MELLITUS AND PERIODONTITIS - A REVIEW

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**ABSTRACT:** The association between diabetes and periodontium is complex. Diabetes is a well established risk factor for periodontitis. Periodontitis infection complicates the severity of disease, and the degree of metabolic control of disease. Diabetes is a disease of metabolic dysregulation, primarily of carbohydrate metabolism, characterised by hyperglycemia that results from defects in insulin secretion, impaired insulin action or both. The major efforts should be directed at the prevention of periodontitis in patients at risk of developing diabetes. This proposed dual pathway of tissue destruction suggests that control of chronic periodontal infection is essential for achieving long-term control of diabetes mellitus. This dual relationship of the control of tissue destruction in chronic periodontal infection is essential also for the long term control of diabetes mellitus.

KEY WORDS: Diabetes, Periodontitis, Relation, Two way, Insulin.

### INTRODUCTION

Diabetes is like dynamite that has a devastating effect on the periodontium "The association between Diabetes and periodontium is complex: Diabetes is a well established risk factor for periodontitis. Periodontitis infection complicates the severity of disease, and the degree of metabolic control of disease.

This paper is an attempt to show the two way relationship between the two. This dual relationship of the control of tissue destruction in chronic periodontal infection is essential also for the long term control of diabetes mellitus<sup>1</sup>.

#### What Is Diabetes?

Diabetes is a disease of metabolic dysregulation, primarily of carbohydrate metabolism, charecterised by hyperglycemia that results from defects in insulin secretion, impaired insulin action or both.

### **Classification of Diabetes**

Diabetes is classified as follows:

- Type 1 diabetes (Insulin Dependent Diabetes Mellitus )
- 2. Type 2 diabetes ( non insulin Dependent Diabetes Mellitus)
- 3. Gestational Diabetes

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#### Other types of diabetes

- Genetic defects in beta cell function
- Genetic defects in insulin action
- Pancreatic disease or injuries: pancreatitis , neoplastic, cystic fibrosis, trauma, pancreatectomy,
- Infections :congenital rubella
- Drug induced or chemical induced

Largely two types of diabetes type 1 and type 2 are discussed :

Type 1 accounts for about 5 to 10% of the cases, and these patients with symptoms traditionally associated with diabetes including polyphagia ,polydypsia, polyuria ,and predisposition to infection.

Type 2 accounts for 90 to 95 % of cases and usually has an adult onset generally occurs in obese individuals. The major efforts should be directed at the prevention of periodontitis in patients at risk of developing diabetes<sup>2</sup>.

# Diabetes Mellitus And Periodontitis The Two Way Relationship:

Periodontitis is the sixth complication of diabetes (loe 1993). Infection-mediated upregulation cycle of cytokine synthesis and secretion by chronic stimulus from lipopolysaccharide (LPS) and by-products of

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periodontopathic organisms may amplify magnitude of the advanced glycation end product (AGE) mediated cytokine response in diabetes mellitus. The combination of these two pathways, infection and AGE-mediated cytokine upregulation , helps explain the increase in tissue destruction seen in diabetes ,and how periodontal infection may complicate the severity of diabetes and the degree of metabolic control, resulting in a 2 way relationship between diabetes mellitus and periodontal disease/infection.

This proposed dual pathway of tissue destruction suggests that control of chronic Periodontal infection is essential for achieving long-term control of diabetes mellitus. Connective tissue destruction taking place in periodontitis results from the interaction of bacteria and their products with mononuclear phagocytic cells and fibroblasts , triggering activation and local secretion of catabolic inflammatory mediators including primarily IL-1b,PGE2,TNF-a, and IL-6. It is well established that diabetics are more likely to develop periodontal disease, and that the disease severity is related to the duration of diabetes<sup>3</sup>.

The control of diabetes is therefore directed at controlling the blood glucose levels within normal limits, and there is clear evidence that complications can be prevented by the meticulous control of hyperglycemia. The monitoring of the effectiveness of this control is done by measuring the levels of glycated serum proteins, especially glycated -hemoglobin(HbA1c), which because of its incorporation into the red blood cells, gives an indication of the serum glucose levels over the proceeding 2 to 3 months<sup>4</sup>.

# Biological Mechanism For Diabetes Having Severe Periodontal Disease

Plausible biological mechanism why diabetes have more severe periodontal disease is the glucose- mediated AGE accumulation would affect migration and phagocytic activity of mononuclear and polymorphonuclear phagocytic cells, resulting in the establishment of a more pathogenic subgingival flora. The maturation and gradual transformation of the subgingival microflora into an essentially Gram-negative flora will in turn constitute, via the ulcerated pocket epithelium, a chronic source of systemic challenge in turn, triggers both an "infectionmediated" pathway of cytokine upregulation , especially with secretion of TNF-a and IL-1, and a state of insulin resistance ,affecting glucose-utilising pathways<sup>5</sup>.

#### Enhanced Interaction Of Advanced Glycation End Products With Their Cellular Receptor Rage

The prevalence and severity of periodontal disease is increased in patients with both Insulin-deficient and insulin-resistance forms of diabetes. A critical consequence of hyperglycemia is non-enzymatic glycation and oxidation of proteins and lipids. After a series of reversible reactions which lead to the generation of Schiff bases/Amadori products, a further series of complex molecular rearrangements ensues which results in the formation of the irreversible AGEs. AGEs accumulate during the process of normal ageing in the plasma and tissues, but to an accelerated degree in patients with diabetes. A central means by which AGEs are believed to impart their pathogenic effects is via interaction with specific cellular receptors : the best-characterized of these receptor for AGE is RAGE<sup>6</sup>.

RAGE , a member of the immunoglobulin superfamily of cell surface molecules ,is present in increased levels or target cells in diabetes ,such as endothelial cells and monocytes .One consequence of AGE-RAGE interaction is the generation of enhanced cellular oxidant stress, a means by which cell signaling pathways may be activated ,thereby resulting in altered cellular phenotype and cellular dysfunction<sup>7</sup>.

#### Enhanced Oxidant Stress Is an Important Sequelae Of Age-Rage Interaction and a means by which to perturb cellular function

AGES are present in human diabetic gingival tissue along with evidence of enhanced oxidant stress. Gingival tissue harvested from adult patients with diabetes undergoing surgery for moderate to advanced periodontal disease manifested increased AGE- immunoreactive material, compared with non- diabetic counterparts<sup>8</sup>.

# Hypothesis Proposed By Evanthia Lalla, Ira B. Lamster And Ann Marie Schmidt

Hypothesis states that AGEs accumulate in the gingival tissue of diabetic human subjects and mice. Enhanced expression of RAGE on critical target cells, such as MPs and ECs , may set into motion a cascade of events leading to a number of proinflammatory sequelae . The hypothesis is that AGE-MP RAGE interaction results chronic MP activation, with generation in of proinflammatory mediators such as TNF-∞, IL-1b ,and IL-6, mediators whose ultimate effects may result in activation collagenases of osteoclasts and /matrix metalloproteinases, therby leading to bone and connective tissue destruction. Furthermore, enhanced interactions of AGEs and EC RAGE may result, in part, in an environment in which further perpetuation of the inflammatory response is favored, for example, by enhanced EC expression of VCAM-1.Its speculated that, at least in part,an important cellular sequel of AGE-RAGE interaction is initiation of cell-signalling mechanisms by the generation of reactive oxygen intermediates<sup>9</sup>.

### Hypothesis proposed by fusanori nishimura et al

A hypothetical model for this varying VLA-5 expression due to up or down regulation of the glucose level , and the subsequent functional impairments in periodontal ligament cells, are presented here. Both hyper and hypoglycemia could modulate the biological cellular

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functions of periodontal ligament cells by inducing different levels of fibronectin receptors , both of which directly altered the repair system of periodontal connective tissues against inflammatory tissue destruction. The mechanism of VLA-5 regulation via varying glucose levels is still unknown . Recently ,however degradative enzymes such as collagenase IV ,cathepsin B ,and cathepsin D were reportedly decreased in retinal mesangial cells when cultured in a medium containing a high concentration of glucose (540 mg/dl). Consequently ,we speculate that these regulations are mainly mediated by Degrading enzymes for VLA-5, which act to maintain cellular homeostatic mechanisms ,since VLA-5 levels in cells cultured at a physiologically normal concentration of glucose can apparently be maintained consistently throughout the culture period regardless of the density of the cells .Experiments supporting this speculation are currently in progress and will be reported elsewhere<sup>10</sup>.

#### **Antibiotics In The Dual Management:**

Systemic antibiotics may induce positive changes in glycemic control when combined with mechanical debridement . Systemic antibiotics may eliminate residual bacteria following scaling and root planing , further decreasing the bacterial challenge to the host. For example Tetracyclines are known to suppress glycation of proteins and to decrease activity of tissue-degrading enzymes such as MMPs .These changes may contribute to improvement in metabolic control of diabetes .conversly, moderately well-controlled individuals with diabetes and periodonitis who are treated by mechanical therapy without adjunctive use of antibiotic , significant changes in glycemic control are less common . Thus ,although the routine use of systemic antibiotics in the treatment of chronic periodontitis is not justified, patients with poorly controlled diabetes and severe periodontitis may constitute one patient group for whom such treatment is appropriate<sup>[11]</sup>.

#### **CONCLUSION:**

To achieve good periodontal health which is our ultimate and final goal, a seemingly positive effect of periodontal therapy on the meatabolic control of diabetes is an interesting and important observation because it has far-reaching implications in the control of diabetes.

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