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DIABETES MELLITUS AND PERIODONTAL DISEASES; A TWO WAY RELATIONSHIP

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ABSTRACT

People with diabetes have a higher than normal risk of periodontal diseases. On the other hand, gum disease can often be the first sign of diabetes. Periodontal diseases are caused by dental plaque which consists of colorless soft sticky film of saliva, food particles and bacteria. These bacteria produce toxic substances that cause inflammation of gums. Chronic Periodontitis impairs the body's ability to utilize insulin whereas insulin resistance makes it difficult to achieve and sustain optimal glycemic control resulting in hyperglycemia. Poor glycemic control causes increased susceptibility to re-infection and more severe periodontal disease. That is why the relationship between diabetes and periodontal disease is sometimes referred to as a two-way path. Prevention and control of periodontal disease just like optimal glycemic control is essential in the medical management of diabetes. There is a need for appropriate health education as good oral health is important for diabetic individuals.

KEYWORDS: Diabetes, Gingivitis, Periodontal Diseases, Oral health, Gum diseases.

INTRODUCTION

Diabetes mellitus (DM) is a chronic and progressive syndrome characterized by several metabolic factors which leads to increased blood glucose levels and abnormalities of lipid metabolism due to absence or decreased level of insulin. There are three major types of the disease: Type 1, Type 2, and Gestational Diabetes. Type 1 DM includes diabetes resulting primarily from destruction of the beta cells in the Islets of Langerhans of the pancreas which often leads to absolute insulin deficiency. The cause may be idiopathic or due to a disturbance in the autoimmune process. The onset of the disease is often abrupt, and patients with this type of diabetes are more prone to ketoacidosis with wide fluctuations in plasma glucose levels.

The causes of Type 2 DM range from insulin resistance accompanied by relative insulin deficiency to a predominantly secretary defect with insulin resistance. Its onset is generally more gradual than for Type 1 DM, and this condition is often associated with obesity. Type 2 DM also carries a strong genetic component. Gestational diabetes mellitus (GDM) is a condition in which glucose intolerance begins during pregnancy. The children of mothers with GDM are at greater risk of experiencing obesity and diabetes as young adults.^[1] As well, there is a greater risk of the mother of developing Type 2 DM in the future. With all three, the body can't

make or use insulin. It affects all the body organs and their functions either directly or indirectly.

Periodontal or gum disease is a pathological inflammatory condition of the gum and bone support (periodontal tissues) surrounding the teeth. The two most common periodontal diseases are; Gingivitis which includes the inflammation of the gum at the necks of the teeth, and Periodontitis which includes the inflammation affecting the bone and tissues of the teeth and is the most serious form of the disease. Inflammation of the gum tissue surrounding the teeth is associated with the bacterial biofilm (plaque) that covers the teeth and gums. When periodontal disease affects the bone and supporting tissue, it is termed periodontitis and is characterized by the formation of pockets or spaces between the tooth and gums. The gums pull away from the tooth and supporting gum tissues are destroyed. Bone can be lost, and the teeth may loosen or eventually fall Exiting evidence indicates that inflammation (gingivitis) is required for periodontitis, however some gingivitis never transform to periodontitis. [2-3] This is because bacterial plaque accumulation is necessary for the onset of both entities but individual susceptibility is required to develop periodontitis.[3-4]

Periodontal disease a slowly progressing disease but the tissue destruction that occurs is largely irreversible.

Severe periodontitis, which may result in tooth loss, is found in 5–20% of most adult populations worldwide. [5-6]

Prevalence of Diabetes

According to International Diabetes Federation (IDF) 2019 estimates, Approximately 463 million adults (20-79 years) are living with diabetes; by 2045 this will rise to 700 million.^[7] India is currently experiencing an epidemic of DM. According to the World Health Organization, India has the unique distinction of being the country with the largest number of diabetic patients in the world. Type-2 DM accounts for more than 90% of all patients with diabetes worldwide. Government survey reveals 11.8% prevalence of diabetes in India where 12% of males and 11.7% of females were found diabetics. Nearly 40% of known diabetes was diagnosed 1-4 years back while 5.3% of known diabetes cases reported diagnosis within past one-year. The survey conducted during 2015-2019 by Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi also showed that the prevalence of known diabetes cases was 8.0% and new diabetes cases was 3.8%. Males showed a similar prevalence of diabetes (12%) as females (11.7%).^[8]

Factors Affecting Diabetes

One of every four people with diabetes don't know they have it. Type 1 DM occurs in childhood and happens either due to some family history or some infection of pancreas. Whereas, Type 2 DM happens due to obesity, insulin resistance, impaired glucose tolerance, gestational diabetes, family history, sedative life style, polycystic ovary syndrome or age, as per American Diabetic association. [9]

Prevalence of Periodontal Diseases

Periodontal diseases are prevalent both in developed and developing countries and affect about 20-50% of global population. According to recent findings from the Centers for Disease Control and Prevention, half of Americans aged 30 or older have periodontitis, the more advanced form of periodontal disease. [10] India reveals a lot of disparities in terms of ratios, one of which is the field of the oral health. The dentist-to-population ratio in the rural areas is dismally low with less than 2% dentists being available for 72% of the rural population. Statistics present the grim reality that 95% of the population in India suffers from periodontal disease, only 50% use a toothbrush, and just 2% visit the dentist. [11] Literature search revealed that only two notable studies in general population have been carried out till date the first being the National Oral Health Survey and Fluoride Mapping conducted by the Dental Council of India and the second being the multicentric study, carried out under the Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; and WHO joint project. Apart from these studies several of the other studies were conducted in different regions with some of them being hospital-based studies. All of the studies indicate a high prevalence of periodontal

diseases with almost over 70% of the population being affected with some or the other periodontal disease. [12]

Factors Affecting Periodontal Disease

The rate of progression of periodontal disease in an individual is dependent on the virulence (or strength of attack) of the bacterial plaque and on the efficiency of the local and systemic immune-inflammatory responses in the person (host). The overall balance between the bacterial plaque challenge and the body's immune-inflammatory responses is critical to periodontal health.

In this regard, it is common for more severe forms of periodontal disease to be present in individuals with compromised immune systems, e.g., those with diabetes. Other than this tobacco smoking cardiovascular diseases step stress obesity obesity female hormones age and sex are other factors which influence the occurrence of periodontal diseases.

Relationship with Diabetes

Both diabetes and periodontitis are chronic diseases. People with diabetes are more likely to have periodontal disease than people without diabetes, probably because people with diabetes are more susceptible to infections. The risk of periodontitis is increased by approximately threefold in diabetic individuals compared with non-diabetic individuals. [21] In the early 1990s periodontitis was sometimes referred to as the 'sixth complication of diabetes'. [22]

Patients with undiagnosed or poorly controlled Type 1 or Type 2 DM are at higher risk for periodontal disease. Diabetes has many adverse effects on the periodontium, decreased collagen turnover, impaired including neutrophil function, and increased periodontal destruction. Diabetic complications result microvascular 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. [23] A great deal of attention has been directed to potential differences in the immune-modulatory 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.[24-25]

There exists a 'two-way' relationship between diabetes and periodontitis and disease may make it more difficult for people who have diabetes to control their blood sugar. The mechanisms that link diabetes and periodontitis are not completely understood, but involve aspects of inflammation, immune functioning, neutrophil activity, and cytokine biology. That is, not only is diabetes a risk factor for periodontitis, but periodontitis could have a negative effect on glycaemic control. Glycosylated hemoglobin (HbA1c) allows the control of serum glucose levels in an interval of 120 d

and is a useful decision-making tool. The first clear evidence to support this hypothesis came from investigations of individuals in the Gila River Indian community. Severe periodontitis at baseline was associated with an increased risk of poor glycaemic control (HbA $_{1c}$ >9.0%) at follow-up (minimum 2 years), suggesting that severe periodontitis was a risk factor for compromised diabetes management. Further studies of the Gila River Indian Community investigated the effect of periodontitis on the development of overt nephropathy, defined as macro-albuminuria and end-stage renal disease (ESRD), in Type 2 DM. [29]

Periodontitis also progresses more rapidly in poorly controlled diabetics^[30], and early age of onset of the disease is seen as a risk factor for more severe diseases.^[31] Conversely, most well-controlled diabetic patients can maintain periodontal health and will respond favorably to periodontal therapy.^[13] Diabetes has been associated to different oral diseases such as salivary and taste dysfunction, oral bacterial and fungal infections (i.e., candidiasis), and oral mucosa lesions (i.e., stomatitis, geographic tongue, traumatic ulcer, lichen planus.^[32-33] The National Health and Nutrition Examination Survey 2009-2010 reported that prevalence of diabetes was 12.5% among periodontal patients, but only 6.3% in subjects without periodontitis.^[34]

Diabetes has many adverse effects on the periodontium, and conversely periodontitis may have deleterious effects further aggravating the condition in diabetics. The potential common patho-physiologic pathways include those associated with inflammation, altered host responses, altered tissue homeostasis, and insulin resistance. [35]

Two similar but distinct pathogenic pathways may justify the biologic plausibility, a possible common origin of the two diseases which results in a host susceptibility to either disease^[36], or a direct causal relationship in which, through the effects of advanced glycosylation end products (AGEs), diabetes triggers an increased inflammatory phenotype in cells. [37-38] Studies have shown how chronic hyperglycemia produces AGEs that can bind to specific receptors (RAGE, the receptor for advanced glycation end products) on different cells such as fibroblast, endothelial cells and macrophages [39] and produce hyper inflammatory responses, healing increased modifications, altered and predisposition to infections. Chronic periodontitis can lead to exacerbation of insulin resistance, with subsequent deterioration of glycemic control. Periodontal therapy eliminates the inflammation and helps to counteract insulin resistance. [40] Certain organisms within the microbial flora of dental plaque are the major etiologic agents of periodontitis^[41] which produce endotoxins in the form of lipopolysaccharides (LPS) that are instrumental in generating a host-mediated tissue destructive immune response. It is believed that bacterial LPS have a significant effect on insulin sensitivity

although the pathogenesis is poorly understood. [42] The release of interleukin-1 beta (IL-I β) and tumor necrosis factor- α (TNF- α) in response to bacteremia/endotoxemia has numerous metabolic effects in addition to hyperlipidemia. Elevated levels of IL-1 β are thought to play a role in the development of Type 1 DM. TNF- α has been implicated as a causative factor in insulin resistance and Type 2 DM in animal models and in human studies. [43]

Both diabetes and periodontitis can stimulate the chronic release of proinflammatory cytokines that have a deleterious effect on periodontal tissues. The chronic systemic elevation of proinflammatory cytokines caused by periodontitis may even predispose individuals to the development of Type 2 DM. Mechanical treatment of periodontitis (scaling and root planing), when combined with short-term administration of therapeutic levels of tetracycline-type antimicrobials, can temporarily improve glycemic control in diabetic patients, especially in those with advanced forms of periodontitis and poor glycemic control before treatment. [44]

CONCLUSION

Diabetes mellitus and periodontal disease are among the most prevalent human disorders. Frequently these two medical problems are present at the same time as in many people. There appears to be a relationship between the two processes, whereby the consequences of one affect the expression of the other. The relationship between these 2 maladies appears bidirectional; the presence of one condition tends to promote the other, and that the meticulous management of either may assist treatment of the other. There are many aspects of this relationship that remain unclear. The signs, symptoms, and clinical presentation of periodontitis need to be recognized by physicians so that diabetic patients are promptly referred to dentists for treatment and similarly dentists should understand the parameters of glycemia that are used to establish a diagnosis of diabetes and the methods used in diabetic care, thus potentially preventing further complications.

REFERENCES

- Meltzer S, Leiter L, Daneman D, Gerstein HC, Lau D, Ludwig S, Yale JF, Zinman B, Lillie D. 1998 clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. CMAJ, 1998; 159(8): S1-29.
- Listgarten MA, Schifter CC, Laster L. 3-year longitudinal study of the periodontal status of an adult population with gingivitis. J Clin Periodontol, Mar, 1985; 12(3): 225-238.
- 3. Löe H, Anerud A, Boysen H, Morrison E. Natural history of periodontal disease in man. Rapid, moderate and no loss of attachment in Sri Lankan laborers 14 to 46 years of age. J Clin Periodontol, May, 1986; 13(5): 431-445.

- 4. Page RC. Milestones in periodontal research and the remaining critical issues. J Periodontal Res., Oct, 1999; 34(7): 331-339.
- 5. Albandar JM. Epidemiology and risk factors of periodontal diseases. Dent Clin North Am, 2005; 49(3): 517-532.
- Khalili J. Periodontal disease: an overview for medical practitioners. LikSprava, Apr-Jun, 2008; (3-4): 10-21.
- International Diabetes Federation. IDF Diabetic Atlas 9th Edition. Available from URL; https://diabetesatlas.org/en/, retrieved on December 10, 2019.
- 8. Sharma, NC. 10 October 2019. "Government survey found 11.8% prevalence of diabetes in India", Available from URL;https://www.livemint.com/science/health/government-survey-found-11-8-prevalence-of-diabetes-in-india-11570702665713.html, retrieved on December 10, 2019.
- American Diabetic Association. "Good to Know: Factors Affecting Blood Glucose". Clinical Diabetes, Apr, 2018; 36(2): 202-202. Available from URL: https://olinical.diabetesiouspels.org/content/26/2/202
 - https://clinical.diabetesjournals.org/content/36/2/202 , retrieved on December 10, 2019
- 10. American Academy of Periodontology. Periodontal Disease Fact Sheet 2019, "The Prevalence of Periodontal Disease", retrieved on December 11, 2019.Available from URL: https://www.perio.org/newsroom/periodontaldisease-fact-sheet
- 11. Blas E, Kurup AS. Equity, Social Determinants and Public Health Programmes. Geneva: World Health Organization, 2010; 291.
- 12. Kolte A. Periodontal disease prevalence: Right time to address the challenges. J Indian Soc Periodontol, 2018; 22: 194-195.
- 13. Pucher J, Stewart J. Periodontal disease and diabetes mellitus. Curr Diab Rep., Feb, 2004; 4(1): 46-50.
- 14. Kubota M, Tanno-Nakanishi M, Yamada S, Okuda K, Ishihara K. Effect of smoking on subgingivalmicroflora of patients with periodontitis in Japan. BMC Oral Health, Jan 5, 2011; 11: 1.
- Zhu J, Quyyumi AA, Norman JE, Csako G, Waclawiw MA, Shearer GM, Epstein SE. Effects of total pathogen burden on coronary artery disease risk and C-reactive protein levels. Am J Cardiol, Jan, 15, 2000; 85(2): 140-146.
- Merchant AT, Pitiphat W, Ahmed B, Kawachi I, Joshipura K. A prospective study of social support, anger expression and risk of periodontitis in men. J Am Dent Assoc, Dec, 2003; 134(12): 1591-1596.
- 17. Suvan J, D'Aiuto F, Moles DR, Petrie A, Donos N. Association between overweight/obesity and periodontitis in adults. A systematic review. Obes Rev., May, 2011; 12(5): e381-404.
- 18. López-Marcos JF, García-Valle S, García-Iglesias AA. Periodontal aspects in menopausal women undergoing hormone replacement therapy. Med Oral

- Patol Oral Cir Bucal, Mar-Apr, 2005; 10(2): 132-141.
- Genco RJ. Current view of risk factors for periodontal diseases. J Periodontol, 1996; 67(10): 1041-1049.
- 20. Slade GD, Spencer AJ. Periodontal attachment loss among adults aged 60+ in South Australia. Community Dent Oral Epidemiol, Aug, 1995; 23(4): 237-42
- 21. Mealey BL, Oats TW. Diabetes mellitus and periodontal disease. J Periodontol, Aug, 2006; 77(8): 1289-303.
- 22. Löe H. Periodontal disease. The sixth complication of diabetes mellitus. Diabetes Care, Jan, 1993; 16(1): 329-334.
- 23. Zambon JJ, Reynolds H, Fisher JG, Shlossman M, Dunford R, Genco RJ. Microbiological and immunological studies of adult periodontitis in patients with non-insulin dependent diabetes mellitus. J Periodontol, 1988; 59: 23-31.
- Manoucher PM, Spagnuolo PJ, Rodman HM, Bissada NF. Comparison of neutrophil chemotactic response in diabetic patients with mild and severe periodontal disease. J Periodontol, 1981; 52: 410-415.
- 25. McMullen JA, Van Dyke TE, Horoszewicz HU, Genco RJ. Neutrophil chemotaxis in individuals with advanced periodontal disease and a genetic predisposition to diabetes mellitus. J Periodontol, 1981; 52: 167-173.
- 26. Taylor GW. Bidirectional interrelationships between diabetes and periodontal diseases: an epidemiologic perspective. Ann Periodontol, Dec, 2001; 6(1): 99-112.
- 27. Taylor J J, Preshaw P M, Lalla E. A review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. J Clin Periodontol, 2013; 40(14): S113–134.
- Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M, Knowler WC, Pettitt DJ. Severe periodontitis and risk for poor glycemic control in patients with non-insulin-dependent diabetes mellitus. J Periodontol, Oct, 1996; 67(10): 1085-1093.
- 29. Shultis WA, Weil EJ, Looker HC, Curtis JM, Shlossman M, Genco RJ, Knowler WC, Nelson RG. Effect of periodontitis on overt nephropathy and end-stage renal disease in type 2 diabetes. Diabetes Care, Feb, 2007; 30(2): 306-311.
- 30. Seppälä B, Seppälä M, Ainamo J. A longitudinal study on insulin-dependent diabetes mellitus and periodontal disease. J Clin Periodontol, Mar, 1993; 20(3): 161-165.
- Thorstensson H, Hugoson A. Periodontal disease experience in adult long-duration insulin-dependent diabetics. J Clin Periodontol, May, 1993; 20(5): 352-358.
- 32. Saini R, Al-Maweri SA, Saini D, Ismail NM, Ismail AR. Oral mucosal lesions in non oral habit diabetic patients and association of diabetes mellitus with

- oral precancerous lesions. Diabetes Res Clin Pract, Sep, 2010; 89(3): 320-326.
- 33. Sandberg GE, Sundberg HE, Fjellstrom CA, Wikblad KF. Type 2 diabetes and oral health: a comparison between diabetic and non-diabetic subjects. Diabetes Res Clin Pract, Sep, 2000; 50(1): 27-34.
- 34. Arora N, Papapanou PN, Rosenbaum M, Jacobs DR Jr, Desvarieux M, Demmer RT. Periodontal infection, impaired fasting glucose and impaired glucose tolerance: results from the Continuous National Health and Nutrition Examination Survey 2009-2010. J Clin Periodontol, 2014; 41(7): 643-652.
- 35. Grover HS, Luthra S. Molecular mechanisms involved in the bidirectional relationship between diabetes mellitus and periodontal disease. J Indian Soc Periodontol, May, 2013; 17(3): 292-301.
- Emrich LJ, Shlossman M, Genco RJ. Periodontal disease in non-insulin-dependent diabetes mellitus. J Periodontol, 1991; 62(2): 123-131.
- 37. Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. Ann Periodontol, Dec, 2001; 6(1): 91-98.
- 38. Grossi SG, Genco RJ. Periodontal disease and diabetes mellitus: a two-way relationship. Ann Periodontol, Jul, 1998; 3(1): 51-61.
- 39. Brownlee M. Glycation products and the pathogenesis of diabetic complications. Diabetes Care, 1992; 15(12): 1835-1843.
- Genco RJ, Grossi SG, Ho A, Nishimura F, Murayama Y. A proposed model linking inflammation to obesity, diabetes and periodontal infections. J Periodontol, 2005; 76: 2075-2084.
- 41. Liljenberg B, Lindhe J, Berglundh T, Dahlén G, Jonsson R. Some microbiological, histopathological and immuno-histochemical characteristics of progressive periodontal disease. J Clin Periodontol, 1994; 21: 720-727.
- 42. Agwunobi AO, Reid C, Maycock P, Little RA, Carlson GL. Insulin resistance and substrate utilization in human endotoxemia.. J Clin Endocrinol Metab, 2000; 85: 3770-3778.
- Moller DE. Potential role of TNF-alpha in the pathogenesis of insulin resistance and type 2 diabetes. Trends Endocrinol Metab, 2000; 11: 212-217.
- 44. Mealey BL, Rethman MP. Periodontal disease and diabetes mellitus. Bidirectional relationship. Dent Today, Apr, 2003; 22(4): 107-113.