

Role of Resistin, Adiponectin, Glutamic Acid Decarboxylase (GAD) Auto-Antibodies, HbA1c, Lipoproteins, Periodontal Parameters In Periodontitis And Their Correlation With Diabetes Mellitus.

Purnima Dey Sarkar¹, Shiv Narayan Lahariya¹

¹Department of Biochemistry, M. G. M. Medical College, Indore, M.P.(India).

Received: April 2018

Accepted: April 2018

Copyright: © the author(s), publisher. Annals of International Medical and Dental Research (AIMDR) is an Official Publication of “Society for Health Care & Research Development”. It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: The link between periodontal disease and type 2 diabetes Mellitus (T2DM) has been suggested through a number of clinical and epidemiological studies. Several studies have shown that the prevalence, incidence and severity of periodontitis is increased in the presence of diabetes. Thus, diabetes is considered to be a risk factor for gingivitis and periodontitis. **Methods:** For this study newly diagnosed type 2 diabetic and periodontitis patients are selected. BMI of all patients is calculated by using the formula weight in Kg/m². Brief clinical history, Blood pressure, dietary habit and information on physical activity are taken before entry of all patients. **Results:** Resistin, adiponectin, glutamic acid decarboxylase (GAD) auto-antibodies, HbA1c, lipoproteins, periodontal parameters and blood sugar have significant role in periodontitis with diabetes mellitus. **Conclusion:** Diabetes mellitus is a systemic disease with several major complications 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 interrelationships between periodontitis and diabetes provide an example of systemic disease predisposing to oral infection, and once that infection is established, the oral infection exacerbates systemic disease.

Keywords: Periodontitis, diabetes mellitus, lipoproteins, inflammation.

INTRODUCTION

Diabetes is a multifactorial, life-threatening chronic disease characterized by a dysregulation of the endocrine and metabolic pathways involved in the control of blood glucose levels resulting in hyperglycemia. Uncontrolled diabetes gradually impacts on the nervous and circulatory systems, resulting in irreversible long-term complications.

In 2010, approximately 8.3 % of the US population—or 25.8 million people—had diabetes either diagnosed (18.8 million) or undiagnosed (7.0 million) and a further 79 million people were estimated to have pre-diabetes according to the Centers for Disease Control and Prevention.^[1]

The prevalence of diabetes mellitus for all age groups worldwide was estimated to be 2.8% in 2000 and an anticipated 4.4% in 2030. The total number of people in the world with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030.

India ranked number one as the country with the highest number of diabetes patients in 1995, at 31.7 million in 2000, with a projected 57.2 million in 2025, and 79.4 million in 2030, retaining its top position. To a greater extent Asian Indians have a racial predisposition and other unique risk factors to develop diabetes mellitus. Diabetes mellitus has acquired a pandemic status in India.^[2-6]

Chronic hyperglycemia is a hallmark of diabetes regardless of the pathophysiological mechanism of the disease and is regarded as a central player in the development of acute complications—such as hypoglycemic coma, ketoacidotic coma, hyperosmolar non-ketonic coma, myocardial infarction (MI), and stroke—and chronic complications—such as diabetic nephropathy, retinopathy, neuropathy, cardiovascular diseases, peripheral vascular diseases, and periodontal diseases (PDs). The prevalence of diabetes can vary widely depending on geography, age, sex and race.

The link between periodontal disease and type 2 diabetes Mellitus (T2DM) has been suggested through a number of clinical and epidemiological studies.^[7,8] Several studies have shown that the prevalence, incidence and severity of periodontitis is increased in the presence of diabetes.^[9-13] Thus,

Name & Address of Corresponding Author

Dr. Shiv Narayan Lahariya
Department of Biochemistry,
M. G. M. Medical College,
Indore,
M.P.(India).

diabetes is considered to be a risk factor for gingivitis and periodontitis.^[7,14]

Periodontal infection is a complication that can be responsible of damaging systemic physiology in diabetic patients. Periodontitis may be more than a confined oral infection; the consequences have been assumed to be far-reaching. Chronic and severe forms of this condition can follow a systemic response of the bacteria and bacterial result products that are outspread due to the collapse of the periodontal apparatus (that is composed from the ligament attachment around the tooth, the gingival tissues and bone). The interdependency between periodontal disease and diabetes is an example that a systemic disease can predispose to oral infection, and then once that infection is settled, the oral infection can augment the progression of systemic disease.^[15,16]

Periodontal diseases are the most common diseases known to humanity. The two major stages of periodontal diseases are gingivitis and periodontitis. In the early stage of gingivitis, the inflammation is located to the gingiva, and is reversible, can usually be treated with good oral hygiene. The second stage involves the extension of inflammation and results in tissue destruction and alveolar bone resorption, stage called periodontitis.^[17]

Research in several countries indicates that 5 – 20% of any population will have severe periodontal disease and a majority of adults suffer from moderate forms of this disease.^[18] Evidence suggests that one out of two adults above the age of 35 years have periodontal disease in India, and 35% of the teeth extracted are as a consequence of periodontal disease.^[19] One study reported 13.3, 12.5, 29.1, and 97% prevalence of various periodontal parameters.^[20]

The increased prevalence and severity of periodontal disease typically seen in patients with diabetes mellitus, especially those with poor metabolic control, has led to the designation of periodontal disease as the sixth complication of Diabetes.^[21] The American Diabetic Association has officially recognized that periodontal disease is common in patients with diabetes, and the Association's Standards of Care include taking a history of current or past dental infections as part of the medical examination.^[22,23]

MATERIALS AND METHODS

For this study newly diagnosed type 2 diabetic and periodontitis patients are selected with prior permission of ethical committee. Patients are taken from outpatient department of periodontics Govt. Dental College Indore. This study is conducted in the department of Biochemistry; M. G. M. Medical College Indore M.P. Written consent is taken from all patients. BMI of all patients is calculated by using the formula weight in Kg/m². Brief clinical history,

Blood pressure, dietary habit and information on physical activity are taken before entry of all patients.

Sample size

1. Control group (healthy non-diabetic, non-periodontitis) – 100
2. Study group – (a) Non diabetic adults with periodontitis – 150 (b) Diabetic adult with periodontitis – 150

Methodology:

- Estimation of Glycosylated Hb (HbA1c) is done with the help of semi auto-analyzer diagnostic kit.
- Estimation of fasting blood sugar is done by GOD-POD method.
- Estimation of serum Total cholesterol is done by enzymatic method.
- Estimation of serum triglycerides is done by enzymatic method.
- Estimation of high density lipo-protein is done by direct HDL-cholesterol method.
- Low density lipo-protein is done by enzymatic method.
- Serum Glutamic acid decarboxylase auto-antibodies, Resistin & Adiponectin are determined by ELISA method.

RESULTS

Analysis of resistin showed a significant relationship between periodontal disease and in both diabetics and non-diabetics. Serum resistin levels in diabetics with periodontitis is 3.71 ± 1.42 ng/ml, ($p < 0.0001$), While in non-diabetics with periodontitis is 4.59 ± 1.04 ng/ml, ($p < 0.0001$) when compared to control groups (non-periodontitis and non- diabetics) 1.54 ± 0.51 ng/ml.

We confirm that resistin levels with T2DM were significantly higher than those of healthy subjects. Serum resistin showed a significant ($p < 0.0001$) positive correlation with HbA1c.

Serum levels of adiponectin in the diabetics with periodontitis are slightly lower 4.48 ± 0.96 ($\mu\text{g/ml}$) than in non-diabetics with periodontitis is 4.83 ± 1.10 ($\mu\text{g/ml}$) when compared to healthy subjects 6.95 ± 1.21 ($\mu\text{g/ml}$). This relationship showed a significant correlation with diabetes and periodontitis .

BMI is significantly higher in the diabetics with periodontitis ($p < 0.0001$). Other variables of obesity are higher in the diabetics with periodontitis, but the differences are not significant.

Age is not significant with the diabetics with periodontitis 43.33 ± 10.08 and non-diabetics and periodontitis 43.87 ± 7.30 when compared to healthy controls groups 41.53 ± 6.37 and $p < 0.155$.

Periodontal parameters such as probing depth, attachment loss, bleeding index also have significant relationship with diabetics with periodontitis and non

diabetics with periodontitis when compared to healthy control groups and $p < 0.0001$.

Glutamic acid decarboxylase auto-antibodies is found significant relation with the diabetics with periodontitis ($p < 0.030$) when compared to control healthy groups.

The level of Total cholesterol and triglycerides is also found significant correlation with diabetics with periodontitis and non diabetics with periodontitis when compared to healthy control groups and $p < 0.0001$.

Study of low density Lipoproteins (LDL) showed a significant relationship between periodontal disease and in both diabetics and non-diabetics. Serum LDL levels in diabetics with periodontitis is

123.2 ± 3.61 mg/dL, ($p < 0.0001$), While in non-diabetics with periodontitis is 126.41 ± 3.2 mg/dL, ($p < 0.0001$) when compared to control groups (non-periodontitis and non- diabetics) 126.98 ± 4.1 mg/dL. High density Lipoproteins (HDL) showed a significant relationship between periodontal disease and in both diabetics and non-diabetics. Serum HDL levels in diabetics with periodontitis is 35.7 ± 2.35 mg/dL, ($p < 0.0001$), While in non-diabetics with periodontitis is 36.2 ± 2.45 mg/dL, ($p < 0.0001$) when compared to control groups (non-periodontitis and non- diabetics) 37.2 ± 0.72 mg/dL.

Very low density Lipoproteins (VLDL) also showed a significant relationship between periodontal disease and in both diabetics and non-diabetics.

Table 1: Comparison between Three Groups (Diabetes mellitus +Periodontitis, Non-Diabetes mellitus +Periodontitis and Non-Diabetes mellitus +Non-Periodontitis)

Characteristics (mean ±SD)	DM + P (150)	NDM+ P (150)	NDM +NP (100)	F -Value	P -value
Age (years)	43.33 ±10.08	43.87 ± 7.30	41.53 ± 6.37	1.880	0.155
BMI (kg/m ²)	24.30 ± 3.42	23.71 ± 3.78	21.19 ± 3.13	17.780	<0.0001
HbA1c (%)	7.57 ± 1.85	5.53 ± 0.38	4.97 ± 0.23	125.227	<0.0001
PD (mm)	3.48 ± 0.77	3.94 ± 0.63	2.18 ± 0.61	141.203	<0.0001
AL (mm)	2.63 ± 1.81	3.34 ± 1.17	3.68 ± 0.23	15.548	<0.0001
BI	2.53 ± 0.77	2.91 ± 0.75	0.69 ± 0.46	266.248	<0.0001
Adiponectin (µg/ml)	4.48 ± 0.96	4.83 ± 1.10	6.95 ± 1.21	105.220	<0.0001
Resistin (ng/ml)	3.71 ± 1.42	4.59 ± 1.04	1.54 ± 0.51	314.068	<0.0001
HDL (mg/dL)	35.7 ± 2.35	36.2 ± 2.45	37.2 ± 0.721	9.687	<0.0001
LDL (mg/ dL)	123.2 ± 3.61	126.41 ± 3.2	126.98 ± 4.1	117.355	<0.0001
Fasting blood glucose (mg/ dL)	142.3 ± 5.26	102.72 ± 2.36	92.4 ± 3.17	137.252	<0.0001
Triglyceride (mg/dL)	149.2 ± 19.3	127.4 ± 12.6	120.36 ± 2.3	139.152	<0.0001
Total cholesterol (mg/dL)	252 ± 10.6	253.6 ± 9.6	210.1 ± 13.6	269.581	<0.0001
VLDL (mg/dL)	39.5 ± 1.35	37.25 ± 0.29	34.18 ± 1.81	271.723	<0.0001

BMI=Body Mass Index, PD= Probing Depth, AL=Attachment Loss, BI=Bleeding Index, DM=Diabetes Mellitus, P=Periodontitis, NDM=Non Diabetes Mellitus, NP=Non Periodontitis

Table 2: Glutamic acid decarboxylase (GAD) auto-antibodies

	GAD auto-antibodies		Chi Sq	P value
	Present	Absent		
DM+P	69	81	7.03	0.030
NDM+P	78	72		
NDM+NP	67	33		

DISCUSSION & CONCLUSION

Diabetes mellitus is a systemic disease with several major complications 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 interrelationships between periodontitis 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 this case, it may also be possible for the oral infection to predispose to systemic disease. In order to understand the cellular/molecular mechanisms responsible for such a cyclical association, one must identify common physiological changes associated with diabetes and periodontitis that produce a

synergy when the conditions coexist. A potential mechanistic link involves the broad axis of inflammation, specifically immune cell phenotype, serum lipid levels, and tissue homeostasis. Diabetes-induced changes in immune cell function produce an inflammatory immune cell phenotype (upregulation of proinflammatory cytokines from monocytes/polymorphonuclear leukocytes and downregulation of growth factors from macrophages). This predisposes to chronic inflammation, progressive tissue breakdown, and diminished tissue repair capacity. Periodontal tissues frequently manifest these changes because they are constantly wounded by substances emanating from bacterial biofilms. Diabetic patients are prone to elevated low density lipoprotein cholesterol and triglycerides (LDL/TRG) even when blood glucose levels are well controlled. This is significant, as recent studies demonstrate that hyperlipidemia may be one of the factors associated with diabetes-induced immune cell alterations. Recent human studies have established a relationship between high serum lipid levels and periodontitis. Some evidence now suggests that periodontitis itself may lead to elevated LDL/TRG. Periodontitis-induced bacteremia/endotoxemia has been shown to cause elevations of serum proinflammatory cytokines such as interleukin-1 beta (IL-1 beta) and

tumor necrosis factor-alpha (TNF-alpha), which have been demonstrated to produce alterations in lipid metabolism leading to hyperlipidemia. Within this context, periodontitis may contribute to elevated proinflammatory cytokines/serum lipids and potentially to systemic disease arising from chronic hyperlipidemia and/or increased inflammatory mediators. These cytokines can produce an insulin resistance syndrome similar to that observed in diabetes and initiate destruction of pancreatic beta cells leading to development of diabetes. Thus, there is potential for periodontitis to exacerbate diabetes-induced hyperlipidemia, immune cell alterations, and diminished tissue repair capacity. It may also be possible for chronic periodontitis to induce diabetes. Diabetes mellitus has become a global health problem and the risk of diabetes is growing daily. The chances of having other health problems associated with diabetes are also increasing. The prevalence of periodontal disease in diabetes is high as compared to non-diabetics, showing a significant correlation between diabetes and periodontal disease.

REFERENCES

- Centers for Disease Control and Prevention, National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Available at: www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf (accessed June 25, 2012).
- Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes-Estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047-53.
- King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: Prevalence, numerical estimates, and projections. *Diabetes Care*. 1998;21:1414-31
- Pradeepa R, Deepa R, Mohan V. Epidemiology of diabetes in India-current perspective and future projections. *J Indian Med Assoc*. 2002;100:144-8.
- King H, Rewers M. WHO ad hoc diabetes reporting group: Global estimates for prevalence of diabetes and IGT in adults. *Diabetes Care*. 1993;16:157-77.
- Gupta OP, Phathak S. Pandemic trends in prevalence of diabetes mellitus and associated coronary heart disease in India-Their causes and prevention. *Int J Diab Dev Ctries*. 2003;23:37-49.
- Preshaw PM, Foster N, Taylor JJ. Cross-susceptibility between periodontal disease and type 2 diabetes mellitus: an immunobiological perspective. *Periodontol* 2000 45:138-157.
- Preshaw PM. Diabetes and periodontal disease. *International Dental Journal* 2008;58:237-243.
- Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. *Ann Periodontol* 2001;6:91-96.
- Novak MJ, Potter RM, Blodgett J, Ebersole JL. Periodontal disease in Hispanic Americans with type 2 diabetes. *J Periodontol* 2008;79:629-636.
- Fernandes JK, Wiegand RE, Salinas CF, Grossi SG, Sanders JJ, Lopes-Virella MF, et al. Periodontal disease status in gullah african americans with type 2 diabetes living in South Carolina. *J Periodontol* 2009;80:1062-1068.
- Matu NK, Stephen L, Lalloo R. Prevalence and severity of periodontal disease: type 2 diabetics versus non-diabetics. *SADJ* 2009;64:66-68.
- Um YJ, Jung UW, Kim CS, Bak EJ, Cha JH, Yoo YJ, et al. The influence of diabetes mellitus on periodontal tissues: a pilot study. *J Periodontal Implant Sci* 2010;40:49-55.
- Mealey BL, Oates TW. Diabetes mellitus and periodontal diseases. *J Periodontol* 2006;77:1289-1303.
- Southerland JH, George W. Diabetes and Periodontal Infection: Making the Connection, *Clinical Diabetes* October 2005 vol. 23 no. 4 171-178.
- Janket SJ, Wightman A, Baird AE. Does periodontal treatment improve glycemic control in diabetic patients? A meta-analysis of intervention studies. *J Dent Res* 2005.;84:1154-9.
- Grossi SG, Skrepcinski FB, DeCaro T. Treatment of periodontal disease in diabetics reduces glycosylated hemoglobin. *J Periodontol*. 1997; 68:713-719.
- Position paper: Epidemiology of periodontal diseases. American Academy of Periodontology. *J Periodontol*. 1996;67:935-45.
- Kulkarni AT, Sachdeva NI. The problems of Oral Health in India. *Swasth Hind*. 1995;13:62-64.
- Sood M. A study of epidemiological factors influencing periodontal diseases in selected areas of District Ludhiana, Punjab. *Indian J Community Med*. 2005;30:70-1.
- Löe H. Periodontal disease: The sixth complication of diabetes mellitus. *Diabetes Care*. 1993;16:329-34.
- American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 1998;21:S23-31.
- Expert committee on the diagnosis and classification of diabetes mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2003;26:S5-20.

How to cite this article: Sarkar PD, Lahariya SN. Role of Resistin, Adiponectin, Glutamic Acid Decarboxylase (GAD) Auto-Antibodies, HbA1c, Lipoproteins, Periodontal Parameters In Periodontitis And Their Correlation With Diabetes Mellitus. *Ann. Int. Med. Den. Res*. 2018; 4(4):BC01-BC04.

Source of Support: Nil, **Conflict of Interest:** None declared