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Role of adipokines in periodontal disease with diabetes mellitus and without diabetes mellitus

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ABSTRACT

Background: There is general agreement that there is a significant relationship between diabetes and periodontitis. Many studies have shown a high prevalence of periodontitis in diabetic patients. In addition a higher prevalence and more aggressive periodontitis are found in patients with poorly controlled diabetes. The duration of having diabetes is an important factor that affects the progression and severity of periodontitis. In this the adipokines play a significant role in diabetes mellitus type -2 and periodontal disease. **Materials and Methods:** A total of 150 periodontitis patients with diabetes mellitus and 150 periodontitis patients without diabetes mellitus have selected for the study. Fasting blood sugar and HbA1c, Resistin and Adiponectin levels have compared with 100 healthy non-diabetics, non -periodontitis subjects. Fasting blood sugar, HbA1c have done by semi auto-analyzer diagnostic kit and Resistin, Adiponectin by ELISA Method (Kit Method). **Results:** Analysis of resistin has 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 are significantly higher than those of healthy subjects. Serum resistin also 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 (μ g/ml) than in non diabetics with periodontitis is 4.83 ± 1.10 (μ g/ml) when compared to healthy subjects 6.95 ± 1.21 (μ g/ml). This relationship showed a significant correlation with diabetes and periodontitis. BMI is significantly higher in the diabetics with periodontitis ($p < 0.0001$). Age is not significant with the diabetics with periodontitis 43.33 ± 10.08 and non-diabetics with 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 $p < 0.0001$. **Conclusion:** Periodontal disease and diabetes mellitus are closely associated and are highly prevalent chronic disease with many similarities in pathobiology. Diabetes can lead to several health complications, including periodontal disease. Periodontal disease or gum disease is one of the most common causes of teeth loss among diabetic patients.

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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.

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 [1,2]. Several studies have shown that the prevalence, incidence and severity of periodontitis is increased in the presence of diabetes [3-7]. Thus, diabetes is considered to be a risk factor for gingivitis and periodontitis [1,8].

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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[9,10].

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 [11].

This study reviews the relationship between diabetes and oral health, particularly focusing on periodontal diseases. Periodontitis is more prevalent and severe in patients with diabetes than in normal population. Periodontitis and diabetes are associated with each other. [10]

Materials and Methods:

The study protocol has in keeping with the ethical guidelines of the 1975 declaration of Helsinki and all the patients have gave written informed consent to the study. Patients have taken from outpatient department of Periodontics, Govt. Dental College Indore. This study has conducted in the department of Biochemistry; M.G.M. Medical College Indore M.P. 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 have taken before entry of all patients.

A total of 150 periodontitis patients with diabetes mellitus and 150 periodontitis patients without diabetes mellitus have selected for the study. Fasting blood sugar and HbA_{1c}, Resistin and Adiponectin level have compared with 100 healthy non-diabetics, non-periodontitis subjects. Fasting blood sugar, HbA_{1c} have done by semi auto-analyzer diagnostic kit and Resistin, Adiponectin by ELISA Method (Kit Method).

Observations tables & Results:

TABLE 1: 2005 American Diabetes Association Criteria for the Diagnosis of Diabetes Mellitus

	Normal	Diabetes
Fasting plasma glucose (mg/dl)	<100	≥126
Casual plasma glucose (mg/dl)		≥200 plus symptoms of diabetes
2-hour PG* (mg/dl)	<140	≥200

*2-hour postload glucose (PG) using the 2-hour oral glucose tolerance test

TABLE 2 Correlation between HbA_{1c} Levels and Mean Plasma Glucose Levels

HbA _{1c} (%)	Mean Plasma Glucose (mg/dl)
6	135
7	170
8	205
9	240
10	275
11	310
12	345

The HbA_{1c} test provides an estimate of the average glucose level over the 30 to 90 days preceding the test. It does not account for short-term fluctuations in plasma glucose levels.

TABLE 3. American Diabetes Association Recommendations for HbA_{1c} Levels

HbA _{1c} (%)	Interpretation
<6	Normal value
<7	Treatment goal for patient with diabetes; diet, exercise, and/or medications should control glucose levels well enough to maintain HbA _{1c} values <7%
>8	Physician intervention in diabetes management regimen is recommended to improve glycemic control

TABLE 4. Comparison between Normal Healthy Controls and Study Groups

Parameters	Normal healthy controls N=100	Periodontitis with diabetes mellitus N=150	Periodontitis without diabetes mellitus N=150	P-Value
	Mean ± S. D.	Mean ± S. D.	Mean ± S. D.	
FBG(mg/dl)	92.4±3.17	142.3±5.26	102.72±2.36	<0.0001
HbA _{1c} (%)	4.97±0.23	7.57±1.85	5.53±0.38	<0.0001
Resistin(ng/ml)	1.54±0.51	3.71±1.42	4.59±1.04	<0.0001
Adiponectin (µg/ml)	6.95±1.21	4.48±0.96	4.83±1.10	<0.0001
BMI(kg/m ²)	21.19±3.13	24.30±3.42	23.71±3.78	<0.0001
PD(mm)	2.18±0.61	3.48±0.77	3.94±0.63	<0.0001
AL(mm)	3.68±0.23	2.63±1.81	3.34±1.17	<0.0001
BI	0.69±0.46	2.53±0.77	2.91±0.75	<0.0001
Age(years)	41.53±6.37	43.33±10.08	43.87±7.30	0.155

BMI: body mass index; FBG: fasting blood glucose; PD: probing depth; AL: attachment loss; BI: bleeding index.

Results:

Analysis of resistin has 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 are significantly higher than those of healthy subjects. Serum resistin also 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 (μ g/ml) than in non-diabetics with periodontitis is 4.83 ± 1.10 (μ g/ml) when compared to healthy subjects 6.95 ± 1.21 (μ g/ml). The present study has demonstrated significant difference in adiponectin among diabetes mellitus type 2 and periodontitis group, non-diabetes and periodontitis group, and healthy control group.

BMI is significantly higher in the diabetics with periodontitis ($p < 0.0001$).

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 $p < 0.0001$.

Discussion and Conclusion:

The present study has demonstrated significant difference in adiponectin, resistin among periodontitis with diabetes mellitus group, periodontitis without diabetes mellitus group, and healthy group.

The relationship between periodontitis and type 2 diabetes mellitus has been discussed widely in the past several decades. Many studies showed that diabetes is an independent risk factor of periodontitis [12] and periodontitis has been thought to be the sixth complication of diabetes [13], while, on the other hand, periodontitis could worsen the metabolism of diabetes [14]. Although the detail of this bidirectionally association is not clear yet, the adipokines may play an important role during the process [15].

In our study, patients in periodontitis without diabetes mellitus group have lower level of adiponectin, and higher level of resistin in serum than healthy people, while patients in periodontitis with diabetes mellitus group have even lower level of adiponectin and lower level of resistin in compared to periodontitis without diabetes mellitus group, which meant that periodontitis could influence the level of adipokines in serum and the effect would be enhanced combining with type 2 diabetes. Some finding are reported by Xu Jing Ling [16] and T. Saito [17] who also reported significant difference in adipokines in periodontal disease with diabetes mellitus and without diabetes mellitus.

Adiponectin has insulin-sensitizing and anti-inflammatory properties [18]. It inhibits IL-6 and TNF- production by macrophages and increases the production of important anti-

inflammatory factors such as IL-10 or IL-1RA by human monocytes, macrophages, and dendritic cells [19].

The role of resistin in insulin resistance and diabetes has been well-established in mice [20], but in rats and humans, its role and relationship are controversial. However, recent studies indicating an abundance of resistin in peripheral blood mononuclear cells and macrophages suggest an important role for resistin in the inflammatory process [21]. Moreover, periodontitis is a common chronic subclinical inflammation of the periodontal tissues, with widespread distribution of gram-negative bacteria in deep pockets. The increase in circulating resistin levels shown in our study may result from the local involvement of monocytes and macrophages in periodontal inflammation.

The inflammatory mechanism has now been considered to be an important part of the pathogen of diabetes and be closely linked with insulin resistance. The increasing of inflammatory cytokines such as TNF-, IL1-, and IL-6 could impair insulin signaling pathways as well as reduce the function of mitochondria and result in insulin resistance [22].

In our investigation, strong correlations have observed between adipokines and periodontal parameters. This phenomenon suggests potential relationship between periodontal inflammation and insulin resistance while further studies in larger populations are required.

In conclusion, periodontitis could influence the level of adipokines in serum and the effect would be enhanced combining with type 2 diabetes. What is more, the ratio of adipokines have strong positive correlation with periodontal parameters and gave a hint of potential relationship between periodontal inflammation and insulin resistance.

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