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Study of serum high sensitivity C - reactive protein, adipokines, HbA1c, and fasting blood glucose level in patients of diabetes mellitus type II with periodontal disease

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ABSTRACT

Background: Diabetes is a systemic disease with several complications affecting both the length and quality of life. One of these complications is periodontal disease (periodontitis). The periodontal diseases are considered as the "sixth complication of diabetes mellitus". The results of this study indicate the presence of a significant relationship between periodontitis and diabetes mellitus.
Materials and Methods: A total of 155 periodontitis patients with diabetes mellitus and 137 periodontitis patients without diabetes mellitus were selected for the study. Hs-CRP (High sensitivity C – Reactive Protein), Adipokines, HbA1c, and Fasting Blood sugar levels were compared with 160 healthy non-diabetics; non-periodontitis (control) subjects.
FBS (Fasting Blood sugar) & HbA1c were done by semi auto-analyzer diagnostic kit and Adipokines by ELISA method (Kit method) and Hs-CRP (High sensitivity C - Reactive Protein) was estimated by Immunoturbidimetric method. For this study newly diagnosed type 2 diabetic and periodontitis patients were selected.
Results: FBS and HbA1c in both study groups were higher than that in control group. Statistical analysis showed that periodontitis with at least one tooth that displayed a probing pocket depth of > or = 6mm was significantly associated with higher blood sugar (P=0.005) and positive correlations are found between mean periodontal disease and HbA1c (P = 0.009). Adipokines, HbA1c, Hs-CRP (High sensitivity C - Reactive Protein), and periodontal parameters have significant role in periodontitis with diabetes mellitus.
Conclusion: The link between periodontal disease and type 2 Diabetes mellitus (T2DM) has been suggested through a number of clinical and epidemiological studies. Many studies have shown that the prevalence and severity of periodontitis is increased in the presence of diabetes mellitus. Thus, diabetes is considered to be a risk factor for gingivitis and periodontitis.

1. Introduction

Diabetes is the most common systemic disease that leads to many major complications affecting longevity of life.[1] As per estimates of The International Diabetes Federation in year 2011 about 366 million people had diabetes and by year 2030 it will rise to 552 million people worldwide. A major concern of diabetes is the various complications which arise due to the disease.[2] Type-2 diabetes mellitus constitute 90% of the cases. Prolonged uncontrolled hyperglycemia in diabetes leads to multiorgan damage that predominantly involves kidneys, heart, blood vessels, nerves and eyes.[3]

Diabetes which has become major health problem globally is associated with multiple organ involvement

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and complications like nephropathy, microvascular disease, neuropathy and delayed wound healing.[4] Of all the complications periodontal diseases is sixth common condition in diabetes mellitus.[5] Periodontitis is an advanced stage of irreversible gum disease with bone loss. It can lead to damage to gum tissue and bone surrounding and supporting teeth making them loose and fall out. Unattended gingivitis in later stage leads to periodontitis.

Diabetics have more frequent and severe form of periodontitis which is also a known risk factor for type II diabetes mellitus.[6,7]

2. Materials and Methods

The study protocol was in keeping with the ethical guidelines of the 1975 declaration of Helsinki and all the patients gave written informed consent to the study. Patients are taken from outpatient department of Periodontics. This study was conducted in the Biochemistry department of Mahatma Gandhi Memorial Medical College, Indore; M.P. BMI of all patients was calculated by using the formula weight in Kg/m^2. Brief clinical history, Blood pressure, dietary habit and information on physical activity were taken before recruiting study participants.

2.1. Sample size

1. Study group
   (a) Adults having periodontitis but not Type II DM – 137.
   (b) Adults having periodontitis & also Type II DM – 155.
2. Control group
   (a) Healthy adults non-diabetic, non periodontitis – 160.

2.2. Methodology

1. Estimation of Hs-CRP (High sensitivity C - reactive protein) was done by Immunoturbidimetric method.
2. Estimation of Glycosylated Hb (HbA1c) was done with the help of semi auto-analyzer diagnostic kit.
3. Fasting blood sugar was estimated by Glucose Oxidase Peroxidase method.
4. Serum Resistin &Adiponectin (adipokines) were determined by ELISA method.

3. Observations & Results

In our study the periodontal parameters in control group when compared to both the study groups were found to be statistically significant ($p < 0.0001$)

The mean values of high sensitivity C- reactive protein in patients having periodontal disease and diabetes mellitus type II (0.60±0.90 mg/dl) and without diabetes mellitus type II (0.94±1.92 mg/dl) was found to be statistically significant ($p<0.0001$) when compared to control group (0.18±0.32 mg/dl). Mean resistin levels showed strong positive association with periodontal disease in both diabetics (3.71 ± 1.42 ng/ml) and non-diabetics (4.59 ± 1.04 ng/ml) in comparison to the control group (1.54 ± 0.51 ng/ml) ($p<0.0001$). Thus in present study resistin levels in both the study groups of adults having periodontitis with and without Type II Diabetes mellitus was significantly higher compared to healthy volunteers. Serum Resistin showed a significant ($p<0.0001$) positive correlation with HbA1c.

Mean levels of serum Adiponectin was lower in adults having periodontitis and type II diabetes mellitus (4.48 ±0.96 μg/ml) and in non-diabetic adults with periodontitis (4.83 ± 1.10μg/ml)as compared to healthy subjects (6.95 ± 1.21μg/ml). The levels of Adiponectin were inversely proportional to periodontitis in diabetics & non diabetics.

The obesity variable: body mass index was found to be significantly higher in adults having periodontitis and Type II diabetes mellitus when compared to adults having periodontitis but not Type II diabetes mellitus and also when compared to the control group ($p<0.0001$).

4. Discussion & Conclusion

The relationship of type 2 diabetes mellitus with periodontitis has been studied since a few decades. Diabetes has been shown to be a risk factor for development of periodontitis.[8] Apart from the known common complications of Type II diabetes mellitus, periodontitis is an additional sixth complication of diabetes,[9] at the same time it is been hypothesized that periodontitis can worsen the metabolism of diabetes.[10] Adipokines are being postulated to play major role in this process of bidirectional association between diabetes and periodontitis.[11]

In present study adults having periodontitis with and without Type II diabetes mellitus had low levels of Adiponectin when compared to the control group. Resistin levels were significantly higher in periodontitis cases with and without diabetes in comparison to the control group. The observations in the present study suggest that the presence of periodontitis influences the levels of serum adipokines and the presence of type 2 diabetes mellitus further enhances this effect.

Study by Xu Jing Ling et al[12] and T. Saito et al[13] have shown significant difference in adipokines in adults having periodontitis in comparison to the control group. The anti-inflammatory properties of Adiponectin and its insulin sensitizing properties may play role in this effect.[14] Adiponectin suppresses the production of inflammatory markers like TNF- α and IL-6, while it causes an increased secretion of antiinflammatory cytokines like IL- 10 by monocytes, macrophages and dendritic cells.[15]

Table 1: Parameter wise comparison among the three studygroups

Parameter(mean ±SD)	Study Group (a) (137)	Study Group (b) (155)	Control Group (160)	F -Value	*P* -value
Body Mass Index (kg/m2)	23.71 ± 3.78	24.30 ± 3.42	21.19 ± 3.13	17.780	<0.0001
HbA1c (%)	5.53 ± 0.38	7.57 ± 1.85	4.97±0.23	125.227	<0.0001
Probing Depth (mm)	3.94 ± 0.63	3.48 ± 0.77	2.18 ± 0.61	141.203	<0.0001
Attachment Loss (mm)	3.34 ± 1.17	2.63 ± 1.81	3.68±0.23	15.548	<0.0001
Bleeding Index	2.91 ± 0.75	2.53 ±0.77	0.69 ±0.46	266.248	<0.0001
Adiponectin (μg/ml)	4.83 ± 1.10	4.48 ±0.96	6.95 ± 1.21	105.220	<0.0001
Resistin(ng/ml)	4.59 ± 1.04	3.71 ± 1.42	1.54 ± 0.51	314.068	<0.0001
HsCRP(mg/dL)	0.94±1.92	0.60±0.90	0.18±0.32	14.182	<0.0001
Fasting blood glucose (mg/dL)	102.72±2.36	142.3±5.26	92.4±3.17	137.252	<0.0001

Resistin induced insulin resistance is studied by experiments in mice,[16] and the role of Resistin in rats and humans and its relation with diabetes has shown varied results. Few of the recent studies have shown high Resistin levels in blood and macrophages which support the theory of Resistin playing important role in inflammatory process.[17] Widespread distribution of bacteria (gram negative) in deep pockets characterizes Periodontitis. Increased blood levels of Resistin in our study may be the result of increase release from monocytes and macrophages present in large numbers in periodontal inflammation.

Development of insulin resistance and diabetes is considered to be result of chronic inflammation. It is hypothesized that increased levels of inflammatory cytokines like, IL-1, IL-6 and TNF cause impairment of insulin signaling pathway and reduce the mitochondrial functioning leading to insulin resistance.[18]

C-reactive protein (CRP) is synthesized and released by liver as acute phase reactant protein as result of action of inflammatory cytokines.CRP acts as an important biomarker of inflammation and acts like a parameter to monitor the progression of systemic diseases like diabetes, coronary heart disease, cancer and others. CRP has emerged as robust and reliable marker for inflammation. The Hs-CRP test is a highly sensitive quantification of CRP that detects minimal quantity.

In present study we have found that mean levels of Adiponectin and Resistin were significantly different among periodontitis with and without diabetes groups as compared with control group.

Diabetes mellitus and periodontal diseases show close association and many similarities in pathophysiology. It is hypothesized that Periodontal disease is an independent risk factor for the causation of type 2 diabetes mellitus. World Health Organization has projected that nearly 4.4% of the world population will be suffering from diabetes by year 2030. Periodontitis is an established complication associated with type 2 diabetes mellitus leading to teeth loss.

In our study we found positive association between diabetes mellitus and periodontitis. Similar positive association among the two has been reported by Aruna et al[19] and Lacopino AM et al.[1] The relationship between periodontal disease and type 2 diabetes mellitus may be related to pre-existing conditions like obesity and insulin resistance. Inflammation has a pivotal role in such association, and it is now getting revealed by various studies. It is proposed that presence of type 2 diabetes mellitus leads to an increased risk of periodontitis, and the various possible bio physiological processes are being studied extensively. It is yet not clear that what is the effect of periodontitis on glycemic control and what is its mechanism of action. It is possible that periodontitis may have a role in the initiation or propagation of insulin regulation further dysregulating glycemic control. Further studies are required to verify and establish the relationship between type 2 diabetes mellitus and periodontal diseases.

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6. Conflict of Interest

The authors declare they have no conflict of interest.

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