Evaluation of Periodontal and Hematological Findings in Diabetes Patients-A Case-Control Study

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Abstract

Background

Periodontal disease is a chronic inflammatory disease initiated by bacterial pathogens and modified by various risk factors. Various studies have elucidated the converse side of the relationship between systemic health and oral health proving the adverse effect of systemic health on periodontal disease and vice-versa. Amongst all, a strong correlation has been shown between periodontal disease and diabetes, revealing that periodontitis is a proven sixth complication for diabetes. There is emerging evidence to support the existence of a two-way relationship between diabetes and periodontitis, with diabetes increases the risk for periodontitis and its inflammation affecting the glycemic control.

Method

The aim of this case-control study was to evaluate the periodontal and hematological manifestations in diabetic and non-diabetic patients. The sample size was estimated as n=264 with n=132 in each group. 2.5 ml of blood was withdrawn from each of the patient for hematological evaluation: HbA1c values, Hb%, RBC count, the differential count, and total leukocyte count. Periodontal evaluations were assessed by probing pocket depth, clinical attachment level, and Russell's periodontal score.

Results

There was statistically significant (p=0.000) difference in the diabetic group than the control group with respect to smoking, alcohol consumption, Hb%, HbA1c levels, differential counts, total leukocyte count, probing pocket depth, clinical attachment level, and Russell's periodontal score. RBC count and gender revealed no significance.

Conclusion

There were a higher periodontal manifestation corresponding to the altered hematological findings in diabetic patients than non-diabetic patients with higher prevalence in smokers and alcohol consumers.

Abbreviations: RBCs: Red Blood Cells; WBC: White Blood Cells; AGEs: Advanced Glycation End-products; VEGF: Vascular Endothelial Growth Factor; RAGE: Receptor for Advanced Glycation End-products; PGE2: Prostaglandin E2

Introduction

Periodontitis is a chronic inflammatory disease of the supporting structures of teeth caused by microbial load, containing predominantly Gram-negative anaerobic bacteria. Periodontal host immune response plays a major role in tissue destruction and if left untreated results in tooth loss. Periodontitis is initiated by the microbial load, progressed by poor oral hygiene and it can be aggravated by various risk factors such as smoking, systemic diseases, environmental and genetic factors.

Diabetes is a progressive chronic condition with multifactorial pathophysiological alterations. It greatly increases the risk of 5 major known complications: retinopathy, neuropathy, nephropathy, ketoacidosis, and cardiovascular disease. When left uncontrolled, it is a major cause of mortality [1]. It is the epidemic of the century and without effective diagnostic methods at an early stage will rise to alarming level [2]. However, early diagnosis and modification of lifestyle can prevent its progression and serious complications. Though

it can be controlled, it threatens to be an important risk factor for periodontitis.

Examination of the available data reveals the same. The level of glycemic control appears to be an important determinant in this relationship [3,4]. Type 1 diabetics exhibited more gingival inflammation and plaque accumulation compared to non-diabetic subjects [5]. The gingival inflammation in adults with type 2 diabetes seems to be directly proportional to poor glycemic control. In association with earlier studies conducted to examine the correlation between diabetes and periodontitis, epidemiologic studies in diabetic adults have often shown an increase in the extent and severity of periodontitis [6-9]. A study conducted among Pima Indians of Arizona, a population with the highest occurrence of type 2 diabetes, suggested a greater prevalence and severity of periodontal attachment loss and bone loss [7,8]. In multivariate risk analysis, diabetic subjects had 2.8 to 3.4 fold increased odds of having periodontitis. Smaller cross-sectional and case-control studies generally confirmed the same findings [10-14]. The aim of this present study was to evaluate the hematological and periodontal findings in patients with and without diabetes and to confirm the positive association between diabetes and periodontitis.

Materials and Methods

The case-control study was designed to evaluate and confirm the association between diabetes and periodontitis. Based on the power analysis (80%), the sample size was assigned as n=264 in this study [15]. The study subjects were divided as cases group (patients with diabetes) and control group (patients without diabetes) with n=132 in each group. The study was conducted in the period of July 2018 to September 2018, after obtaining approval from the Institutional ethical committee, Priyadarshini Dental College and Hospital, Tiruvallur.

Inclusion criteria

- Patients of both genders with 30-70 years of age
- Patients with HbA1c levels greater than 6.5% were included in the diabetic study group
- Patients with HbA1c levels of less than 6.5% were included in the non-diabetic control group

Exclusion criteria

- Patients who had undergone periodontal therapy within the previous 6 months
- Patients with other systemic diseases specifically inflammatory conditions
- Patient with premalignant lesions or conditions and oral malignancy
- Patients with immunosuppressive disorders

The sample subjects were randomly selected and segregated into the respective groups based on their HbA1c values, as it is considered as a standard confirmatory test for diabetic assessment reflecting the glycemic level of past 3 months precisely and accurately [16]. Both the group patients were screened at Priyadarshini dental college and hospital, Tiruvallur. They were explained about the study procedure in detail. Individuals willing to participate in the study were included and written informed consent were obtained. The demographic variables such as age, sex, address, usage of tobacco in any form such as pan/ gutkha/tobacco chewing and alcohol consumption were recorded. Following this, the periodontal parameters such as probing pocket depth, clinical attachment level, and Russell's periodontal index were evaluated using William's probe. After considering their complete medical history, blood investigations were done. 2.5ml of blood was drawn from the patient, fasting blood sugar and postprandial blood sugar levels were measured to screen their glycemic level and confirmed by HbA1c values. Following this, Hb%, Red Blood Cells (RBCs), total leukocyte count and differential counts (Granulocytes and Agranulocytes) were examined for both the groups. The results were collected and statistically analyzed.

Statistical Analysis

The results were statistically analyzed by SPSS-2017 software. Student "t" test was done. p<0.05 was considered statistically significant.

Results

Table 1 shows the demographic details of diabetic and non-diabetic patients. There was no significant difference between genders of both groups indicating, no prevalence is seen in both the groups. There was a significant difference observed in the diabetic group in relation to age and also in tobacco consumption and alcohol intake, showing its increased prevalence in the diabetic group.

		Cases group	Control group	p-value
Age (Years)		51.69 ± 11.6	45.33 ± 11.178	.000 *
Gender	Male	51.50%	47.70%	0.538
	Female	48.50%	52.30%	0.623
Use of tobacco		37.90%	3%	.000 *
Alcohol consumption		29.50%	2.30%	.000 *
*Statistically significant i.e. p<0.05; Statistical test used: Chi square test				

Table 1: Demographic details.

Table 2 shows the hematological parameters in the study group. HbA1c levels, hemoglobin content, differential count (Granulocytes and Agranulocytes) and total leukocyte count were statistically significant between the groups, whereas the RBC count did not reveal any significant difference between them.

	Group	Mean	p-value	Standard Error Mean
HbA1c (%)	Cases (Diabetic Patients)	9.960 ± 2.5558	0.000*	0.2225
	Controls (Non Diabetic Patients)	4.917 ± 0.5605		0.0488

Red Blood Cell Count (in millions)	Cases (Diabetic Patients)	4.730 ± 0.5894	0.158	0.0513
	Controls (Non Diabetic Patients)	4.623 ± 0.6414		0.0558
Hemoglobin%	Cases (Diabetic Patients)	12.845 ± 1.9481	0.000*	0.1696
	Controls (Non Diabetic Patients)	13.704 ± 1.9403		0.1689
Granulocytes	Cases (Diabetic Patients)	57.55 ± 6.444	0.000*	0.561
	Controls (Non Diabetic Patients)	52.03 ± 10.706		0.932
Agranulocytes	Cases (Diabetic Patients)	48.05 ± 10.674	0.000*	0.929
	Controls (Non Diabetic Patients)	37.27 ± 8.337		0.726
Total Leukocyte Count	Cases(Diabetic Patients)	7450.76 ± 1981.190	0.000*	172.44
	Controls (Non Diabetic Patients)	6608.71 ± 1351.455		117.629
*Statistically significant i.e. $p<0.05$; Statistical test used: independent t-test				

Table 2: Haematological parameters of the study group.

Table 3 shows the periodontal manifestations in the study groups. There was a significant increase in average probing depth, clinical attachment level and Russell's periodontal score in the diabetic group than the non-diabetic group.

	Group	Mean	p-value	Standard Error Mean
Teeth present	Cases (Diabetic Patients)	21.91 ± 5.889	00.000 *	0.513
	Controls(Non Diabetic Patients)	24.98 ± 3.602		0.314
Probing Pocket Depth (millimetres)	Cases (Diabetic Patients)	5.2061 ± 1.2058	0.000 *	0.10495
	Controls (Non Diabetic Patients)	3.2386 ± 0.74201		0.06458
Clinical Attachment Level (millimetres)	Cases (Diabetic Patients)	6.9428 ± 1.79674	0.000 *	0.15698
	Controls (Non Diabetic Patients)	1.8181 ± 1.34113		0.11673
Russell's Periodontal Index Score	Cases (Diabetic Patients)	5.7097 ± 1.29504	0.000 *	0.11272
	Controls (Non Diabetic Patients)	3.6648 ± 1.27494		0.11097
*Statistically significant i.e. $p<0.05$; Statistical test used: independent t-test				

Table 3: Periodontal parameters of study groups.

Discussion

Diabetes is considered to be a disorder of carbohydrate metabolism. As literature suggests, with aging, the human body's capacity to absorb and utilize glucose becomes gradually less, leading to glucose intolerance. On progression, it leads to insulin resistance and results in increased glucose level causing hyperglycemia [17]. In this present study, the results supported the fact that there was an increase in the prevalence of diabetes with age. There was no statistical significance observed in gender variance, indicating gender prevalence.

This study also showed higher periodontal manifestations amongst smokers and alcohol consumers in diabetic than non-diabetic individuals. Various studies have also supported this result suggesting that smoking influences inflammation and oxidative stress. Evidence strongly suggests that inflammation and oxidative stress may also be related to an increased risk of diabetes [18,19]. A study by Novak, et al. states that smokers are almost three times more prone to have periodontal destruction than non-smokers [20]. Vascular alterations, altered neutrophil function, decreased IgG production and increased prevalence of periopathogens are found to be the possible mechanisms for periodontitis among smokers.

Numerous studies show that acute or chronic alcohol consumption can antagonize insulin-stimulated glucose disposal, thereby has the risk of developing insulin dependent diabetes [21,22]. Impairment of neutrophil function, stimulation of bone resorption and suppression of bone turnover may be the underlying mechanisms of periodontitis among alcohol consumers.

The subjects were separated into two groups depending on their HbA1c values and showed potential significance with mean HbA1c levels of 9.960 ± 2.5558 in diabetic patients and 4.917 ± 0.5605 in non-diabetic patients. In this study, the HbA1c was assessed as it is the standard test and it gives the estimated glycohaemoglobin levels over the preceding 30-90 days period. Glycohemoglobin forms

continuously in erythrocytes. The binding of glucose to hemoglobin is highly stable. Hence, hemoglobin remains glycated for the lifespan of the erythrocytes [23]. There was also a significant decrease in the levels of Hb% in patients with diabetes. Previous studies suggest that RBCs are stiffened by chronic hyperglycemia that has adverse effects on the vasculature and the hemorheological changes in the microcirculation of diabetics, which could be potential predictive markers of diabetes [24]. But this study revealed no significant changes in the RBC count.

Our study showed a significant increase in total leukocyte count along with increased inflammatory responses in diabetic patients. As studies suggested, White Blood Cell (WBC) levels were increased in diabetic patients. This could be due to systemic inflammation characterized by an elevated WBC count in venous blood due to higher endotoxin levels detected in the plasma of periodontitis patients [25]. Gediminas, et al. [26] study shows that there is an increase in total leukocyte and lymphocyte counts with no significant increase in neutrophils, monocytes and eosinophil count in periodontitis patients. Al-Rasheed's [27] study reveals that there is an increase in the mean WBC counts among patients with periodontitis.

In this study, we have analyzed the WBCs as granulocytes and agranulocytes and it is found to have a significant increase in their levels among diabetic patients. This could be due to the accumulation of granulocytes accompanied by the release of granular proteins. These granule proteins are seeded on the endothelium and it allows direct activation of granulocytes followed by the adhesion of monocytes. This supports the recruitment of the inflammatory cells at the inflammatory sites during the beginning of inflammation [28]. Our study result was also supported by another explanation which stated that there is a decrease in granulocyte chemotaxis as well as defective granulocyte apoptosis leading to increasing in the retention of granulocytes in diabetic patients [29].

Association between periodontitis and diabetes are clearly demonstrated in multiple studies and it is strongly proven by Papapanou [3]. Tervonen, et al. [9] concludes that type 1 diabetic subjects with poor metabolic control over the preceding 2-5 years have a significantly greater prevalence of deep probing depth and advanced attachment loss than subjects with good glycemic control.

In this study, increased periodontal probing depth, clinical attachment loss, and Russell's score were seen in diabetic patients which indicated a statistically significant presence of periodontitis amongst diabetics than healthy controls. The possible mechanism attributed may be due to the action of Advanced Glycation End-products (AGEs) in individuals with sustained hyperglycemia. Collagen is cross-linked by AGE formation, which makes the collagen less soluble and less likely to be normally repaired or replaced. Tissue integrity is impaired as a result of damaged collagen that remains in the tissues for long periods. As a result, collagen in the tissue of poorly controlled diabetes is more susceptible to pathogenic periodontal breakdown. AGE formation was also found to be associated with increased production of Vascular Endothelial Growth Factor (VEGF) that played a major role in microvascular complications of diabetes [30]. Increased oxidative stress has also been demonstrated in the gingiva of diabetic subjects in association with an increased accumulation of AGEs [31]. The interaction between the Receptor for Advanced Glycation End-products (RAGE) and AGEs in periodontal tissues resulted in the marked elevation of IL-1β, TNF-α and Prostaglandin E2 (PGE2) in GCF of diabetic subjects compared to non-diabetic individuals [32].

To the best of our knowledge, this is the first study evaluating the periodontal manifestations and hematological alterations of diabetic patients in the population of Tiruvallur district, Tamil Nadu. The limitations in this present study are the smaller sample size; the complete differential count evaluation; the hematological analysis of differential count and blood sugar levels and clinical variation after periodontal therapy being not evaluated.

Conclusion

To conclude, there was a higher periodontal manifestation corresponding to the altered hematological findings in diabetics than non-diabetic patients with higher prevalence in smokers and alcohol consumers. Though variations in hematological findings stand as a common underlying factor for all the six complications of diabetes, this paper clearly states that it has a direct impact on periodontal manifestations by altering the host immune response. Being a chronic inflammatory condition, both periodontal disease and diabetes mellitus share common similarities in pathophysiology and are interdependent on each other when presenting together. Thus, poor glycemic control can aggravate periodontal destruction and a controlled glycemic level enhances the need for maintenance of healthy periodontium.

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