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RESEARCH ARTICLE

PRE-DIABETIC AND TYPE 2 DIABETIC RISK IN CHRONIC PERIODONTITIS PATIENTS

[1*]Dr. Aditi Mahajani, [2]Dr. Menaka KB and [3]Dr. Vinayak Kumbhojkar

[1]Post Graduate, Department of Periodontics, KAHER's KLE VK Institute of Dental Sciences, Belagavi, Karnataka (575001)
[2]Reader, Department of Periodontics, KAHER's KLE VK Institute of Dental Sciences, Belagavi, Karnataka (575001)
[3]Professor and Head, Department of Periodontics, KAHER's KLE VK Institute of Dental Sciences, Belagavi, Karnataka (575001)

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ABSTRACT

Background: The two way relationship between diabetes and periodontitis offers an opportunity for the detecting undiagnosed pre diabetes and diabetes. The present study assesses pre-diabetic and diabetic risk in chronic periodontitis patients. Methods: A sample of 100 patients diagnosed with chronic periodontitis was enrolled into the study. Patients with Periodontal Disease Index (PDI) score >4 were subjected to collection of blood samples in 2ml EDTA vacutainers were sent for HbA1c analysis to Thyrocare® Laboratory. The patients were then diagnosed as pre-diabetic or diabetic. Results: The study population revealed that 39% of the total population was pre-diabetic while 13% were diabetic of the total population was overweight. Strength of association of PDI scores with pre-diabetic and diabetic risk, a moderate statistical significance was noted. Conclusion: Screening for pre-diabetes and diabetes in patients with periodontal disease may help in identification of individuals with pre-diabetes and diabetes mellitus at early stages allowing for a wholesome treatment approach.

Key words: Chronic periodontitis, Pre-diabetes, Diabetes, HbA1c.

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INTRODUCTION

Periodontitis is a slowly progressive chronic disease with a multi-factorial etiology. The immune inflammatory response that develops in the gingival and periodontal tissues in response to plaque bacteria, results in destruction of structural components of the periodontium leading, ultimately, to clinical signs of periodontitis (Pihlstrom, 2005). Although disease progression is usually slow, but can be accelerated in presence of systemic (diabetes, osteoporosis), environmental (smoking) or behavioral risk factors (stress) (Newman). One such example is the increased prevalence and severity of periodontitis observed in patients suffering with poor metabolic control as seen in diabetes mellitus. This has led to the designation of periodontal disease as the "sixth complication of diabetes (Newman)". Conversely, severe periodontal disease predisposes an individual to insulin resistance specially when left untreated. The substantial increase in gram negative flora induces release of pro-inflammatory markers that impede insulin activity and hence cause insulin resistance. Such a sequence of events prompts development of a dysglycemic state. Diabetes mellitus is a metabolic disease characterized by dysregulation of carbohydrate, protein, and lipid metabolism. The primary feature of this disorder is elevation in blood glucose levels (hyperglycemia), resulting from either a defect in insulin secretion from the pancreas, a change in insulin action, or both (Lynch, 1994). An increase in body fat is generally associated with increased risk of metabolic diseases such as type 2 diabetes mellitus, hypertension and dyslipidaemia (Bays, 2007). Periodontal infections are often chronic in nature colonized essentially by gram negative organisms. Such an infection poses a systemic challenge to the host defense system. As periodontal destruction progresses, cytokine upregulation occurs. Cytokines mainly TNF-α and IL-lß and various endotoxins induce insulin resistance and decrease insulin action apart from widespread connective tissue destruction (Grossi, 1998). This insulin resistance resulting due to chronic inflammation of the periodontium results in accumulation of Acetylated Glycation End (AGE) products. As a consequence, migration and phagocytic activity of monocytes and neutrophils is affected knocking down the host defense system further and establishing a more pathogenic sub gingival microflora. As a gradual shift occurs to a more predominantly gram negative flora, oral periodontal disease becomes a long standing source of impaired glucose metabolism in the body. Hence, a close inter-relationship between a localized chronic inflammatory periodontal disease and diabetes is established (Grossi, 1998).

Corresponding author: **Dr. Aditi Mahajani,**
Post Graduate, Department of Periodontics, KAHER's KLE VK Institute of Dental Sciences, Belagavi, Karnataka (575001).

Considering periodontitis as a risk factor in the pathogenesis of diabetes, early identification of pre-diabetes and diabetes in patients diagnosed with chronic periodontitis may prove exceedingly beneficial. Diabetes is usually preceded by a stage of impaired glucose metabolism called pre-diabetes. The range of fasting plasma glucose between 100 and 125 mg/dl, 2 hours post 75 gm glucose plasma sugar value between 140 and 199 mg/dl and HbA1c level between 5.7-6.4% are used to define pre diabetes (Maji, 2010). HbA1c reflects average plasma glucose over the previous 8 to 12 weeks. It can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made HbA1c the diagnostic tool of choice for assessing glycemic control in people with diabetes and pre-diabetes (World Health Organization).

While abundant documentation exists about periodontal disease in patients diagnosed with diabetes mellitus, not much has been elucidated about diagnosis of pre-diabetes and diabetes in periodontal patients who do not report any other contributing factors precluding them to a diagnosis of diabetes mellitus (Lalla *et al*., 2011; Lalla *et al*., 2013; Herman, 2015). Early diagnosis and intervention of undetected pre-diabetes and diabetes mellitus in patients with periodontal disease can prevent the common microvascular and macrovascular complications and proves to be cost-effective. In addition, early diagnosis and treatment of pre-diabetes may also benefit the treatment of periodontitis. As dentists, we play a pivotal role in identifying pre-diabetic and diabetic state among patients diagnosed with poor oral health and chronic periodontitis. Thus, the present study aimed at assessment of pre-diabetic and type 2 diabetic risk in patients diagnosed with chronic periodontitis.

MATERIALS AND METHODS

The study was conducted in the Department of Periodontics, KAHER's KLE V.K. Institute of Dental Sciences, Belagavi. An ethical clearance was obtained from the Institutional Ethical Committee.A total of 100 patients of either gender reporting to the outpatient department, Department of Periodontics, KAHER's KLE V.K. Institute of Dental Sciences, Belagavi diagnosed with chronic generalized periodontitis (According to the Periodontal Disease Index, 1959) were included in the study. Inclusion criteria included patients diagnosed above 30 years of age, systemically healthy, with or without family history of type 2 diabetes mellitus. Patients with bleeding disorders, pregnant or lactating women and those who had undergone periodontal therapy in the last 6 months were excluded from the study. A written informed consent was obtained from patients before enrolling in the study. A brief general and medical history was recorded for all the patients.

Patients participating in the study were screened for the full mouth periodontal evaluation using University of Michigan Number 0 probe. The gingival and periodontal component of the Periodontal Disease Index (1959) was used for assessment of chronic periodontitis.

After detailed periodontal examinations and recordings, blood sampling was done for patients with PDI score ≥4. Two ml of venous blood was drawn under aseptic conditions, from antecubital fossa. The blood sample was transferred immediately to K3 EDTA vacutainers and transported to Thyrocare® Laboratory for estimation of HbA1c levels. Patients were grouped as non diabetic, pre diabetic and diabetic according to American Diabetic Association (2010) specifications (American Diabetes Association, 2010).

Patients were informed of their glycaemic status. Patients who were pre-diabetic were advised lifestyle and diet modification along with close monitoring and consultation from a General Practitioner (GP) so as to prevent further disease progression. Patients diagnosed as diabetic were referred to the GP for necessary pharmacotherapy.

Statistical Analysis

Statistical analysis was done using SPSS Chicago, IL (Version 22). The comparison between the diabetic groups for PDI scores was done using Kruskal Wallis test. The strength of relationship for diabetes status with PDI scores was done using Pearson's Correlation test.

RESULTS

A larger number of the study population was pre-diabetic when compared to diabetics (Table 1). Comparison of PDI score among the diabetic groups did not show any statistical difference (Table 2). Moderate statistical significant association was observed between HbA1c and PDI score. (Table 3). Patients who reported a family history of diabetes were statistically more likely to be aware of their diabetic status as compared to those who did not have a family history (Table 4).

Table 1: Characteristics and frequencies of study population (n = 100):-

	%	Mean	S.D.	Range
Age	100	43.7	12.9	30 - 75
Gender				
Male	56	N/A	N/A	N/A
Female	44	N/A	N/A	N/A
PDI scores				
Total	100	5.3	0.3	4.5 - 6
HbA1c				
<5.7% (Non-diabetic)	48	5.3	0.2	4.5 - 5.6
5.7–6.4% (Pre-diabetic)	39	5.9	0.2	5.7 - 6.4
≥6.5% (Diabetic)	13	8.5	1.9	6.5 - 12.5
Total	100	5.9	1.3	4.5 - 12.5

Table 2: Comparison of PDI for diabetes risk by Kruskal Wallis test

	Diabetes groups	N	Mean Rank	X^2	df	p value
PDI score	Non diabetic	48	45.29	3.941	2	0.139
	Pre diabetic	39	53.06			
	Diabetic	13	62.04			
	Total	100				

Table 3: Pearson Correlation between periodontitis (PDI score) and diabetes risk (HbA1c)

Correlation between	Correlation co-efficient	p-value
HbA1c – PDI score	.322**	.001

**p value<0.005

Table 4. Prevalence of awareness of having HbA1c values in the pre-diabetes/diabetes ranges and elevated HbA1c (in %)

Characteristic	Persons with >5.7% HbA1c	Persons aware that they have diabetes or pre diabetes	% aware that they have diabetes or pre diabetes	95% confidence interval	Significance (P-value)
Gender					
Male	25	4	16%	6.0 – 7.1	0.267
Female	27	2	7.4%	6.0 – 7.2	
Family history					
No	35	3	8.6%	6.6 – 9.8	0.008*
Yes	17	3	17.6%	6.0– 11.2	

*p value<0.05

DISCUSSION

Tooth loss in adult population is most commonly precipitated due to periodontitis, a chronic inflammatory condition characterized by destruction of periodontal tissues. Many studies have demonstrated the association between diabetes mellitus and oral conditions, most common being chronic periodontitis. When compared to a healthy population, periodontitis is two or even three times more prevalent in patients with diabetes (Mealey, 2006). Also, periodontitis and uncontrolled diabetes mellitus are strongly associated (Garcia, 2015; Taylor, 2008). There is abundant literature which suggests that periodontal disease can worsen glycemic control in diabetic individuals (Newman; Taylor, 1996; Collin, 1998). Oral and periodontal findings offer an opportunity for identification of affected individuals who are unaware of their glycemic status. Pre-diabetic status of an individual can quickly transcend to diabetes if left unattended. Subjects with uncontrolled diabetes mellitus are more susceptible to infections and impaired wound healing. A vast majority of the population remains undiagnosed with diabetes. A fairly scant research exists in regard to pre-diabetic state of an individual being influenced by periodontal disease. Diagnosing pre-diabetes in chronic periodontitis and patients with poor oral health can help illustrate the effect of periodontal disease on glycemic status of an individual. Hence, awareness of dysglycemic state can help retard progression to an established diabetic state and aid in maintaining periodontal and oral health as well (Tabák, 2012; Fonseca, 2007).

This cross-sectional study was undertaken to identify individuals with undiagnosed pre-diabetes and diabetes among patients diagnosed with chronic periodontitis. The age group selected ranged from 30-75 years with a mean age of 43.7±12.9. (Table 1) Dallo *et al*. (2003) recommended that African, Asian and Hispanic races should be tested for undiagnosed diabetes after 30 years of age. Studies by Lalla *et al*. (2013) and Herman *et al*. (2015) also used the same age criteria in their study and stated that presence of periodontal disease among these subjects precluded them to have underlying pre-diabetes or diabetes. The present study involved 56% males and 44% females. A notable percentage of study population was diagnosed with pre-diabetes (39%) and diabetes (13%) according to ADA specifications (2010). (Table 1) No specific gender predilection was observed. These findings were in accordance with studies conducted by Zhang *et al*. (2015) Herman *et al*. (2014) Genco *et al*. (2014) and Rosedale *et al*. (2015) Individuals who were diagnosed as pre-diabetic or diabetic were referred to the general practitioner for further diagnostics and diet modification as deemed necessary by the physician. The periodontal status of patients in the present study was assessed using Periodontal Disease Index (PDI) developed by Sigurd P Ramfjord in 1959.

Studies by Lalla *et al*. (2011) Deepika *et al*. (2013) Zhang *et al*. (2015) and Teeuw *et al*. (2017) used a diverse range of criteria to record periodontal status in their study population and concluded that periodontal status could indicate presence of pre diabetes or diabetes. A mean PDI score of 5.4±0.3 was observed in pre-diabetic group and 5.4±0.4 was seen in the diabetic group. Inter-group analysis of PDI scores for diabetes risk was done using Kruskal Wallis test. PDI scores between the groups, i.e. non-diabetes, pre-diabetes and diabetes did not show any statistical significance. (Table 2) This could be attributed to smaller sample size of the study. However, when Pearson's correlation test was applied to assess the strength of association between HbA1c and PDI score, a moderate and statistical significance was noted (Table 3). Similar findings were seen in a study conducted by Hayashida *et al*. where the mean HbA1c was associated with periodontal status, but did not reach statistical significance (Hayashida, 2009). Another study by Deepika *et al*. (2013) found a positive correlation between HbA1c values and plaque scores. This correlation can be attributed to long standing periodontal disease is characterized by colonization of deep pockets by increasingly pathogenic gram negative microorganisms which release cytokines like TNF-α and IL-1β which induce insulin resistance and decreased insulin action.

TNF-α has been suggested as a mediator of insulin resistance in infection by suppressing tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1), thus impairing insulin action (Grossi, 1998). A brief medical history was recorded for all patients regarding their awareness of pre-diabetic or diabetic status and presence of any family history of diabetes. Among 52 individuals with HbA1c values >5.7% only 6 individuals were aware of their diabetic status. The subjects were significantly more likely to be aware of elevated glucose levels if they had a family history of diabetes than those who didn't. (Table 4) A fair majority of the population were unaware of their dysglycemia. Various studies by Hayashida *et al*. (2009) Lalla *et al*. (2011); Lalla *et al*., 2013; Genco *et al*. (2014) Herman *et al*. (2015) and Teeuw *et al*. (2017) have successfully concluded that undiagnosed diabetic status can be identified in a dental office using periodontal status as a marker. Thus the current findings of this study make it imperative to encourage screening for diabetes in patients diagnosed with periodontal disease. In the present study, a significant proportion of the population was diagnosed with pre-diabetes and diabetes. A positive correlation was observed between diabetic status and PDI score implying that presence of periodontal disease can put an individual at a risk for pre-diabetes and type 2 diabetes mellitus. Comparison of PDI scores within the diabetic groups did not show statistical significance. This finding could be attributed to a relatively smaller sample size of the study. However, the results of the present study can be further validated by using a larger sample size.

Conclusion

It can be concluded that routine assessment of HbA1c especially for patients presenting with poor oral health and severe chronic periodontitis in a dental setting can help in identification of undiagnosed pre-diabetes and diabetes mellitus in its preliminary stages. Such a finding can promote a methodical inter-disciplinary approach to expertly prevent progression of periodontal disease and worsening of glycemic status.

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