COMPARATIVE EVALUATION OF PERIODONTAL INFLAMED SURFACE AREA (PISA) IN DIABETICS WITH PERIODONTITIS AND NON-DIABETICS WITH PERIODONTITIS: A CLINICAL STUDY

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Abstract

Aim: To evaluate and compare the Periodontal Inflamed Surface Area (PISA) in diabetics with periodontitis and non-diabetics with periodontitis.

Materials and Methods: A total of 42 patients with Chronic Generalized Periodontitis, with and without type 2 diabetes mellitus, reporting to the Department of Periodontology, Sri Siddhartha Dental College and Hospital, Tumkur were selected for the study, taking into consideration the inclusion and exclusion criteria. Complete clinical examination of patients was carried out including probing pocket depth (PPD), Clinical attachment level (CAL), Gingival recession and Bleeding on probing (BOP). Data on all the 4 periodontal parameters, mentioned above, was assessed at six sites per tooth and entered in a spreadsheet to calculate PISA for each patient. HbA1c levels were estimated for all the patients by Glycosylated Hemoglobin kit. SPSS (Statistical Package for Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011]) was used to perform the statistical analysis.

Results: There was a linear correlation obtained between PISA and HbA1c in both the groups. And the correlation was statistically higher, in diabetic group (p=0.003), when compared to the non-diabetic group (p=0.001).

Conclusion: From the results of the study, it can be concluded that there exists a dose-response relationship between the PISA and HbA1c levels. And the periodontal inflamed surface area (PISA) increases exponentially with the increase in HbA1c levels.

Keywords: PISA, Diabetes, HbA1c, Periodontitis.

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Introduction

Periodontitis is a multifactorial chronic inflammatory disease that affects the supporting structures of the teeth, which results in the destruction of periodontal connective tissue and the alveolar bone.[1] Often, the periodontal disease progression can be altered by the presence of systemic disorders. One such systemic condition, which has a crucial role in the aetiology of periodontal disease is diabetes mellitus.[2]

Studies show a high prevalence and severity of periodontal disease in patients suffering from diabetes than in non-diabetic individuals.The chronic low grade systemic infection and inflammation associated with periodontitis are thought to contribute to the development and deterioration of diseases like cardiovascular diseases[3,4] and diabetes mellitus[5,6]. Periodontitis increases serum levels of CRP, IL-6 and TNFα, which may for example lead to insulin resistance and thereby to poor control of blood glucose in patients with type 2 diabetes mellitus (DM2) as well as healthy individuals[7-9]. Therefore, periodontitis appears to be a chronic low-grade source of infection and inflammation that may endanger overall health by contributing to development of diseases like diabetes mellitus.

The measurement of haemoglobin A1c (HbA1c) levels in the blood, provides an estimation of glycaemic control. A two-way association between glycaemic control of diabetic patients and periodontal disease exists. Probing pocket depth (PPD) and Clinical attachment level (CAL) are not the most appropriate measures, for the assessment of the relationship between periodontitis and glycaemic control (HbA1c levels) in type 2 diabetic patients.

Hence, a new parameter, as a measure of periodontitis, namely the Periodontal Inflamed Surface Area (PISA) has been developed by Nesse et al (2009). The periodontal inflamed surface area, aids in quantification of the inflammatory burden posed by periodontitis, and therefore, can be clinically applied. It represents the surface area of bleeding pocket epithelium in millimetre square.[10] The sum of the probing pocket depth (PPD) of bleeding on probing (BOP)- positive sites for the total dentition, represents the Periodontal Inflamed Surface Area (PISA). Therefore, the current study was performed to establish an association between periodontitis and diabetes, and to assess the relationship between inflammatory burden posed by the periodontitis and glycemic control. The study was aimed at comparing the Periodontal Inflamed Surface Area in diabetics with periodontitis and non-diabetics with periodontitis, along with establishing a correlation between HbA1c levels and PISA.

Materials and methods

The clearance from Institutional Ethical committee was obtained prior to the study (ethical committee clearance reference number: SSMC/Dent/IEC-1/Dec-2020) and the ethical principles as enumerated in the Helsinki declaration 2008 were meticulously followed throughout the course of the study. A sample of Forty-two patients, 21 Type 2 diabetics with periodontitis, and 21 non-diabetics with periodontitis, from the OPD of the Dept. of Periodontology, Sri Siddhartha Dental College and Hospital, Tumkur, were included in this study. All the patients met the following criteria:

For control group, systemically healthy patients between the age of 30-50 years; Patients with Chronic Generalized Periodontitis, as diagnosed by marked redness, edema, spontaneous bleeding on probing and at least 30% of remaining teeth having a probing pocket depth of $\geq$ 5mm; Patients who had not taken antibiotics medication 6 months prior to the study and Patients who had not undergone any periodontal therapy in the past 6 months.

For experimental group, Patients with a history of type 2 diabetes mellitus, having HbA1c levels>6.5mg/dl; Patients with Chronic Generalized Periodontitis, as diagnosed by marked redness, edema, spontaneous bleeding on probing and at least 30% of remaining teeth having a probing pocket depth of $\geq$ 5mm; Patients who had not taken antibiotics medication 6 months prior to the study and Patients who had not undergone any periodontal therapy in the past 6 months.

Exclusion Criteria included: Patients who were on antibiotics/ immuno-suppressants; Chronic smokers /alcoholics /tobacco users; Pregnant/ lactating women and Patients with systemic conditions, other than type 2 diabetes mellitus, that affect the periodontal health.
Subjects were selected as per the inclusion and exclusion criteria. All the subjects were informed about the nature of the study and a signed informed consent was obtained. Subjects underwent a thorough medical history and examination by a physician.

Clinical Assessment

Clinical periodontal parameters such as Bleeding on Probing (BOP); Probing Pocket Depth (PPD);

Clinical Attachment Level (CAL); and Gingival Recession were recorded for each patient (Fig. 1). Attachment Loss Surface Area (ALSA), Periodontal Epithelial Surface Area (PESA) and Periodontal Inflamed Surface Area (PISA) were derived from Clinical attachment level (CAL), recession and bleeding on probing (BOP) measurements. Excel Spreadsheets that are specially designed for this purpose were downloaded and utilized.

Fig 1: Clinical periodontal parameters measurement using UNC-15 probe

Collection of Blood

All the patients underwent a screening for glycemic status, by the estimation of HbA1c levels. The patients were referred to the Department of Biochemistry, Sri Siddhartha Medical College, Tumkur, or to other Pathology labs based in Tumkur, for the testing of HbA1c levels, based on patient's convenience.

Blood samples were collected in the morning between 8:30 and 9:30, following an overnight fasting. About 2ml of blood was collected using SST II Advance BD Vacutainer Flashback Blood Collection Needle (BD, Franklin Lakes, NJ, USA). The HbA1c Assay was performed using Diazyme Direct Enzymatic HbA1c kit.

The subjects were divided into two groups: Group A were the patients with type 2 diabetes mellitus (having HbA1c>6.5mg/dl, in accordance with the current WHO guidelines for Diabetes mellitus), with chronic generalized periodontitis and Group B were systemically healthy patients (without type 2 diabetes mellitus), with chronic generalized periodontitis.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011]) was used to perform the statistical analysis. Data was entered in the excel spread sheet. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation, median and IQR (based on data distribution) for quantitative variables, frequency and proportions for qualitative variables.

Inferential statistics like: Independent sample t test / Man-Whitney test was applied to compare the periodontal inflamed surface area and HbA1C between the groups. Pearson's correlation / Spearman's correlation was used to correlate the periodontal inflamed surface area with HbA1C within each group. The level of significance was set at 5%.

Results

Table 1 and graph 1 depicts the comparison of the PISA between the groups.

When the Periodontal Inflamed Surface Area was compared between both the groups, the intergroup comparison revealed, statistically significant differences in the PISA values with the p value of 0.001 which is ≤ 0.001 (p≤ 0.001, considered statistically significant). And the diabetic group, accounted for higher PISA values than non-diabetic group. The PISA value for the diabetic group had a median of 1018.800 (IQR=1206.4-859.2), whereas the non-diabetic group had a median PISA value of 675.500 (IQR=719.4-617.2).

Table 1: Comparison of the PISA between the groups using Mann Whitney test

Groups	Minimum	Maximum	Median	Interquartile Range	p value
Diabetic	859.2	1206.4	1018.800	138.9	0.001*
Non-diabetic	617.2	719.4	675.500	52.5	

*significant

Graph 1: Comparison of the PISA between the groups using Mann Whitney test

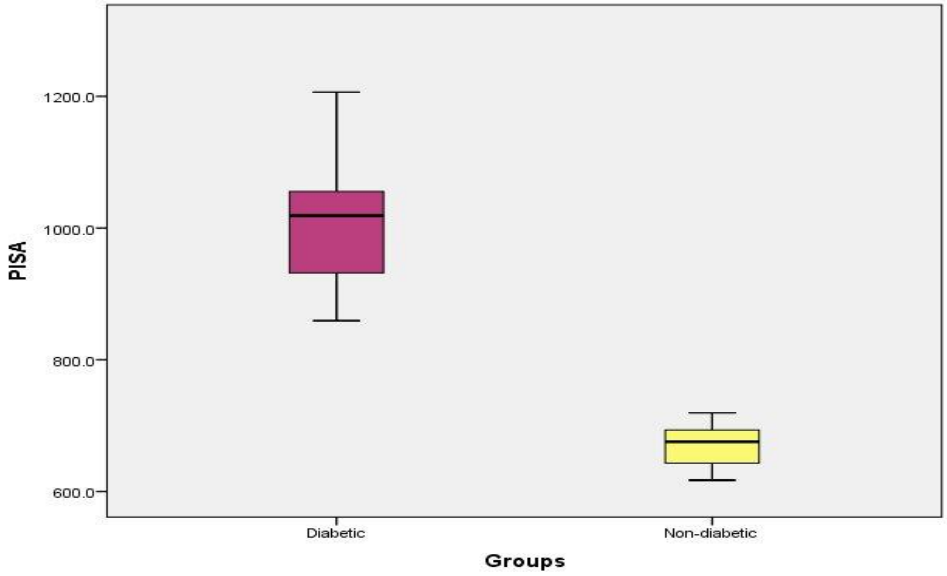


Table 2 and graph 2 depict the comparison of the HbA1c levels between the groups.

When the HbA1c levels were compared between both the groups, the intergroup comparison revealed, statistically significant differences in the HbA1c levels with the p value of 0.001 which is ≤ 0.001 (p≤ 0.001, considered statistically significant). And the diabetic group, accounted for higher HbA1c levels than non-diabetic group. The diabetic group had an a median of 7.30 (IQR=11.5-6.1), whereas the non-diabetic group had a median HbA1c level of 5.00 (IQR=5.5-4.2).

Table 2: Comparison of the HbA1c between the groups using Mann Whitney test

Groups	Minimum	Maximum	Median	Interquartile Range	p value
Diabetic	6.1	11.5	7.30	1.3	0.001*
Non-diabetic	4.2	5.5	5.00	.4	

*significant

Graph 2: Comparison of the PISA between the groups using Mann Whitney test.

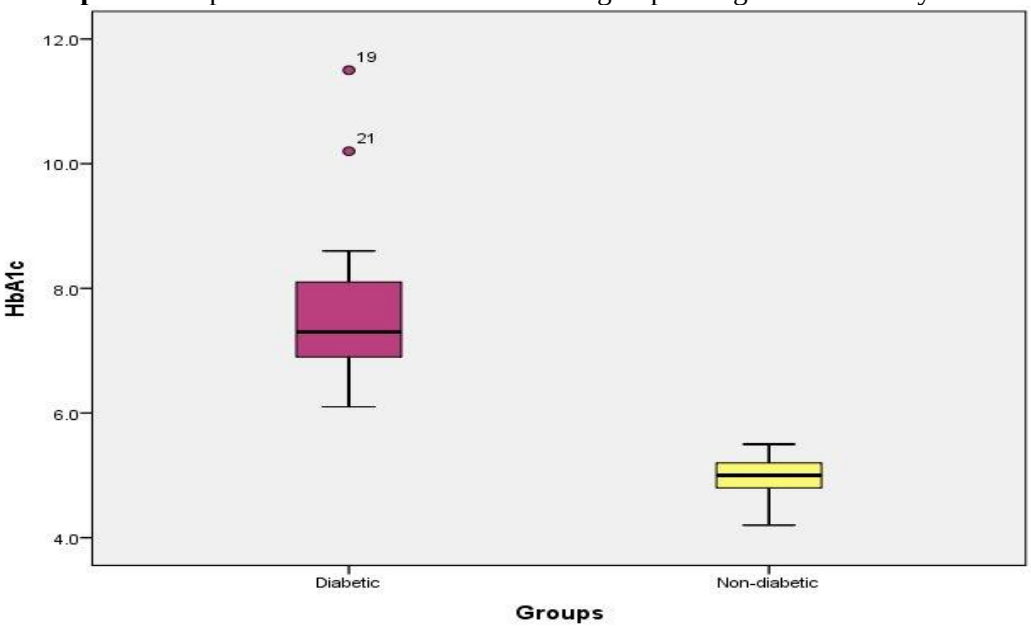


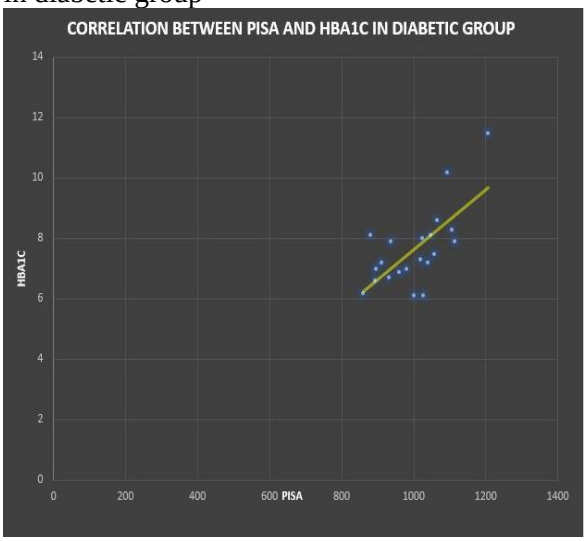
Table 3 depicts the correlation between PISA and HbA1c within the Diabetic and Non-Diabetic group. Graph 3.1 depicts the correlation between PISA and HbA1c in diabetic group. Graph 3.2 depicts the correlation between PISA and HbA1c in non-diabetic group.

Table 3: Spearman's correlation between PISA and HbA1c within the diabetic and non-diabetic group

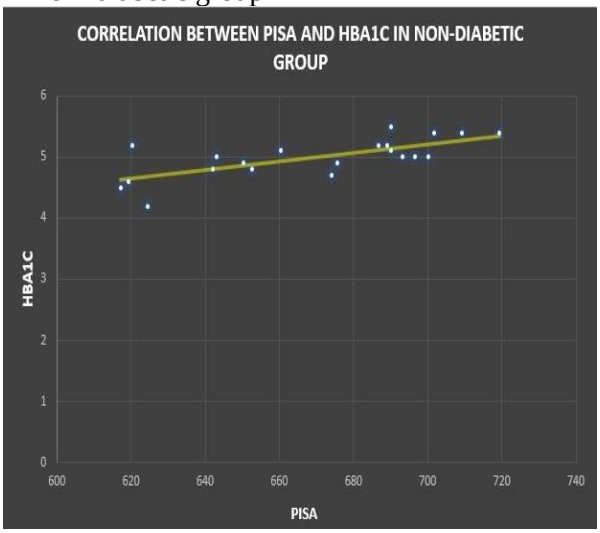
Groups		PISA Vs HbA1c
Diabetic	rho value	0.609
	p value	0.003*
Non-Diabetic	rho value	0.683
	p value	0.001*

*significant

Graph 3.1: Correlation between PISA and HbA1c in diabetic group



Graph 3.2: Correlation between PISA and HbA1c in non- diabetic group



When the correlation analysis between the PISA values and HbA1c levels was done within the diabetic group, the intra group comparison revealed a statistically significant value, indicating a positive correlation between the PISA values and HbA1c levels within the diabetic group. The p value obtained was 0.003, which is less than 0.001 ($p \leq 0.001$, considered statistically significant).

Also, the correlation analysis between the PISA values and HBA1c levels within the non-diabetic group also revealed a statistically significant difference, indicating a positive correlation between PISA values and HbA1c levels within the non-diabetic group as well. The p value obtained was 0.001, which is less than 0.001 ($p \leq 0.001$, considered statistically significant).

Upon the inter group comparison, for the correlation between PISA values and HbA1c levels, a statistically significant difference was obtained between both the groups, with the diabetic group having a greater statistical significance compared to the non-diabetic group.

Discussion

Periodontitis and diabetes mellitus have been linked as having a bidirectional cyclical association, with periodontitis aggravating hyperglycemia and diabetes causing periodontal destruction. With an increased prevalence and severity in diabetic patients, periodontitis is considered as the sixth significant consequence of diabetes.[11]

According to the research (McMullen et al 1981), chronic infections like periodontitis may cause a long-lasting state of insulin resistance, which would lead to poor glycemic management, further contributing to the cycle of hyperglycemia, non-enzymatic irreversible glycation, and protein-binding AGEs.

Löe suggested that periodontitis was the sixth consequence of diabetes mellitus in 1993.[12] From a clinician's view point, random glucose and fasting blood glucose are of limited value since they indicate the glucose concentration at a point of time. The most common of the available tests for monitoring the long- and short-term control of glucose is the estimation of Glycated Haemoglobin.[13] HbA1c assay indicates the plasma glucose over 6-8 weeks (for the average half-life of RBC is 60 days)

Several studies have revealed correlation between plasma HbA1c and periodontal disease severity. However, many studies comparing HbA1c levels with periodontal diseases severity, have expressed periodontitis in terms of probing pocket depth and clinical attachment level.[14] PPD, CAL do not quantify the amount of diseased or inflamed periodontal tissue.

The great variation in periodontal classifications used in the various studies and the lack of a tool that adequately assesses the inflammatory burden of periodontitis is a major drawback of the studies published on the periodontal inflammation – systemic disease interaction. Therefore, a new measure for quantifying the inflammatory status has been researched. The current study researches PISA (Periodontal Inflamed Surface Area), to

evaluate the surface area of bleeding pocket epithelium in square millimetres.

The scarcity of literature for the comparative association of HbA1c levels with periodontal disease severity, especially when the latter is expressed in terms of PISA, substantiates the need for and the appropriateness of the current study.

In the current study, the median PISA value for the non-diabetic group was found to be 1018.800 (IQR=1206.4-859.2) and that for the diabetic group was 675.500 (IQR=719.4-617.2). On statistical comparison of the PISA values between the Diabetic group with periodontitis and non-diabetic group with periodontitis, the differences were found to be statistically significant (p=0.001). The results of the current study, depict a higher PISA value in the diabetics with periodontitis group as compared to the non-diabetics with periodontitis group. This is attributed to the impaired adherence, chemotaxis, and phagocytosis of neutrophils in diabetic patients, which prevents neutrophil mediated destruction of bacteria in the periodontal pocket, thereby increasing periodontal destruction.[8] The current study is first of its kind, wherein the periodontal inflamed surface area has been compared between the diabetics and non-diabetics with periodontitis.

Various biochemical tests are available to assess the glycaemic status of the patients. However, out of all of the available biochemical tests, HbA1c is regarded as the gold standard test, to monitor the glycaemic control. As a standard of care (SOC) for diagnosing and managing diabetes, specifically type 2 diabetes, the HbA1c is now advised. The American Diabetes Association, in 2010, instituted the use of HbA1c as a more accurate and stable parameter for the diagnosis of diabetes, than the fasting plasma glucose estimation or oral glucose tolerance test.[15]

In the present study, the correlation test (Spearman) between PISA and glycemic control (HbA1c) for diabetic group, revealed a p value of 0.003, which is highly statistically significant. For the non-diabetic group, the p value obtained was 0.001, which is statistically significant. The intergroup comparison revealed a strong statistical correlation between the PISA and HbA1c levels in the diabetic group. Also, it was noted, with the rise in HbA1c levels, the PISA values increased as well, which was statistically significant (p=0.003). Correlation in the rise in HbA1c levels, with an increase in PISA values, was not much pronounced in the non-diabetic group (p=0.001). The results are in accordance with the study conducted by Negishi J et al[16] in 2004, which detected the high value of HbA1c to be significant factor related to advanced periodontitis in diabetic patients. A positive correlation has been reported between mean PD and HbA1c in diabetic cases by Lim et al[17] in 2004 ($r=0.26$, $p< 0.05$). However, in an investigation on 26 type I diabetic patients, Pinson et al in 1995, found no significant association between the level of control of diabetes (Glycated Hb) and probing depths, clinical attachment levels or recession.[18]

The results of non-diabetic controls showed a statistically higher correlation between HbA1c levels and PISA, but lesser than that observed for the diabetic group, with the diabetic group depicting a highly statistically significant result (p=0.003). Similar are the findings of Hayashida et al (2009)[19] and Wolf et al (2009)[20] who found a significant relationship between periodontal status and Plasma HbA1c levels in non-diabetic individuals.

The results of the present study, indicate that the PISA values exponentially increase with the rise in HbA1c levels, therefore it can be inferred that a strong correlation exists between the PISA values and HbA1c levels in diabetics with periodontitis. The results go in hand with the study by Nesse et al in 2009, who assessed a dose–response relationship between PISA and HbA1c levels in forty type 2 diabetics.[14]

PISA can be easily calculated using routine periodontal charting. It is an indication of level of periodontal inflammation in a quantitative aspect and it can be used as a parameter to differentiate patients with active inflammatory sites from those with non-inflamed or healed periodontium.

One of the limitations of the study is low sample size. Further studies can be done, using a larger sample size and assessing variables such as smoking, stress, socio-economic status etc., and its correlation with glycemic status and periodontal inflammatory condition.

Conclusion

From the results of the study, it can be concluded that there exists a dose-response relationship between the PISA and HbA1c levels. And the periodontal inflamed surface area (PISA) increases exponentially with the increase in HbA1c levels. Further studies can be done, using a larger sample size and assessing variables such as smoking, stress, socio-economic status etc., and its correlation with glycemic status and periodontal inflammatory condition.

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