# PERIODONTAL INFLAMED SURFACE AREA IN NON-DIABETIC AND DIABETIC PERSONS WITH OBESITY

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# ABSTRACT

*Objectives:* The purpose of this research was to evaluate the periodontal inflamed surface area (PISA) in persons with clinically severe obesity with or without diabetes. The PISA is thought of as the main contributor to any systemic inflammatory burden posed by periodontitis. The aforementioned disease is a chronic inflammatory condition characterized by a shift in the microbiological ecology and an increase in the inflammatory host response. This condition may affect more than teeth and their supporting structure. A relationship is thought to exist between periodontitis and systemic health; thus, periodontitis is thought to be a risk factor for various disorders such as diabetes.

*Methods:* This study analyzed the baseline data of individuals participating in a prospective study investigating whether diabetes alters the subgingival microbial composition and/or bacteria RNA expression by comparing bacteria obtained from patients with and without diabetes both before and after bariatric surgery. Patients from Temple University's Hospital Bariatric Surgery Program were selected based on inclusion and exclusion criteria for the parent study and analyzed in the present study. Medical data including BMI, HbA1c and fasting glucose were obtained. Following the dental examination, the periodontal epithelial surface area (PESA) affected by bleeding on probing (BOP) was quantified. PESA and PISA for each patient was calculated (Neese et al., 2008). Statistical analysis comparing non-diabetics and diabetics was performed using the non-parametric Mann-Whitney U Test.

*Results:* Of the 8 participants, 25% were diabetic and 75% were non-diabetic. The mean PESA was $1785.20 \pm 728.18$ mm$^2$ and $1544.80 \pm 204.73$ mm$^2$ in patients with and without diabetes, respectively. The mean PISA was 875.10 ± 653.50 $mm^2$ and 568.78 ± 181.38 $mm^2$ in patients with and without diabetes, respectively. While both PESA and PISA were higher among those with diabetes, the differences did not reach statistical significance.

*Conclusions:* These findings suggest that the inflammatory burden posed by periodontitis is greater in diabetics with obesity compared to non-diabetics with obesity. A larger sample size would be required to have appropriate statistical power to confirm the present findings. Such a study would provide a better understanding of the underlying systemic implications of periodontitis in diabetic and non-diabetic persons with clinically severe obesity.

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# CHAPTER 1

# INTRODUCTION

Diabetes is a chronic metabolic disease, which can be characterized by a lack of insulin production by the pancreas due to destruction of β-cells (type 1 diabetes) or results from insulin resistance as the body cannot effectively use the insulin (type 2 diabetes) (Mealy et al., 2006). Type 2 diabetes is actually the most common form, and accounts for 90% of all diabetes cases. Since 1980, the global prevalence of the disease has increased from 4.7% to 8.5% among adults aged 18 years and older (WHO, 2018). Interestingly, a major risk factor for developing type 2 diabetes is obesity, which affects over 650 million adults (WHO, 2020). The risk of a person with obesity developing type 2 diabetes is 20-fold greater (Field et al., 2001); the risk is even greater among those with clinically severe obesity, operationalized as a BMI $\geq 35$ kg/m$^2$ (Colditz et al., 1995). A greater BMI is associated with a larger accumulation of free non-esterified fatty acids, increase in secretion of inflammatory cytokines and adipokines and mitochondrial dysfunction (Levine, 2013). While the factors involved in increased insulin resistance are still unclear, the production of adipokines, including IL-6 and TNFα, are implicated (Krogh-Madsen et al., 2006).

People with diabetes have an increased risk of developing a number of serious health problems. Consequently, as blood glucose levels continue to increase, this can lead to complications such as cardiovascular disease, nephropathy, neuropathy, retinopathy, and periodontitis (WHO, 2016). Of particular interest is periodontitis, as it described to be the 11$^{th}$ most prevalent disease globally (IDF, 2020). Periodontitis is a chronic inflammatory condition initiated by a shift in the microbiological ecology (Marsh, 1994).

Besides the role of periodontopathogens, the host immune response is also thought to play an important role in the progressive destruction of tissues that both surround and support teeth (Socransky et al., 1992). However, beyond the oral cavity, periodontitis is considered a risk factor for a broad range of systemic diseases, which includes diabetes (Saremi et al., 2005). Periodontitis is described as the sixth major complication of diabetes (Loe, 1993). Thus, there has been much emphasis on the two-way relationship between diabetes and periodontitis; therefore, not only is diabetes a risk factor for periodontitis, but periodontitis could have a negative effect on glycaemic control (Grossi & Genco, 1998, Preshaw et al., 2012).

A fundamental feature of periodontitis is the formation of a periodontal pocket, which can be defined as the pathological deepening of the gingival sulcus (Bosshardt. 2017). Page and Schroeder (1976) detailed the pathogenesis of periodontal disease from the conversion of the junctional epithelium to pocket epithelium. These degenerative alterations can be characterized by loss of connective tissue and a disruption in cellular continuity of the epithelium (Schroeder & Listgarten, 1997). Concurrently, the epithelium becomes thinner and ulcerated. These changes are of importance as the defense system is compromised, and as result, provides a direct entry for bacteria to enter into the systemic circulation leading to systemic disease. Evidence suggests that the persistence of certain Gram-negative bacteria such as *Porphyromonoas gingivalis* affect the glycemic level (Maikura et al., 2008). Furthermore, these bacteria act as a constant source of systemic challenge, and therefore can trigger inflammatory mediators, IL-6, TNFα and IL-1 to enter the systemic circulation, altering the metabolism of glucose (Preshaw et al., 2007, Shi et al., 2019). Alternatively, the host inflammatory response to the bacteria or their byproducts may be related to the pathogenesis of glycemic control and increasing the risk of diabetic complications (Winning & Linden, 2015).

Periodontitis is associated with chronic infection and inflammation that may induce insulin resistance and negatively impact glycemic control, which Neese et al. (2008) defines as inflammatory burden. This burden is thought to be related to the amount of inflamed periodontal tissue; therefore, the greater the amount of inflamed periodontal tissue is, the larger the chances of periodontitis leading to bacteremia and systemic inflammatory responses. Although various studies define periodontitis based on its severity (mild, moderate or severe) or by using clinical parameters such as pocket depth or attachment levels, the aforementioned do not measure the amount of inflamed tissue (Neese et al., 2008). Secondary to the lack of tools to quantify the inflammatory burden, Neese et al. (2008) proposed that by determining the periodontal epithelial surface area (PESA) that is affected by bleeding on probing (BOP), the periodontal inflamed surface area (PISA) can be quantified.

The currently available literature on PISA as a periodontal index suggests that it is positively correlated with conventional periodontal classifications and with periodontal indexes (Park et al., 2017). A PISA value of greater than or equal to 130.33 $mm^2$ is predicted the presence of periodontitis with a sensitivity of 98% and a specificity of 100% (Leira et al., 2017). Nevertheless, the literature on PISA as an indicator of inflammatory burden is limited; and thus, there is a lack of research on the relationship between PISA and diabetes. As a result, the purpose of this research study was to investigate the PISA in non-diabetic and diabetic persons with clinically severe obesity.

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# CHAPTER 2

# MATERIALS AND METHODS

## Study Subjects

This study was a subgroup analysis of data from an ongoing, prospective study investigating whether diabetes alters the subgingival microbial composition and/or bacteria RNA expression by comparing bacteria obtained from diabetic and nondiabetic individuals before and after bariatric surgery. The research had been reviewed and approved by Temple University's Institutional Review Board.

Patients from this study population came from Temple University's Hospital Bariatric Surgery Program. The inclusion criteria included men and women participants, 25 to 65 years old, and BMI equal to or greater than 35 $kg/m^2$. Diabetes was operationalized as fasting plasma glucose equal to or greater than 126 mg/dl and HbA1c equal to or greater than 6.75 %. The dental criteria for inclusion were a minimum of 8 posterior teeth and at least two posterior teeth with 4-6 mm periodontal pockets and two teeth with 2-3 mm periodontal pockets.

The exclusion criteria included subjects with a diagnosis of type 1 diabetes maturity onset diabetes of the young, or latent autoimmune diabetes in adults, daily insulin requirements of 100 units, pregnant women (or those considering pregnancy during the study period), women who are currently breastfeeding, history of chronic inflammatory or autoimmune diseases or who are taking medications that affect immune function or affect body weight such as chronic systemic steroids, individuals who are nonambulatory (unable to walk 50 feet without assistance), currently smoke more than 10 cigarettes per day, individuals with prosthetic joints (hips, knee, shoulder, etc.) that require treatment with antibiotics prior to dental probing, cardiac valvopathy in cardiac transplant recipients, congenital heart disease repaired within the previous six months with prosthetic material or device (whether placed by surgery or by catheter), repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or device, unrepaired cyanotic congenital heart disease (include palliative shunts and conduits).

## Data Collection

As a part of standard care at Temple University Hospital for patients undergoing bariatric surgery, pre-operative and post-operative testing was performed. The enrolled participant's medical history was reviewed, and laboratory values (BMI, fasting blood glucose, HbA1c) were collected. The subject's height was measured in centimeters (cm) and their weight was recorded in kilograms (kg) to determine the BMI (kg/m$^2$). A venapuncture to obtain blood samples was also performed to produce a reading of each subject's fasting blood glucose and HbA1c.

## Periodontal Tooth Assessment

At Temple University Kornberg School of Dentistry, a full mouth oral examination was performed, which included dental charting of only pocket probing depth (PPD) and recording of sites with bleeding on probing (BOP) (Newman et al., 2015) in order to calculate the PISA (Neese et al., 2008). The dental examination was performed by a calibrated and blinded periodontal resident (W.C.).

PPD was measured in millimeters (mm) from the gingival margin to the base of the sulcus with a UNC-15 periodontal probe at six sites per tooth. A walking stroke was used to locate the deepest pockets. Values were rounded up to the higher mm. The probe was kept as nearly as parallel to the tooth surface as possible to ensure correct measurement. For buccal and palatal/lingual surfaces, the probe was walked up and down along the surface between the mesial and distal line angles. The deepest measurement was recorded as the probing depth. For interproximal sites, the probe was walked in the sulcus as far into the interproximal contact as possible (Persson, 1991). The probe may be tilted slightly to enable the probe to reach under the contact point (up to 30°).

BOP was assessed 30 seconds after probing each of the three pockets on the buccal and on the palatal/lingual surfaces of each tooth.  A dichotomous scoring system was used.  Yes or No for presence or absence, respectively.

Periodontal Inflamed Surface Area (PISA)

Hujoel et al. (2001) described an estimation of dentogingival epithelial surface area (DGES) ($mm^2$) by using polynomial formulas to relate typical root lengths (mm) to root surface area ($mm^2$). Based on these findings, Neese et al. (2008) constructed a Microsoft Excel spread sheet that first calculates the PESA, which quantifies the surface area of both healthy and inflamed pocket epithelium. The healthy pocket epithelium contains few inflammatory cells and serves as a protective barrier against bacteria (Takata et al., 1988). The inflamed part of the PESA may pose as an inflammatory burden to overall systemic health. Histologic studies have demonstrated that BOP was associated with a decrease in collagen connective tissue (Greenstein et al., 1981), thinned or ulcerated epithelium and inflammatory infiltration (Davenport et al., 1981). PISA can then be defined by the part of PESA that is affected by BOP. The Microsoft Excel spread sheet developed by Neese et al. (2008) can be retrieved from the following website: https://www.parsprototo.info.

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | tooth | 18 | 17 | 16 | 15 | 14 | 13 | 12 | 11 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | tooth | |
| PPD | buccal | | | | | | | | | | | | | | | | | buccal | PPD |
| | palatinal | | | | | | | | | | | | | | | | | palantinal | |
| | lingual | | | | | | | | | | | | | | | | | lingual | |
| PPD | buccal | | | | | | | | | | | | | | | | | buccal | PPD |
| | tooth | 48 | 47 | 46 | 45 | 44 | 43 | 42 | 41 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | tooth | |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| tooth | 18 | 17 | 16 | 15 | 14 | 13 | 12 | 11 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | tooth |
| surface area (mm2) | 0 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0 | surface area (mm2) |
| surface area (mm2) | 0 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0 | surface area (mm2) |
| tooth | 48 | 47 | 46 | 45 | 44 | 43 | 42 | 41 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | tooth |

| tooth | PESA | nr of sites with BOP | PISA (mm2) |
|---|---|---|---|
| 18 | 0 | | 0.00 |
| 17 | 0 | | 0.00 |
| 16 | 0 | | 0.00 |
| 15 | 0 | | 0.00 |
| 14 | 0 | | 0.00 |
| 13 | 0 | | 0.00 |
| 12 | 0 | | 0.00 |
| 11 | 0 | | 0.00 |
| 21 | 0 | | 0.00 |
| 22 | 0 | | 0.00 |
| 23 | 0 | | 0.00 |
| 24 | 0 | | 0.00 |
| 25 | 0 | | 0.00 |
| 26 | 0 | | 0.00 |
| 27 | 0 | | 0.00 |
| 28 | 0 | | 0.00 |

| tooth | PESA | nr of sites with BOP | PISA (mm2) |
|---|---|---|---|
| 38 | 0 | | 0.00 |
| 37 | 0 | | 0.00 |
| 36 | 0 | | 0.00 |
| 35 | 0 | | 0.00 |
| 34 | 0 | | 0.00 |
| 33 | 0 | | 0.00 |
| 32 | 0 | | 0.00 |
| 31 | 0 | | 0.00 |
| 41 | 0 | | 0.00 |
| 42 | 0 | | 0.00 |
| 43 | 0 | | 0.00 |
| 44 | 0 | | 0.00 |
| 45 | 0 | | 0.00 |
| 46 | 0 | | 0.00 |
| 47 | 0 | | 0.00 |
| 48 | 0 | | 0.00 |

| Total **Periodontal Epithelial Surface Area** (mm2) |
|---|
| 0.0 |

| Total **Periodontal Inflamed Surface Area** (mm2) |
|---|
| 0.0 |

Figure 1. Excel spread sheet used to record PISA from https://www.parsprototo.info

1. After filling in PPD measurements at sites per tooth in the Excel spread sheet, the computer calculated the periodontal epithelial surface area (PESA) for that specific tooth.
2. The PESA for a particular tooth was then multiplied by the proportion of sites around the tooth that was affected by BOP, in order to determine the PISA for that specific tooth.
3. The sum of the individual PISAs was calculated, amounting to the total PISA within a patient’s mouth.

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | tooth | 18 | 17 | 16 | 15 | 14 | 13 | 12 | 11 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | tooth | |
| PPD | buccal | | 3 2 3 | 3 2 4 | 4 2 3 | 3 2 3 | 3 1 2 | 2 1 2 | 3 1 2 | 2 1 2 | 3 1 2 | 2 1 2 | 4 1 3 | 3 1 4 | 4 2 5 | 5 2 3 | | buccal | PPD |
| | palatinal | | 3 2 5 | 5 3 4 | 3 3 3 | 3 2 3 | 3 2 3 | 3 2 2 | 2 2 3 | 3 2 2 | 2 1 3 | 3 2 3 | 3 2 4 | 3 2 4 | 4 2 3 | 3 3 3 | | palantinal | |
| | lingual | | | | 2 3 4 | 4 3 4 | 3 2 2 | 2 1 2 | 2 2 2 | 2 1 3 | 2 1 2 | 2 2 3 | 2 2 3 | 3 2 3 | 3 2 2 | | | lingual | |
| PPD | buccal | | | | 2 1 2 | 2 1 2 | 2 1 3 | 3 1 2 | 2 1 2 | 2 1 2 | 2 1 2 | 2 1 2 | 2 1 2 | 2 2 3 | 3 2 2 | | | buccal | PPD |
| | tooth | 48 | 47 | 46 | 45 | 44 | 43 | 42 | 41 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | tooth | |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| tooth | 18 | 17 | 16 | 15 | 14 | 13 | 12 | 11 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | tooth |
| surface area (mm2) | 0 | 88.7854 | 102.5321 | 76.8744 | 50.0550 | 44.4681 | 34.0448 | 31.6255 | 28.7190 | 34.0448 | 41.0567 | 53.0695 | 73.8546 | 94.3231 | 94.7704 | 0 | surface area (mm2) |
| surface area (mm2) | 0 | 0.0000 | 0.0000 | 47.3676 | 50.0548 | 42.5089 | 28.6267 | 28.1682 | 28.1682 | 26.0392 | 39.7053 | 38.5875 | 51.3313 | 28.5505 | 0.0000 | 0 | surface area (mm2) |
| tooth | 48 | 47 | 46 | 45 | 44 | 43 | 42 | 41 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | tooth |

| tooth | PESA | nr of sites with BOP | PISA (mm2) |
|---|---|---|---|
| 18 | 0 | | 0.00 |
| 17 | 88.785 | | 0.00 |
| 16 | 102.53 | 3 | 51.27 |
| 15 | 76.874 | 3 | 38.44 |
| 14 | 50.055 | 2 | 16.69 |
| 13 | 44.468 | | 0.00 |
| 12 | 34.045 | | 0.00 |
| 11 | 31.625 | | 0.00 |
| 21 | 28.719 | | 0.00 |
| 22 | 34.045 | | 0.00 |
| 23 | 41.057 | | 0.00 |
| 24 | 53.069 | | 0.00 |
| 25 | 73.855 | 1 | 12.31 |
| 26 | 94.323 | 6 | 94.32 |
| 27 | 94.77 | 1 | 15.80 |
| 28 | 0 | | 0.00 |

| tooth | PESA | nr of sites with BOP | PISA (mm2) |
|---|---|---|---|
| 38 | 0 | | 0.00 |
| 37 | 0 | | 0.00 |
| 36 | 28.55 | 1 | 4.76 |
| 35 | 51.331 | | 0.00 |
| 34 | 38.587 | 1 | 6.43 |
| 33 | 39.705 | | 0.00 |
| 32 | 26.039 | 1 | 4.34 |
| 31 | 28.168 | | 0.00 |
| 41 | 28.168 | | 0.00 |
| 42 | 28.627 | | 0.00 |
| 43 | 42.509 | | 0.00 |
| 44 | 50.055 | 1 | 8.34 |
| 45 | 47.368 | 2 | 15.79 |
| 46 | 0 | | 0.00 |
| 47 | 0 | | 0.00 |
| 48 | 0 | | 0.00 |

| Total **Periodontal Epithelial Surface Area** (mm2) |
|---|
| 1257.3 |

| Total **Periodontal Inflamed Surface Area** (mm2) |
|---|
| 268.5 |

Figure 2. Example of completed Excel spread sheet used to record PISA for patient #1

## Statistical analysis

Statistical analysis of the BMI, PESA and PISA between the two groups, diabetics and non-diabetics, was performed using the non-parametric Mann-Whitney U Test. A p value < 0.05 was considered statistically significant.

# CHAPTER 3

# RESULTS

A summary of the patients' characteristics is presented in Table 1. Although both men and women were eligible to participate in the study, all 8 participants in this sample were women. The mean age was 39.88 ± 8.72 years; they had a BMI that ranged from 31.10 $kg/m^2$ to 52.59 $kg/m^2$. The mean BMI was 44.63 ± 5.70 $kg/m^2$ and 44.17 ± 2.35 $kg/m^2$ in non-diabetics and diabetics, respectively.

The HbA1c ranged from 5.10 % to 7.10 %, and the fasting glucose ranged from 73 mg/dl to 142 mg/dl. Of the 8 patients, 2 (25 %) were diagnosed with type 2 diabetes with a mean HbA1c of 6.70 ± 0.57 % and a mean fasting glucose of 132.50 ± 13.43 mg/dl. The other 6 (75 %) patients were classified as non-diabetic with a mean HbA1c of 5.63 ± 0.45 % and had a mean fasting glucose of 85.50 ± 11.33 mg/dl.

Based on the dental charting, increased PPD greater than 3mm and clinical signs of inflammation indicated by the presence of BOP, all the patients were diagnosed with periodontitis (AAP Task Force, 2015).

Table 1. Patient characteristics

| Patient # | Gender | Age | BMI (kg/m$^2$) | HbA1c (%) | Fasting Glucose (mg/dl) | PESA (mm$^2$) | PISA (mm$^2$) |
|---|---|---|---|---|---|---|---|
| 1 | F | 45 | 37.10 | 5.20 | 91 | 1257.30 | 268.50 |
| 2 | F | 44 | 49.90 | 6.10 | 80 | 1495.00 | 196.70 |
| 3 | F | 27 | 40.60 | 5.60 | 74 | 1733.90 | 459.20 |
| 4 | F | 26 | 42.98 | 5.10 | 96 | 1497.80 | 568.80 |
| 5 | F | 39 | 45.83 | 6.30 | 142 | 1270.30 | 221.60 |
| 6 | F | 49 | 52.59 | 6.20 | 99 | 1826.00 | 1429.10 |
| 7 | F | 46 | 42.51 | 7.10 | 123 | 2300.10 | 1528.60 |
| 8 | F | 43 | 44.90 | 5.60 | 73 | 1458.80 | 490.40 |

A summary of the total PISA within each patient's mouth is presented in Table 1. Table 2 is the PESA and PISA of diabetic subjects. Table 3 is the PESA and PISA of non-diabetic subjects. In diabetics, the PESA ranged from 1270.30 $mm^2$ to 2300.10 $mm^2$ and the PISA ranged from 221.60 $mm^2$ to 1528.60 $mm^2$. In non-diabetics, the PESA ranged from 1257.30 $mm^2$ to 1826.00 $mm^2$ and the PISA ranged from 196.70 $mm^2$ and 1429.10 $mm^2$.

Table 2. PISA of diabetic subjects

| Diabetes status | Patient # | PESA ($mm^2$) | PISA ($mm^2$) |
| --- | --- | --- | --- |
| Diabetic (HbA1c ⩾6.75%) | 5 | 1270.30 | 221.60 |
| | 7 | 2300.10 | 1528.60 |

Table 3. PISA of non-diabetic subjects

| Diabetes status | Patient # | PESA ($mm^2$) | PISA ($mm^2$) |
|---|---|---|---|
| Non-diabetic (HbA1c <6.75%) | 1 | 1257.30 | 268.50 |
| | 2 | 1495.00 | 196.70 |
| | 3 | 1733.90 | 459.20 |
| | 4 | 1497.80 | 568.80 |
| | 6 | 1826.00 | 1429.10 |
| | 8 | 1458.80 | 490.40 |

The PESA values in non-diabetics and diabetics were a mean of 1544.80 ± 204.73 $mm^2$ and 1785.20 ± 728.18 $mm^2$, respectively (Figure 3).

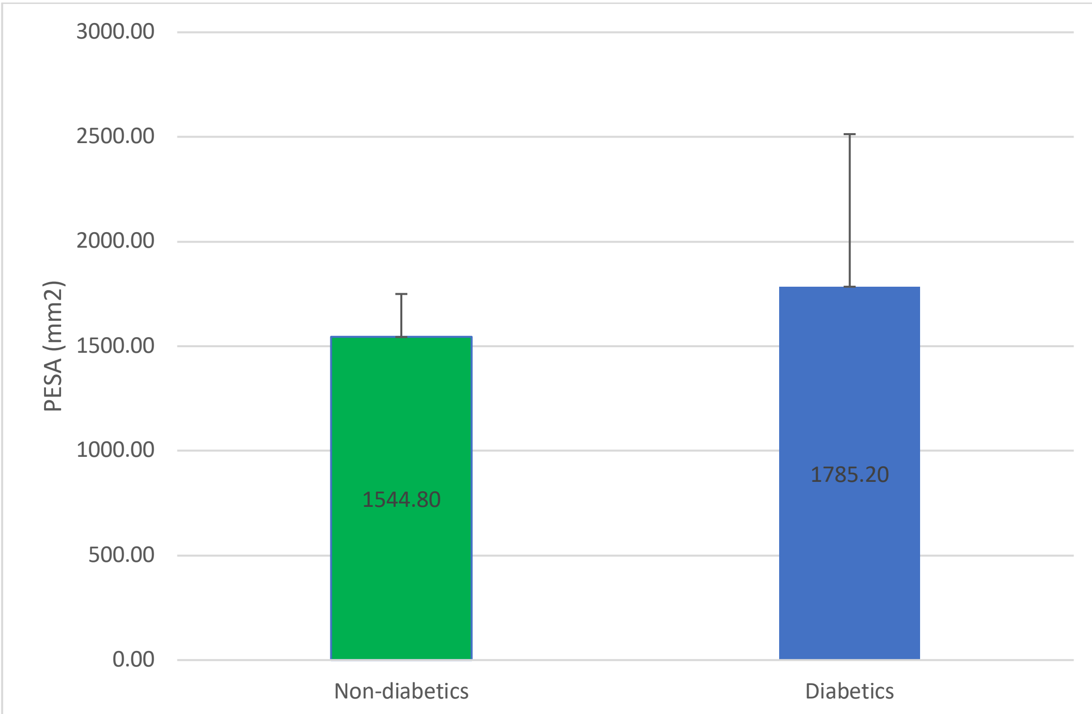


Figure 3. Comparing the mean PESA of non-diabetic and diabetic subjects. The Mann-Whitney U value was 5.000 and the p-value was 0.857. Statistical significance was set at $p < 0.05$. Thus, the difference between the groups did not reach statistical significance.

The PISA values in non-diabetics and diabetics were a mean of 568.78 ± 444.28 $mm^2$ and 875.10 ± 924.19 $mm^2$, respectively (Figure 4).

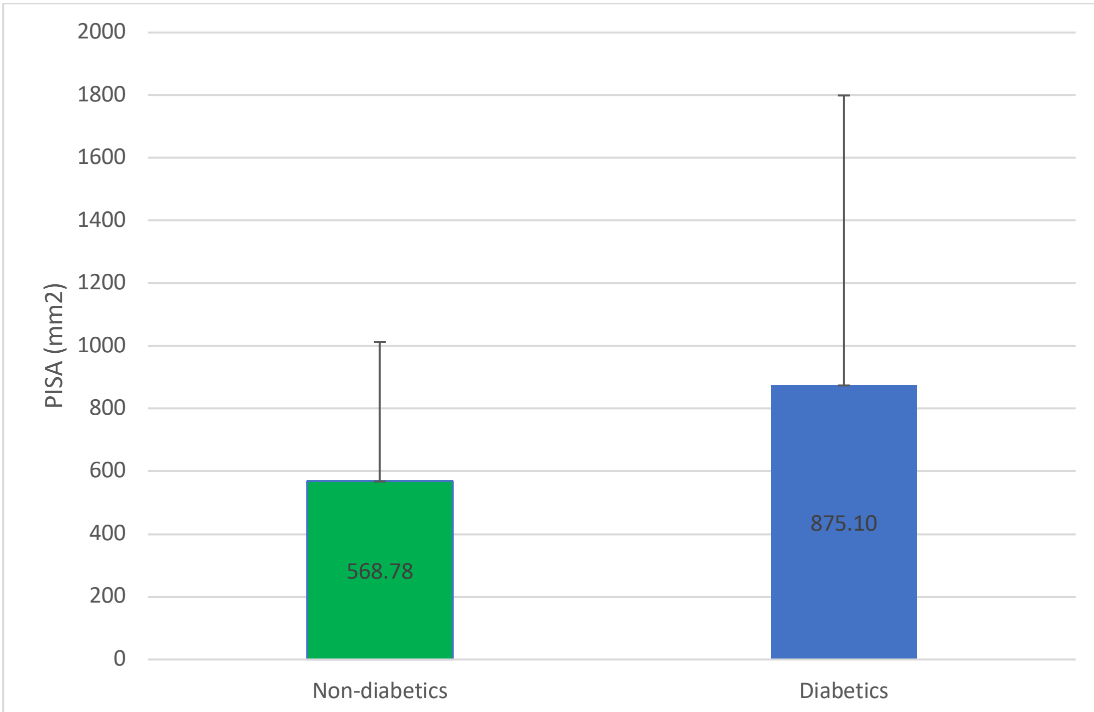


Figure 4. Comparing the mean PISA of non-diabetic and diabetic subjects. The Mann-Whitney U value was 5.000 and the p-value was 0.857. Statistical significance was set at $p \leq 0.05$. Thus, the difference between the groups did not reach statistical significance.

Statistical analysis of the data was performed using the Mann-Whitney U Test and using a p-value of 0.05. The mean BMI of non-diabetics with obesity could not be statistically differentiated to that of diabetics with obesity, with a p-value of 1.000. The mean PESA in non-diabetics compared to diabetics could not be significantly differentiated with a p-value of 0.857. The mean PISA between the two groups could not be statistically differentiated with a p-value of 0.857.

CHAPTER 4

DISCUSSION

The present study suggests that PISA is greater in women with clinically severe obesity that are diabetic compared those that are non-diabetic. In the diabetic group, the PISA ranged from 221.60 $mm^2$ to 1528.60 $mm^2$, with a mean of 875.10 ± 924.19 $mm^2$. In comparison to the non-diabetic group, the PISA ranged from 196.70 $mm^2$ and 1429.10 $mm^2$, with a mean of 568.78 ± 444.28 $mm^2$. However, these differences did not reach statistical significance.

The present findings appear to be in line with currently available knowledge about PISA and HbA1c. In a study by Neese et al. (2009), a dose–response relationship between HbA1c over time and the PISA in type 2 diabetics was found. In that study, the authors had observed that an increase in PISA of 333 $mm^2$ is associated with an increase in HbA1c by 1.0%. In contrast, Susanto et al. (2012) found that the PISA did not predict the HbA1c in patients with type 2 diabetes but did predict the HbA1c in healthy patients. Interestingly, in that same study, the extent and severity of periodontitis did not contribute significantly as a predictor to HbA1c. Given that the PISA reflects the amount of inflamed periodontal tissue, it was suggested that it more accurately predicts the infectious and inflammatory burden compared to other methods used to define periodontitis (Neese et al., 2008, Neese et al., 2018).

Although the effect of periodontal treatment on diabetic control and systemic inflammation are unknown, the present findings are important as various treatment studies using non-surgical periodontal therapy have highlighted a positive effect on glycemic control and changes in clinical periodontal parameters of inflammation. For example, Kiran et al. (2005) found that scaling and root planning resulted in a 50 % reduction in gingival bleeding and significant reduction in HbA1c, from 7.5 % to 6.5 %. From the perspective of diabetes control, a 1 % reduction appears to be modest but its impact on systemic health may in fact be more significant. To this point, Balady et al. (2007) found that a 1 % decrease in HbA1c is associated with a 25% reduction in mortality risk from cardiovascular diseases. Another study by Stratton et al. (2000) estimated that each 1 % reduction in HbA1c is associated with reduction in risk of 21 % for diabetes related deaths, 14 % for myocardial infarction, and 37 % for microvascular complications. Therefore, there is a potential benefit of reducing the PISA and the inflammatory burden of periodontitis through periodontal therapy. This underlines the importance of maintaining periodontal health and the need for oral health evaluation to become an integral part of patient care. Co-management by dental and medical teams may be needed for those diagnosed with periodontitis, diabetes and obesity.

The limitations of this study include the small sample size that left the study underpowered to detect statistical significance. Trends in the expected direction were observed; however, in order to confirm these relationships, it would be necessary to increase the power of this study by having a larger sample size. By increasing either the entire sample size of diabetic and non-diabetic patients or by raising the non-diabetic-to-diabetic ratio, levels of significance may demonstrate that the PISA is greater in clinically severe obese persons that are diabetic compared those that are non-diabetic. Also, all the patients in the present study were women, and a possible confounding variable would be menopause status and the possible use of hormone replacement therapy that was not controlled. Given the mean age of 39.88 ± 8.72 years of the participants, a study by Shen et al. (2017), suggests that women with earlier menopausal age (equal to or less than 45years) is associated with a 20% increased risk of diabetes compared to the average menopausal age of 49.5 years. A suggestion for future studies would be to increase the sample size, control for menopause status and include men.

The advantage of the PISA index is that it can be easily applied and implemented in a clinical evaluation as it only requires PPD and BOP as parameters. Knowing that the inflamed epithelial surface area is of interest, it should not be important the apico-coronal location of the gingival margin/epithelium relative to the cemento-enamel junction. Furthermore, full mouth assessment of clinical attachment levels is time consuming and technically demanding. The PISA also has its shortcomings as there are measurement errors related to examiner, instrument and patients' teeth. Additionally, the calculation of PISA uses population based mean values of both root surface areas and root lengths, and therefore does not take individual variations into account. Finally, PISA may not adequately predict the probability of periodontitis to cause other diseases, such as diabetes, even if it would be possible to measure precisely the amount of inflamed periodontal tissue. As previously alluded to, it would be necessary to take into consideration the presence of certain inflammatory mediators, such as IL-6, IL-1 and TNF$\alpha$, as well as certain Gram-negative oral microorganisms that have been shown to play key roles.

# CHAPTER 5

# CONCLUSION

The results from the present study may provide insight into the inflammatory burden posed by periodontitis in diabetic persons with obesity compared to non-diabetic persons with obesity. The PISA was greater for diabetics than for non-diabetics, but the difference was not statistically significant. Further studies are warranted with a larger sample to confirm this result. Additional studies are also required to better understand the relationship between periodontitis and diabetes in general. Clarity is needed specifically on how periodontitis may trigger or aggravate glycemic control and the mechanisms through which this occurs. Furthermore, investigating the influence of obesity as risk factor for both periodontitis and diabetes, and the potentially beneficial effects of weight loss, whether through lifestyle changes or bariatric surgery would be of interest.

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