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Periodontal Disease in Patients with Type 2 Diabetes and Its Relationship with Dry Mouth Condition

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ABSTRACT

This study aimed to determine the prevalence and severity of chronic periodontitis (CP) and the relationship between periodontal status and dry mouth condition in patients with type 2 diabetes mellitus (T2DM). A cross-sectional study was conducted on 66 controlled T2DM patients, determined by HbA1c level ≤ 9%. Plaque index (PI), gingival index (GI), periodontal pocket depth (PPD), and clinical attachment loss (CAL) were recorded. Subjects were given questionnaire for self-evaluation of dry mouth followed by collection of saliva. Data were analysed using SPSS version 22.0. Results showed that the prevalence of CP was 93.9% with severity ranging from mild (41.9%), moderate (30.6%), to severe (27.5%). Most subjects (74.2%) had normal stimulated salivary flow rate although 15.9% reported having less saliva. There was no significant association between periodontal parameters and salivary flow rate. In conclusion, T2DM patients exhibited high prevalence of CP despite having controlled glycaemic status. Dry mouth condition was not a common symptom and was also not associated with periodontitis. To ensure appropriate management of diabetics, collaboration between medical colleagues and dental practitioners is important to control progression of periodontal disease.

Keywords: *Diabetes mellitus; mouth dryness; periodontitis; xerostomia.*

INTRODUCTION

Recently, a new definition for periodontitis has been published by Tonetti *et al.* (2018). The authors stated that the clinical definition for periodontitis is characterised by "microbially-associated, host-mediated inflammation that results in loss of periodontal attachment", which is detected as clinical attachment loss. Traditionally, periodontal disease is known as a chronic inflammation of the periodontium (which includes gingiva, periodontal ligament, alveolar bone, and root cementum) due to presence of bacterial plaque. It started as gingivitis and is reversible if patients can maintain good oral hygiene. However, if this condition is left untreated, the inflammation spreads to the underlying structures, causing tissue destruction and bone resorption (Flemmig, 1999). Thereafter, collagen fibres of the periodontal ligaments will break down, and periodontal pocket develops. Although these processes progress slowly, the

tissue destruction that occurs is permanent (Seymour *et al.*, 2015). Unfortunately, periodontal disease is very common, but its occurrence is often unnoticed by patients. In advanced stage, it negatively impacts many aspects of daily living and quality of life, in terms of confidence, social interactions, and food choices, such as having semisolid meals because patient cannot tolerate solids (O'Dowd *et al.*, 2010).

Diabetes is one of the major risk factors for periodontitis (Preshaw *et al.*, 2012), where diabetics are three to four times more likely to have periodontal disease compared to non-diabetics (Emrich *et al.*, 1991). Prolonged tissue exposure to hyperglycaemia results in the production of advanced glycation end products, which leads to an increase in collagen cross-linking and the generation of reactive oxygen intermediates, such as free radicals. Over time, these collagen fibres accumulate in the tissues and thickened the basement membrane, a condition which could impair oxygen diffusion, waste elimination, leukocyte migration, and the diffusion of immune factors. These disorders would then contribute to the pathogenesis of periodontitis (Lalla *et al.*, 1998; Molina *et al.*, 2016).

Besides periodontitis, the other oral complication of diabetes mellitus (DM) is dry mouth condition, also known as xerostomia. It is defined as the subjective perception of dry mouth. The perception of dry mouth is sometimes, but not always, associated with a reduced salivary flow. The normal saliva quantity is important in the maintenance of the integrity of oral tissues, as saliva plays an important role in defense mechanism. The normal stimulated salivary flow rate is defined as a rate ≥ 1.0 ml/min. Hyposalivation is considered when salivary flow rate is < 0.1 ml/min at rest or < 0.7 ml/min under stimulation (Navazesh and Kumar, 2008; Löfgren *et al.*, 2012).

Dentists have long been aware of the importance of a diagnosis of diabetes in their patients, as many oral conditions are associated with this disease. Bajaj *et al.* (2012) reported that T2DM patients were observed to have periodontal disease (34%), oral candidiasis (24%), tooth loss (24%), and dental caries (24%). Other complications include xerostomia and salivary gland hypofunction in 14% of their subjects.

There is association between oral health and diabetes. Studies evaluating the association between the level of glycaemic control in patients with T2DM and their salivary flow reported that patients with poor glycaemic control produce less saliva (Chávez *et al.*, 2000; Chávez *et al.*, 2001). The authors speculated that the altered salivary flow rate in poorly-controlled DM is associated with autonomic neuropathies, hormonal imbalances, and microvascular changes (Chávez *et al.*, 2000). They then extended their study in the elderly patients (aged 54–90 years old) and reported similar findings; that is, older patients with poorly-controlled diabetes have impaired salivary flow when compared to better-controlled diabetes and non-diabetes. However, they did not report significant complaints of xerostomia (Chávez *et al.*, 2001). Hoseini *et al.* (2017) also reported lower salivary flow rate and higher xerostomia in DM patients compared to healthy controls. The underlying aetiology of xerostomia may be due to systemic diseases such as endocrine, autoimmune, infectious, and granulomatous diseases (Millsop *et al.*, 2017).

Although studies regarding relationship between periodontitis and DM are numerous in the field, the influence of these with dry mouth condition is under reported. We hypothesised that poor periodontal status is significantly correlated with dry mouth condition in diabetic patients. Thus, this study was conducted to assess the periodontal status and dry mouth condition in patients with controlled T2DM, determined by HbA1c level ≤ 9%.

MATERIALS AND METHODS

This was a cross-sectional observational study on diabetic patients attending Hospital Universiti Sains Malaysia, Kelantan, Malaysia. The study protocol was approved by the Human Research Ethics Committee of USM, at which the study was conducted; reference number: USMKK/PPP/JEPeM [266.3.(13)]. All participants signed written informed consent and agreed to participate in the study. Patient's information was kept confidential by assigning numbers to each of them.

The inclusion criteria were patients with controlled T2DM determined by HbA1c level ≤ 9% (Tsai *et al.*, 2002) and had been diagnosed with T2DM for more than three years. Patients with HbA1c < 7.0% will be considered as having well-controlled diabetes and the rest of the patients with HbA1c > 7% and ≤ 9% will be considered as having controlled diabetes. Patients with uncontrolled systemic diseases, pregnant, smokers, and those who have received periodontal treatment for the past three months prior to the study, were excluded.

The measurement of periodontal pocket depth and clinical attachment loss on one quadrant (where at least seven teeth were present) was done repeatedly on three patients by two examiners before the study started. The intra-examiner calibration was done on two patients with the same criteria. The reproducibility and reliability of the examiners were analysed using intra-class correlation coefficient. The results showed an agreement with Cronbach's alpha of 0.78 for inter-examiners and 0.85 for intra-examiner calibration.

From the medical records, patients who have recent HbA1c level ≤ 9% were selected based on the inclusion and exclusion criteria. They were informed about the study and written informed consent was obtained. Patients were given an appointment at the dental clinic for oral examination. Prior to the appointment, they were advised to refrain from eating, drinking, and performing oral hygiene measures at least one hour before saliva collection. During the appointment, the assessment of dry mouth was done by using self-administered questionnaire (Grisius and Fox, 1998) with the help of the researcher. Questions included were: (i) Do you have difficulty swallowing dry foods? (ii) Does your mouth feel dry while eating a meal? (iii) Do you sip liquids to aid in swallowing dry foods? and (iv) Does the amount of saliva in your mouth most of the time seem to be too little, too much, or you don't notice it?

The collection of stimulated saliva was carried out based on guidelines by Navazesh and Kumar (2008). The container and chewing gum were pre-weighted prior to data collection sessions. In upright position, patients chewed a chewing gum for two min to the sound of Metronome app (Mobile Metronome for Android version 1.2.4F) to standardise the chewing stroke at 65 beats/min. The stimulated saliva was spit twice into the container, once after one min and another at the end of the two min. However, patients could spit more frequently if they were unable to hold their saliva in the mouth. Both container and chewing gum were then weighted again. The difference in weight was taken as the weight of saliva. The rate of stimulated salivary flow (mg/min) was calculated by dividing this weight by two. The mg/min unit is equivalent to ml/min, since over 99% of saliva is composed of water (Navazesh and Kumar, 2008).

Following saliva collection, periodontal assessment was carried out with the patient on the dental chair in supine position. The measurements of periodontal parameters such as plaque index (Silness and Loe, 1964), gingival index (Loe and Silness, 1963), probing pocket depth (PPD), and clinical attachment loss (CAL) were assessed using William's periodontal probe with grading of 1, 2, 3, 5, 7, 8, 9, and 10 mm, using gentle pressure (probe's power = 0.25 N) and visual examination. Alveolar bone loss relative to root

length (in millimetre) was measured from orthopantomogram radiograph using Planmeca Romexis software. The assessments were performed by a calibrated examiner and all data were recorded in a data collection form.

PPD and CAL were determined at six sites per tooth; that is, disto-buccal, mid-buccal, mesio-buccal, disto-lingual, mid-lingual, and mesio-lingual (Armitage, 2004). The PPD was measured using a periodontal probe, in which the depth from the gingival margin to the base of the pocket was recorded. The total PPD measurements from all teeth were then averaged to get a mean score for each subject.

CAL is the clinical parameter to detect loss of periodontal attachment and to determine the severity of periodontitis. It is measured from the cementoenamel junction (CEJ) to the base of the pocket (in millimetre) at six sites per tooth, as for PPD. When the CEJ can be seen clinically, CAL is calculated by adding the depth of periodontal pocket to the gingival recession measurement. Gingival recession is the distance between the CEJ and gingival margin. CAL measurements were then used to determine the presence of periodontal disease and its severity, based on the American Academy of Periodontology (1999) classification (Armitage, 1999). Chronic periodontitis (CP) is deemed to be localised when less than 30% of sites are affected and generalised when more than 30% of sites are affected. For severity of CP, it was considered mild when CAL is 1–2 mm, moderate when CAL is 3–4 mm, and severe when CAL is ≥ 5 mm.

All data were entered and analysed using the Statistical Package for the Social Sciences (SPSS) version 22.0 software. Descriptive analyses of demographic variables were expressed as means and standard deviations (SD), or frequencies and percentages. The prevalence of periodontal disease was determined at 95% confidence interval (CI). Mann-Whitney test was used to compare the means of periodontal parameters between the different groups of HbA1c level. Chi-squared test was used to test for association between the levels of the group's glycaemic control with (i) number of patients with PPD and (ii) salivary flow rate. The Pearson's correlation coefficient was used to determine the correlation between periodontal status and dry mouth condition in T2DM patients. A p value of < 0.05 was considered as statistically significant.

RESULTS

A total of 66 patients with the mean age of 54.9 (SD 6.71) years old participated in this study, in which 59% of them were males. More than 86% were Malays, who made up the majority of the population in this part of the country. The mean HbA1c level was 7.3% (SD 0.89). Out of the 66 patients, 26 (39.4%) were in well-controlled diabetic status (HbA1c < 7.0%).

The prevalence of CP among T2DM patients was 93.9% (95% CI: 0.88, 1.0). Among them, 41.9% had mild CP, 30.6% moderate CP, and 27.5% had severe CP based on CAL. There were 56 (84.8%) patients presented with mean PPD ≥ 3 mm. The records of periodontal parameters in these patients are shown in Table 1. Sixty-three percent of all patients presented with at least one site of PPD ≥ 5 mm; most of them were in the HbA1c group of ≥ 7.0%. However, there was no significant association between HbA1c level and PPD; $\chi^2(1) = 0.57$, $p = 0.812$ (Table 2).

Table 1 Periodontal status of the patients with pocket depth ≥ 3 mm (n = 56)

Periodontal parameter	Mean (SD)	Range (min-max)
PI	1.68 (0.52)	0.5–3.0
GI	1.88 (0.52)	0.4–3.0
PPD (mm)	4.83 (0.81)	3.0–8.6
CAL (mm)	3.69 (1.46)	2.1–9.1

PI = Plaque index; GI = Gingival index; PPD = Probing pocket depth; CAL = Clinical attachment loss.

Table 2 The association between HbA1c level and PPD (n = 66)

Variable	Mean (SD)	HbA1c < 7.0% (n)	HbA1c ≥ 7.0% (n)	χ^2 (df)	*p* value*
PPD < 5 mm	3.44 (1.85)	9	15	0.57 (1)	0.812
PPD ≥ 5 mm	5.60 (0.86)	17	25		

*Chi-squared test, PPD = Periodontal pocket depth.

The mean stimulated salivary flow rate was 1.63 (SD 0.94) mg/min, in which 74.2% have a normal stimulated salivary flow rate (≥ 1.0 mg/min). Female subjects have slightly higher salivary flow rate compared to male subjects, 1.71 (SD 1.01) mg/min and 1.58 (SD 0.82) mg/min, respectively. The salivary flow rate was slightly higher in patients with well-controlled DM [1.73 (SD 0.91) mg/min] compared to controlled DM group [1.59 (SD 1.01) mg/min]. However, it was found that there was no significant association between the level of HbA1c and salivary flow rate; $\chi^2(1) = 2.414$, $p = 0.12$. In terms of self-rated saliva quantity, most of the subjects rated as having normal amount of saliva (Table 3). Plaque index, gingival index, PPD, and CAL were not correlated with stimulated salivary flow rate among T2DM with periodontitis (Table 4).

DISCUSSION

The impact of DM to the periodontal tissues has been widely reported. The pathophysiological changes would likely be the reason for the higher prevalence of CP seen in this study, which coincides with a report from National Oral Health Survey of Adults 2010 (NOHSA 2010) in Malaysia (Oral Health Division, Ministry of Health Malaysia, 2013). Previous studies had also suggested that the risk of periodontitis in diabetic patients was higher compared to healthy patients (Emrich *et al.*, 1991; Tsai *et al.*, 2002; Mittal and Teeluckdharry, 2010; Garcia *et al.*, 2015).

Table 3 Evaluation of the saliva quantity based on patient's perception (n = 66)

Saliva quantity	Frequency (%)
Normal	30 (45.5)
Much	23 (23.8)
Less	11 (16.7)
Not sure	2 (3.0)

Table 4 The association between stimulated salivary flow rate and periodontal parameters in patients with pocket depth ≥ 3 mm (n = 56)

Periodontal parameter	Correlation coefficient (*r*)	*p* value*
PI	0.51	0.686
GI	0.79	0.526
PPD (mm)	0.12	0.937
CAL (mm)	-0.43	0.732

*Pearson coefficient correlation test; PI = Plaque index; GI = Gingival index; PPD = Probing pocket depth; CAL = Clinical attachment loss.

Saliva is an important fluid in the oral cavity; one of its many functions is to clear the oral cavity of bacteria, which could potentially harm the periodontium. Many studies have shown that DM and periodontal disease are biologically linked together (Preshaw *et al.*, 2012; Casanova *et al.*, 2014; Molina *et al.*, 2016). Moreover, xerostomia and salivary gland hypofunction have also been reported in DM subjects (Chávez *et al.*, 2000; Chávez *et al.*, 2001; Moore *et al.*, 2001; Bajaj *et al.*, 2012), which could be more damaging to the periodontium. However, we could not find any association between CP and dry mouth condition in this study, probably because we studied patients who have controlled T2DM with HbA1c level ≤ 9.0% (Chávez *et al.*, 2000; Tsai *et al.*, 2002).

Various methods have been used to collect saliva. Salivary flow rates are usually measured for at least five min after an overnight fast or two hours after a meal (Löfgren *et al.*, 2012). Other study proposed collection of saliva using pre-weighted cotton rolls at the orifice of major salivary glands, and re-weigh them after collection time (Leal

et al., 2010). In this study, the collection of stimulated saliva was carried out based on guidelines by Navazesh and Kumar (2008). The stimulated saliva was induced by using chewing gum, instead of paraffin wax. The chewing gum was chosen as it is easier to chew, more widely available in the market, and more acceptable to the patients, compared to paraffin wax. As this study was designed to be used in a clinical setting in the future, the use of easily available chewing gum is a better option than paraffin wax. The chewing method is also the simplest way to assess salivary flow rate (Navazesh and Kumar, 2008). Stimulated salivation by chewing the gum increases the crevicular fluid, adding to the volume of saliva produced in these patients. Chewing gum is known to be one of the saliva stimulants for dry mouth, based on its mechanism of action of oral stimuli; namely, taste and mastication. Both of this stimulation provide instant relief from dry mouth as they increase salivation (Inui, 2015). Despite the advantages of using chewing gum, it may also influence the chewing masticatory stroke in patients with less number of teeth remaining in their mouth. Besides, the elderly patients seemed to be unfamiliar to gum chewing, which may affect the stimulation of saliva and its flow rate.

Whole saliva was collected as it is the most frequently used fluid to diagnose alterations in salivary output compared to saliva from a specific gland. It is a non-invasive procedure, cost-effective with limited training, and requires no special equipment for its collection. The early detection of salivary hypofunction will potentially be valuable for the management of xerostomia in preventing other oral and pharyngeal complications. Some older patients may not be aware of their reduced salivary flow due to dementia or other medical conditions; thus, this assessment would be of greater value in this population.

Salivary Flow Rate and Dry Mouth Condition

In this study, 25.8% of the patients had reduced salivary flow rate, which correlates with some studies that showed the prevalence of xerostomia in both T1DM and T2DM varies from 24% to 76% (Moore *et al.*, 2001; Carda *et al.*, 2006; Busato *et al.*, 2012; Prathibha *et al.*, 2013). However, there is considerable disagreement in the literature whether there is an effect of DM on alterations to salivary flow rates. Dodds and Dodds (1997) reported that patients with poorly-controlled T2DM did not have impaired salivary output. The authors found no differences in unstimulated and stimulated parotid saliva flow between diabetics and non-diabetics, although the unstimulated saliva was less in DM patients compared to non-diabetics. Nonetheless, they did not consider the medication taken by the patients, which could also influence the salivary output (Xu *et al.*, 2019).

This study showed that controlled diabetes patients had a normal stimulated salivary flow rate, in line with Chávez *et al.* (2000) who reported similar findings. They mentioned that patients with poorly-controlled diabetes (HbA1c ≥ 9%) had lower stimulated parotid flow than patients with controlled diabetes and non-diabetes group. Moreover, the authors concluded that there was no significant difference in dry mouth complaints in terms of the level of glycaemic control and salivary flow rate. Since some of the patients in the present study presented with reduced salivation, this impairment could be related to the diabetes complications of neuropathy. Salivation is stimulated via the autonomic nervous system; thus, when neuropathies present, salivation may also be affected. Indeed, Carda *et al.* (2005) has demonstrated that acinar cells of the salivary gland are smaller in patients with DM.

Chávez *et al.* (2001) investigated salivary flow rate among diabetics who complained of xerostomia using a standardised xerostomia

questionnaire. They reported that older people with poorly-controlled diabetes may have reduced salivary flow compared to better-controlled diabetes and normal people; however, there were more patients complaining of thirst rather than xerostomia. Thirst is associated with dehydration, and reduced salivary flow is also related to dehydration. Thus, it was suggested that thirst may be related to hypofunction of the salivary gland in these patients.

There may also be other variables that could influence the salivary flow which give rise to the different value in salivary flow rate; some of these were our study limitations. These factors include: (i) medication taken by the patients which has some xerogenic effects on the salivary flow, (ii) the time of saliva collection which was not at its peak production time, (iii) the difference in fluid or food intake prior to the test, and (iv) the amount of residual saliva that was swallowed during saliva collection. In this present study, timing of saliva collection was set in the morning between 8.30 am to 11.30 am, although there were a few patients who could not conform to it.

Association between Periodontal Parameters and Dry Mouth Condition

The present study found no association between periodontal parameters and dry mouth condition in the study subjects. Although the prevalence of CP is high, it does not show any effect on the salivary flow rate which was found to be within the normal range. In contrast, Farsi *et al.* (2008) found an association between periodontitis and salivary flow rate; hence, concluded that periodontal disease is strongly linked to salivary flow rate. Meanwhile, Márton *et al.* (2008) who assessed the prevalence of xerostomia and its relation to other symptoms of oral dryness suggested that subjects with less saliva might have a higher risk for caries and gingivitis, but not for periodontitis. They also reported that gingival bleeding and plaque indices were significantly higher in patients with low saliva; thus, there is an increased risk for plaque build-up and gingivitis in patients with hyposalivation. The salivary flow rate and periodontitis was not significantly associated in this present study.

There are some arguments on how the dry mouth can increase the risk of periodontitis. When there is reduced saliva, there will be an increase in bacterial plaque accumulation and food debris, as the cleaning effect of saliva is affected (Dodds *et al.*, 2015). This might predispose the subject to periodontal disease. Moreover, the high glucose environment in diabetes patients can possibly alter the plaque microflora which favours the periodontal pathogen, thus increasing the risk for periodontal destruction. It was thought that saliva does not have a direct influence on periodontal pathogens within the periodontal pocket since there is an outward flow of crevicular fluid, and the antibacterial components that are contained in the saliva are able to fight against the pathogenic periodontal pathogens (Faran Ali and Tanwir, 2012). However, in patients with reduced salivary flow, bacterial clearance is reduced; therefore, there will be more bacterial colonisation on the periodontal tissue. In this study, subjects with normal stimulated salivary flow rate were the majority; hence, the presence of CP could be due to dental biofilm and other factors, for example diabetic status, age, and oral hygiene. Plaque accumulation has been shown to be associated with CP (Lertpimonchai *et al.*, 2017).

CONCLUSION

This present study concluded that: (i) there was high prevalence of CP in controlled T2DM patients with moderate to advanced stage of severity, (ii) controlled T2DM patients have normal salivary flow rate, and (iii) there was no association between periodontal disease and dry mouth condition in controlled T2DM patients. Both dental and medical counterparts should collaborate to improve patient care; referral both ways

are critical in the management of these patients. The periodontal examination needs to be a part of diabetes management and assessment. If glycaemic status does have effects on salivary dysfunction, then preventive and intervention therapy will be necessary to reduce the related oral problems. Therefore, early referral by medical colleagues for dental assessment is crucial to prevent and control the disease progression, thus improving quality of life of the patients.

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