Original Article

Prevalence of Oral Mucosal Lesions in Patients with Type 2 Diabetes Attending Hospital Universiti Sains Malaysia

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Abstract

Objectives: **Diabetes mellitus is associated with a greater likelihood of developing certain oral mucosal disorders. This study was aimed at assessing the prevalence of oral mucosal lesions (OMLs) in patients with type 2 diabetes (DM2) and to investigate the association of such lesions with metabolic control of the disease.**

Methods: **This cross-sectional study involved 391 patients with DM2 and 391 non-diabetic control subjects. Demographic information and data on the duration and type of diabetes, glycosylated hemoglobin (HbA1c) values, medical history, and current use of medication were obtained from medical records. Detailed oral examination was performed in accordance with international criteria.**

Results: **The prevalence of OMLs was significantly higher among diabetic patients (45.5%) than among control subjects (38.4%) ($P = 0.042$). Patients with diabetes had a higher prevalence of geographic tongue (GT) ($P = 0.017$), denture stomatitis ($P = 0.018$), and angular cheilitis ($P = 0.006$) than controls. Overall, diabetic patients with poor metabolic control had a significantly higher prevalence of OMLs and xerostomia than patients with moderately and well-controlled disease ($P < 0.05$).**

Conclusions: **The prevalence of OMLs was significantly higher in diabetic patients than in control subjects. Higher occurrence of OMLs was significantly associated with poor metabolic control.**

Keywords: *diabetes mellitus type 2, prevalence, mouth mucosa, oral pathology*

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterised by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (1). The World Health Organization (WHO) recognises 2 major clinical forms: insulin-dependent diabetes mellitus (IDDM), or type 1 diabetes, and non-insulin-dependent diabetes mellitus (NIDDM), or type 2 diabetes (DM2).

Diabetes mellitus currently affects 246 million people worldwide, and it is expected to affect a staggering 380 million people by 2025 (2). An estimated 3-fold rise in the prevalence of the disease is expected in Asia—especially in China and India. Similarly, other rapidly developing Asian countries including Malaysia, Singapore, and Thailand will also see a dramatic increase in the number of DM cases (3).

Diabetic complications account for most of the socio-economic burden of the disease (4). DM is considered the leading cause of blindness, renal failure, lower-limb amputation, and deaths due to cardiovascular disease (5). Chronic hyperglycemia induces structural changes in tissues (6) and is associated with impaired wound healing, higher susceptibility to infections (7), and microvascular and macrovascular dysfunctions (8).

Similarly, a number of oral health complications are frequently associated with DM (9). These include various inflammatory diseases, reduced saliva secretion, and oral mucosal pathologies. Further, inflammatory diseases such as gingivitis, periodontitis, candidiasis, stomatitis, benign migratory glossitis or geographic tongue (GT), median rhomboid glossitis, and angular cheilitis have been reported frequently in various studies (10–13). DM predisposes an individual to bacterial and fungal infections as well, including those caused by *Candida* species (14).

DM is believed to promote periodontitis through an exaggerated inflammatory response

to the periodontal microflora and hyperglycemia-induced vascular changes (15). Oral soft tissue abnormalities that are associated with DM include fissured tongue, irritation fibroma, traumatic ulcers, and parotid gland enlargement (16,17).

Certain studies have reported a possible association between DM and potentially malignant disorders such as leukoplakia (18,19), erythroplakia (19,20), and lichen planus (16,18,21, 22). However, other studies neither demonstrated this association nor found any influence of DM on the duration, distribution, or type of lesion (23,24). These conflicting results stem from several variations in the sample populations with regard to age, type of diabetes, time of diabetes onset, level of metabolic control, and daily consumption of drugs. Additionally, comparing the sample population with an appropriate control group is fundamental when investigating the prevalence of oral mucosal alterations in patients with DM.

Hence, the purpose of this investigation was to study the prevalence of oral mucosal lesions (OMLs) in DM2 and non-diabetic control subjects in the Malay population and to determine the association between OMLs and metabolic control of the disease.

Materials and Methods

Research design

The present study was approved by the Human Ethics Research Committee of the School of Dentistry, Universiti Sains Malaysia (USM), Kelantan, Malaysia. The study was conducted in full accordance with the ethical principles of the World Medical Association Declaration of Helsinki (2002). All volunteers were informed of the aims and methods of this study, and written consent was obtained.

Malaysia is a multiracial country with a predominant Malay ethnic group in the state of Kelantan. This cross-sectional study involved 391 Malay patients with DM2 and 391 Malay non-diabetics as control subjects. The sample size of the study was calculated using a single formula, which was based on the proportion of oral lesions in diabetic patients from a previous study (16). The precision was set at 0.05 with a 95% confidence interval and a Z score of 1.96. Diabetic patients were recruited from the endocrinology clinic of the University Hospital, which is situated in the same complex that houses the medical and dental schools. Non-diabetic control subjects, identified by their normal fasting blood glucose levels, were recruited from the outpatient department of the dental clinic. Both patients and control subjects with immunosuppressive disease, or oral habits such as smoking, alcohol consumption, or tobacco or betel nut chewing, were excluded from the study.

Data collection sheets were used to gather demographic data, education level, medical and dental history, subjective xerostomia, and past and current use of medications. Data on the duration of disease, type of diabetes, glycosylated hemoglobin (HbA1c) values, any major complications, and type of diabetes therapy were retrieved from medical records. The patients were categorised into 3 groups according to their mean HbA1c values recorded in the past year (25). These were:

Well-controlled	HbA1c < 7.5%
Moderately controlled	HbA1c = 7.6% to 8.9%
Poorly controlled	HbA1c > 9%

Oral examination

Visual examination of the mouth was carried out by a single examiner who was supervised and assessed by an oral medicine specialist. Extraoral and intraoral examination was performed under electrical overhead lights using a mouth mirror, tweezers, gauze, and a wooden tongue depressor. Diagnostic criteria for abnormalities of the oral mucosa were in accordance with World Health Organization (WHO) guidelines (26). Incision biopsy and histopathological examination were performed when necessary. The number of natural teeth and presence of dentures, either partial or complete, were also recorded. After the oral examination, patients who presented with diabetes-associated lesions were referred for appropriate treatment.

Statistical analysis

Statistical Package for the Social Sciences (SPSS), version 20, was used for data entry and analysis. Differences in categorical variables between diabetic patients and control subjects were compared by chi-square tests, while differences in continuous variables were compared by independent *t* tests. A Chi-square test was also used to determine the association between the frequency of oral lesions and level of metabolic control among diabetic patients. A *P* value of < 0.05 was considered significant.

Results

A total of 391 DM2 patients and 391 non-diabetic control subjects participated in this study. There were more women than men among

both DM2 patients (56.5% women) and control subjects (61.1% women). The mean (SD) age of the DM2 patients was 54.71 years (8.48) and that of the control subjects was 53.04 years (12.06). The demographic characteristics are presented in Table 1.

More DM2 patients (33.2%) than control subjects (16.4%) were on medications for indications other than diabetes. A small percentage of subjects reported taking medications such as sedatives and corticosteroids, which were categorised as "Others".

Diabetes-related variables among DM2 patients are presented in Table 2. The mean (SD) duration of DM was 8.26 years (6.11) from the time of diagnosis, with 41.9% of subjects having DM for less than five years. The mean (SD) value of HbAc1%, indicative of metabolic control, was 8.39 (SD 2.23) with 65% of the subjects having moderately or well-controlled disease. Most patients (70%) were prescribed oral hypoglycemic drugs, while 23.3% were prescribed a combination of insulin and oral drugs, and 6.6% of patients were prescribed insulin alone. Diabetic complications including retinopathy, nephropathy, neuropathy, cardiovascular diseases, and amputations of the lower limbs were observed in 14.6% of diabetic patients.

Approximately one-third of subjects in both groups used either complete or partial dentures. DM2 patients had an average of 14.2 (SD 10.11) remaining teeth, which was significantly less than the average of 18.7 (SD 10.14) remaining teeth in control subjects ($P < 0.001$). The dentition status for both groups is presented in Table 3.

The OMLs observed in DM2 patients and control subjects are shown in Table 4. Twelve types of OMLs observed in DM2 patients were categorised into six main groups: tongue lesions, denture-related lesions, white lesions, ulcerative lesions, benign tumors, and precancerous lesions. The most common lesions in DM2 patients were fissured tongue (26.9%), denture stomatitis (11.5%), and GT (3.6%). OMLs were present in a significantly higher percentage of DM2 patients (45.5%) than control subjects (38.4%) ($P = 0.042$). Specific oral lesions found to occur with significantly higher frequency in DM2 patients than in control subjects included GT ($P = 0.017$), denture stomatitis ($P = 0.018$), and angular cheilitis ($P = 0.006$). The prevalence of traumatic ulcers was higher in DM2 patients than in control subjects, but this difference was not statistically significant ($P = 0.056$).

The distribution of OMLs in DM2 patients according to the level of metabolic control of disease is shown in Table 5. Higher prevalences of OMLs and xerostomia were significantly

Table 1: Demographic data and characteristics of the study groups

Variables	Diabetics (n = 391)		Controls (n = 391)	
	n (%)	Mean (SD)	n (%)	Mean (SD)
Gender				
Male	170 (43.5)		152 (38.9)	
Female	221 (56.5)		239 (61.1)	
Age (years)		54.71 (8.48)		53.04 (12.06)
Education				
No schooling	40 (10.2)		48 (12.3)	
Primary	161 (41.2)		157 (40.2)	
Secondary	190 (48.6)		186 (47.6)	
Medications*				
None	261 (66.8)		327 (83.6)	
Cardiovascular agents	91 (23.3)		42 (10.7)	
Antibiotics	10 (2.6)		4 (1.0)	
NSAID	14 (3.6)		6 (1.5)	
Antiasthmatic	6 (1.5)		7 (1.8)	
Others	9 (2.3)		5 (1.3)	

*Medication other than anti-diabetic drugs.

associated with poor metabolic control of disease ($P < 0.05$).

Discussion

Diabetes mellitus is a complex and pernicious syndrome characterised by abnormalities in carbohydrate, lipid, and protein metabolism resulting from either a profound or an absolute deficiency of insulin. Type 1 diabetes represents less than 5% of primary diabetes cases, and DM2 represents the remainder (25).

A number of specific oral mucosa alterations have been associated with DM (22). In the present study, the prevalence of OMLs was significantly higher in DM2 patients (45.5%) than in non-diabetic control subjects (38.4%) ($P = 0.042$). A similar study of 146 patients with DM2 and 111 non-diabetic control subjects showed that nearly twice the number of diabetic patients (88%) had one or more oral soft tissue lesions as compared to non-diabetic control subjects (45.0%), and the difference was statistically significant ($P < 0.001$) (27). Similarly, Guggenheimer et al., investigated the prevalence of OMLs in 405 patients with type 1 diabetes and 268 control subjects and found that 44% of diabetic patients had one or more oral soft tissue lesions as compared to 25% of control

Table 2: Description of diabetes variables among diabetic patients

Variables	*n* (%)	Mean (SD)
Duration of diabetes (years)		
Duration categories		8.26 (6.11)
< 5 years	164 (41.9)	
6–10 years	128 (32.7)	
> 10 years	99 (25.3)	
Treatment of DM		
Oral agents	274 (70.1)	
Insulin	26 (6.6)	
Insulin + Oral agents	91 (23.3)	
Metabolic control (%)		8.39 (2.23)
Well	170 (43.5)	
Moderate	84 (21.5)	
Poor	137 (35.0)	
Diabetes complications		
Yes	57 (14.6)	
No	334 (85.4)	

Table 3: Comparison of remaining teeth and denture wearing in diabetics and controls

Variables	Diabetics (*n* = 391)		Controls (*n* = 391)		χ^2 Statistics (df)	*P* value
	n (%)	Mean (SD)	*n* (%)	Mean (SD)		
Remaining teeth		14.2 (10.11)		18.7 (10.14)		0.001*
Dentures wearers	157 (40.2)		139 (35.5)		1.76 (1)	0.184**
CD	112 (28.6)		89 (22.8)			
PD	37 (9.6)		48 (12.2)			
PD + CD	8 (2.0)		2 (0.5)			

*independent *t* test.
**Chi Square test.
Abbreviations: CD = complete dentures, PD = partial dentures, PD + CD = partial + complete dentures.

Table 4: Comparison of the prevalence of oral mucosal lesions in diabetics and controls

Variables	Diabetics *n* = 391	Control *n* = 391	χ^2 (df)	*P* value
	n (%)	*n* (%)		
Subjects with 1 or more lesions	178 (45.5)	150 (38.4)	4.12 (1)	0.042
Fissured tongue	105 (26.9)	106 (27.1)	0.006 (1)	0.936
Geographic tongue	14 (3.6)	4 (1.0)	5.69 (1)	0.017
RMG	4 (1.0)	5 (1.3)		1.000*
Denture stomatitis	45 (11.5)	26 (6.6)	5.6 (1)	0.018
Angular chelitis	10 (2.6)	1 (0.3)	7.5 (1)	0.006
Denture granuloma	2 (0.5)	1 (0.3)		0.500*
Frictional keratosis	8 (2.0)	14 (3.6)	1.68 (1)	0.194
Cheek biting	4 (1.0)	4 (1.0)	0.0 (1)	0.637
Aphthous stomatitis	3 (0.8)	3 (0.8)		1.000*
Fibroma	5 (1.3)	5 (1.3)		1.000*
Lichen planus	2 (0.5)	0.0 (0.0)		0.499*
Traumatic ulcers	8 (2.0)	2 (0.5)	3.67 (1)	0.056
Xerostomia	119 (30.4)	58 (14.8)	27.17 (1)	0.001

*Chi-square test.
*Fisher Exact test.

Table 5: Distribution of oral mucosal lesions and xerostomia among diabetic patients according to the level of metabolic control

Lesions	Metabolic Control (*n* = 391)			Total (%)	χ^2 (df)	*P* value
	Well *n* = 170	Fair *n* = 84	Poor *n* = 137			
One or more lesion						
Yes	63 (37.1)	44 (52.4)	71 (51.8)	178 (45.5)	8.7 (2)	0.013
No	107 (62.9)	40 (47.6)	66 (48.2)	213 (54.5)		
Denture Stomatitis						
Yes	16 (9.4)	5 (6.0)	24 (17.5)	45 (11.5)	8.14 (2)	0.02
No	154 (90.6)	79 (94)	113 (82.5)	346 (88.5)		
Geographic Tongue						
Yes	2 (1.2)	4 (4.8)	8 (5.8)	14 (3.6)	5.21 (2)	0.07
No	168 (98.8)	80 (95.2)	129 (94.2)	377 (96.4)		
Traumatic Ulcers						
Yes	2 (1.2)	1 (1.2)	5 (3.6)	8 (2.0)	2.71 (2)	0.26
No	168 (98.8)	83 (98.8)	132 (96.4)	383 (98)		
Angular Chelitis						
Yes	2 (1.2)	4 (4.8)	4 (2.9)	10 (2.6)	3.01 (2)	0.22
No	168 (98.8)	80 (95.2)	133 (97.1)	381 (97.4)		
Xerostomia						
Yes	42 (24.7)	23 (27.4)	54 (39.4)	119 (30.4)	8.22 (2)	0.016
No	128 (75.3)	61 (72.6)	83 (60.6)	272 (69.6)		

Chi-square and Fisher exact test.

subjects; again, the difference was significant (16). Collin et al., investigated the occurrence of diabetic neuropathy in elderly patients with DM2 and examined the mucosal diseases, tooth loss, and temporomandibular joint dysfunction in 45 long-term DM patients and 77 control subjects (28). They showed that 42% of patients with DM had two or more mucosal lesions, as compared to 20% of control subjects (P = 0.008) (28). This higher point prevalence rate of mucosal lesions observed in diabetic patients may be due to slower healing rates observed in these patients, leading to a longer duration of a given lesion, and not be due to an increase in the incidence. In other words, if a lesion takes two months to heal in a diabetic patient and one month to heal in healthy control subject, the prevalence will be higher in patients with DM at a given point of time.

Specific lesions that occurred with significantly greater frequency in the present study included GT, denture stomatitis, and angular cheilitis. An association between GT and DM was suggested initially by Wysocki et al., by linking an increased prevalence of tissue type HLA-B15 with GT and in patients with IDDM. This study of 87 diabetic patients and 105 non-diabetic control subjects showed a 4-fold increase in the prevalence of GT in the diabetic group (12). Another study by Bastos et al., found a higher prevalence of GT in DM2 patients (5.4%) than in control subjects (0.9%), and this difference was statistically significant (P = 0.001) (27). Guggenheimer et al., also found a higher frequency of GT in diabetic patients (5.4%) than in control subjects (3.9%); however, this difference was not statistically significant (16). The cause of increased prevalence of GT in diabetic patients, although still unknown, may be associated with slower repair and delayed healing mechanisms caused by microangiopathy of the oral vasculature and hypoxia in diabetic patients.

The prevalence of denture stomatitis was found to be significantly higher in diabetic patients than in control subjects (P = 0.018). As the percentages of denture wearers in both groups were not significantly different, the prevalence of denture stomatitis was not adjusted for in terms of the differences in denture use between the groups. A literature search revealed conflicting reports about the association of denture stomatitis with DM (29,30). Similarly, the prevalence of angular cheilitis in the present study was found to be significantly higher in diabetic patients than in control subjects (P < 0.05). It is generally acknowledged that diabetic patients are more susceptible to fungal infections, particularly to *Candida albicans* infections, than non-diabetic subjects (31). Hyperglycemia due to poor metabolic control is one possible predisposing factor of oral candidiasis in diabetic patients. This can lead to the growth of *Candida albicans* and enhanced adhesiveness to the oral epithelium (32) in association with other local factors such as the presence of dental prostheses, salivary pH, salivary flow rate, and oral habits (33).

The relationship between lichen planus and DM has been extensively studied, with controversial results (34). This is due to a wide range of prevalence, from 1.6% (24) to 85% (21), of lichen planus in the study populations, and while some studies have verified this association (21,18,35), other studies could not (23,24). In the present study, no association between lichen planus and DM was found. Only 2 cases (0.5%) of lichen planus were found in DM2 patients, and none were found in control subjects. However, Bastos et al., reported a significantly higher prevalence of lichen planus in DM2 patients (6.1%) than in control subjects (27). Van Dis and Park (24) observed lichen planus in 4% of patients with diabetes.

Our results also demonstrated a significant association between metabolic control of disease and the occurrence of one or more oral lesions, denture stomatitis, GT, and angular cheilitis in DM2 patients (P < 0.05). As the level of metabolic control decreased, the possibility of having OMLs increased. Collin et al. (28), reported that patients with fewer than 2 OMLs had a mean HbA1c of 8.3%, while those with 2 or more lesions had a mean HbA1c of 9.5% (P = 0.08) (28). Poor metabolic control has been associated with various diabetic complications (36), including severe periodontitis (37). Uncontrolled DM may lead to many pathological changes such as increased glucose levels in saliva, decreased saliva secretion, vascular changes, delayed healing, inhibition of phagocytosis, and cellular immune responses, which can increase the susceptibility of oral tissues to infection and local irritants (38).

Conclusion

In this study, DM2 patients had a higher prevalence of oral mucosal alterations than control subjects. Higher occurrence of OMLs was significantly associated with poor metabolic control of DM. These findings highlight the necessity of regular clinical examinations to ensure early diagnosis and prompt management of OMLs in DM patients.

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Conflict of Interest

None.

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Authors' Contributions

Conception and design, provision of study materials or patient, obtaining of funding: ARI
Analysis and interpretation of the data, critical revision of the article for the important intellectual content: NMI, ARI
Drafting of the article, administrative, technical or logistic support: AAG
Statistical expertise, collection and assembly of data: SAAM
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