EGYPTIAN DENTAL JOURNAL

VOL. 55, 1:15, APRIL, 2009

I.S.S.N 0070-9484

WWW.EDA-EGYPT.ORG

HYPERGLYCEMIA AND ORAL MUCOSAL LESIONS AMONG DIABETIC PATIENTS IN JEDDAH CITY

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ABSTRACT

Objective: To determine the prevalence of oral mucosal lesions in diabetic patients and its association with glycemic control. Methods: The study comprised 152 diabetic patient (101 = type 2, 51 = type 1) attending KAAUH diabetic clinic and 50 sex and aged matched non diabetic controls. Measurements of total HbA1c was performed in diabetics to determine the level of glycemic control and random blood glucose was measured for control group selection. A complete intraoral soft tissue examination was performed according to the World Health Organization guidelines. Abnormalities were recorded on a checklist of common oral lesions. The relation between HbA1c concentration and prevalence of oral mucosal lesions were analyzed. **Results:** The prevalence of one or more oral mucosal lesions in the diabetic sample was significantly higher than non diabetics. The most frequent lesions among diabetic patient were fissured and burning tongue sensation, followed by taste disturbance and xerostomia. Logistic regression model revealed that xerostomia increased the probability of one or more oral lesions, while age, gender, smoking, medication use, education and social factors had no effect. We have found no correlation between the quality of glycemic control and frequency of oral mucosal lesions. **Conclusion:** We can conclude that oral mucosal lesions are common among diabetic patient in Jeddah city, suggesting the necessity for improved standard of prevention, diagnostic and opportune treatment of these lesions.

INTRODUCTION

Diabetes mellitus is a highly prevalent worldwide disorder. There is a rising prevalence particularly of type 2 diabetes mellitus. It is projected that 221 million people will have diabetes by the year 2010; Africa and Asia are designated as the regions with the greatest potential increases, where the current number is expected to double the number experienced today [1, 2].

Ascertaining underlying systemic diseases from oral symptoms is a valuable tool in discovering occult systemic diseases. The correlation between oral symptoms and systemic diseases provides a means for early diagnosis of such conditions [3].

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Some studies have found no clear association between periodontal disease and DM [4, 5], though the great majority of authors consider that such patients present increased periodontal destruction [6, 7]. Likewise, while some researchers describe no difference in the number of caries between diabetics and non-diabetics [8], others report a comparatively greater prevalence of caries among patients with DM [9, 10].

Many authors also relate DM to the development of oral mucosal lesions [11], with an increased incidence of certain mucosal infections such as oral candidiasis, or comparatively greater difficulties for the healing of oral ulcers or wounds. A number of oral soft tissue abnormalities have been reported to be associated with diabetes mellitus [12]. Other oral manifestations; diminished salivary flow and burning mouth or tongue are common complaints of patients with uncontrolled diabetes mellitus [13]. Concomitant enlargement of parotid glands has been described, possibly as a result of alterations in the basement membranes of parotid ducts or other histopathological changes [14].

Although many studies have evaluated oral mucosal lesions in patients with diabetes mellitus, there have been conflicting findings concerning the prevalence of some conditions [17, 18]. As well as some studies have failed to show any difference between controls and diabetic patients examined for prevalence of oral mucosal lesions [15]. The results of Chavez et al. [16] suggest that older adults with poorly controlled diabetes may have impaired salivary flow in comparison with better-controlled diabetes and non-diabetic patients, yet they may not have concomitant xerostomia complaints. This may be a reflection of the different pathophysiologic behaviors of the clinical types of diabetes mellitus or may reflect variations in glycemic control, duration of disease, or age of the patients.

According to some authors, the duration of the disease influences the severity of periodontal lesions and the loss of epithelial attachment, as well as the development of renal, cardiovascular, and infectious complications [19, 20]. Chronic exposure to raised concentrations of glucose, most accurately measured with hemoglobin A1c (HbA1c), has been postulated to contribute to oral mucosa [23] disease in individuals with diabetes, although this association is controversial. People with diabetes have an increased risk of oral lesions, but whether glycemia independently contribute to the development of oral lesions is still unclear. Metabolic control of diabetes affects the course of periodontal disease; well-controlled diabetic patients (with lower values of HbA1c) are less likely to lose periodontal attachments compared to uncontrolled patients. Patients with high levels of HbA1c have more severe forms of periodontitis [21]. Interestingly, the opposite also seems to hold true: treatment of periodontal disease reduces the percentage of glycosylated hemoglobin [22].

AIM OF STUDY

To assess the prevalence of oral mucosal lesions among diabetic patients in Jeddah city and to study the relationship between the quality of glycemic control **(HbA1c)** and the prevalence of oral mucosal lesions in diabetic patients

MATERIALS AND METHODS

Sampling & Sample Sizes (Table 1)

The research is a clinical / laboratory investigation model conducted at KAAUH, diabetic clinics. The study population consists of 152 diabetic patients (101= type 2, 51= type 1), diagnosed according to the history and selected as they presented clinically at the diabetic clinics of KAAUH for routine follow up without diabetic complications. The non-diabetic (ND) control group consists of age and sex

matched fifty healthy volunteers with no history of diabetes mellitus selected from the dental clinics including patients as well as dental auxiliaries. All subjects in both groups gave informed signed consents to participate in the study. Individuals were excluded from the study if they have received antibiotic or steroids therapy or xerogenic drugs or had been using antiseptic mouthwashes during the last 3 weeks prior to the study. The participants in the study were selected using a random stratified sample by age, gender, and socioeconomic status and covering the program for this study. The study protocol was approved by the Ethics committees of KAAUH. Medical Faculty.

All participants were subjected to the following clinical examinations and laboratory investigations:

I. Oral soft tissue examination

Examiners were 2 full time faculty members from the oral medicine department, King Abdul-Aziz University, they had at least 10 years of experience in oral evaluation. A complete intraoral soft-tissue examination was performed with a dental mirror and gauze square. The diagnosis of any oral soft tissue pathosis was established based on onset, duration, oral habits, clinical appearance, history of trauma, and previous episodes. Abnormalities were recorded on a checklist of common oral lesions. The locations and descriptions of the lesions were also recorded. Before the oral health examination, each subject was interviewed and the investigators controlled the completion of the questionnaire which included questions on personal sociodemographic data, medical history, previous dental visits and salivary function.

Demographic data included age, weight, height, race, gender, income, education, and marital status. The medical history and status of current medical care, and significant previous illness were assessed or collected.

II. Blood Sample

5 mL blood samples were extracted from the anticubital vein from each participant and collected in the phlebotomy lab and analyzed at the hematology laboratory of KAAUH.

For diabetic patients, the sample was used to measure the glycosylated hemoglobin concentrations (HbA1c), which assess the glycemic control of that patient [7], while for non diabetic (control) subjects, the samples were used to measure the random blood glucose level. Those with values greater than or equal to 6.8 mmol/L were excluded from the study. According to guidelines for management of diabetes, subjects with HbA1c < 9.0% were considered as well-to-moderately controlled patients, whereas diabetics with HbA1c > 9.0% were assigned to the poorly controlled group. [24]

III. Salivary Function

Salivary dysfunction was assessed by means of self-report measures, as well as by unstimulated salivary flow determinations [16]. One of the self-report measures of dry mouth used 4 questions previously shown to correlate with salivary dysfunction [19]. Affirmative responses to any of the following were scored for xerostomia: Does your mouth feel dry when eating a meal? Do you have difficulty swallowing dry foods? Do you sip liquids to aid swallowing dry foods? Or is the amount of saliva in your mouth too little most of the time. Additionally, a question developed by Bacic [20] was included: Does your mouth usually feel dry?

IV. Statistical Analysis

All results were coded and computerized database was set up to facilitate analysis using SPSS. Stepwise linear discriminate analysis was used to identify which combinations of factors best predicted the presence or absence of Oral lesion. Logistic regression model were used to assist the influence of the other variables

TABLE (1) (Subjects Demographics) shows the distribution of the characteristics of the sample by gender and age.

		Control Subjects	Diabetic Pt. Type 1	Diabetic Pt. Type 2
No. Subjects		50	51	101
Age	20-30	8	17	4
	30-40	11	12	7
	40-50	16	7	37
	50-60	15	15	53
Sex	Male	34	20	47
	Female	16	31	54

**Significant at 5% level*

RESULTS

One hundred fifty two diabetic patients and fifty non-diabetic control subjects participated in this research. The diabetic cases compromised 101 type 2 and 51 type 1 diabetic patient who is correlated by previous studies stated the less frequency of IDDM. The mean duration of disease of 3.16 years (± 1.09) and 3.57 years (± 1.27) respectively. The difference was not statistically significant. By the design, which is proportional for age and gender to the pattern population, the distribution of demographic characteristics was 101 (50%) woman, 101 (50%) men, 29 individuals who were 20 to 30 years old and 137 individuals who were 30 years older.

There is a significantly greater proportion of diabetics subjects had one or more oral soft tissue lesions than control subjects. The most frequent lesions in our study were fissure tongue (36.2%) and burning tongue (41.3%) respectively (table 2). Also there were more significant complaints of altered taste sensation and xerostomia among diabetic patients than control. Dry mouth was found in 33.6% of the cases and 12% of the control. Atrophic glossitis was higher in diabetic patients than control, but the difference was not significant. Other abnormalities including angular chelitis and lichen planus and denture stomatitis were not found more prevalent in the diabetic group. Ten diabetic patients were denture wearers; three of them having denture stomatitis while 4 controls were denture wearer none of them having stomatitis.

Regarding diabetic groups the study showed that fissured tongue and dry mouth were more significantly prevalent in type 1 diabetics than type 2. Atrophic glossitis was also higher significant among type 1 than type 2. (table 3)

Table 4 shows the relationship between glycaemic control and oral lesions in diabetic's patients. There was no significant relation between the prevalence of oral mucosal lesion and quality of glycaemic control as assessed by glycosylated hemoglobin (table 4).

Logistic regression model was constructed to analyze the variables associated with more probability of having one or more oral mucosal lesions: age, gender, education, medication, smoking, denture use, dry mouth, frequency of the previous dental visits. Only dry mouth significantly increased the probability of having lesions while angular chelitis, denture stomatitis and lichen planus were not analyzed because of their low frequency.

TABLE (2) The distribution of all mucosal disorders observed in the diabetic sample and control.

Signs & Symptom	Case (n=152)	Control (n=50)	P-value
Fissured Tongue	55 (36.2%)	9 (18.0%)	0.017*
Burning Tongue	62 (41.3%)	3 (6.4%)	0.000*
Altered Taste	49 (33.1%)	2 (4.0%)	0.000*
Dry Mouth	51 (33.6%)	6 (12.0%)	0.003*
Atrophic Glossitis	23 (15.1%)	4 (8%)	0.199
Denture Stomatitis	3 (2.0%)	-	0.317
Lichen Planus	3 (2.0%)	-	0.317
Angular Cheilitis	4 (2.6%)	-	0.247

**Significant at 5% level*

TABLE (3) Distribution of oral mucosal lesions among diabetic groups

Oral Lesion	Type I (n=51)	Type II (n=101)	P-value
Fissured Tongue	24 (47.1%)	31 (30.7%)	0.047*
Dry Mouth	27 (52.9%)	24 (23.8%)	0.00*
Atrophic Glossitis	15 (29.4%)	8 (7.9%)	0.00*
Burning Tongue	23 (45.0%)	39 (39.4%)	0.502
Altered Taste	17 (33.0%)	32 (33.0%)	0.966
Denture Stomatitis	2 (3.9%)	1 (1.0%)	0.220
Lichen Planus	1 (2.0%)	2 (2.0%)	0.994
Angular Cheilitis	3 (5.9%)	1 (1.0%)	0.075

**Significant at 5% level*

TABLE (4) Oral mucosal lesions in diabetics according to the level of metabolic control

Signs & Symptom	HbA1c < 9 (n=78)	HbA1c ≥ 9 (n=74)	P-value
Fissured Tongue	33(42.3%)	22 (29%)	0.107
Dry Mouth	23 (29.5%)	28(37.8%)	0.27
Altered Taste	26(34.7%)	23 (31.5%)	0.683
Burning Tongue	34 (44.7%)	28 (37.8%)	0.391
Angular Cheilitis	1 (1.3%)	3 (4.1%)	0.286
Denture Stomatitis	2(2.6%)	1 (1.4%)	0.591
Lichen Planus	2 (2.6%)	1 (1.4%)	0.591
Atrophic Glossitis	9 (11.5%)	14 (18.9%)	0.024

**Significant at 5% level*

Discussion

The present study examined oral mucosal lesions and their revalance to disease activity and state of hyperglycemia among group of adult diabetics. Another strength of our study is the fact that few studies have been investigated both state of glycemic control and mucosal lesions in the same study.

Although many studies have described oral manifestation of diabetes mellitus. The findings have been diverse and various. The correlation between diabetes and oral lesions is debated. Some authors have report higher incidence of oral and mucosal lesions in diabetic patients [13, 14] , while others have not found any correlations between oral mucosal lesions and diabetes.[15]

In the present study, oral soft tissue lesions were encountered more frequently in diabetic population than in the non diabetic group. Specific oral mucosal lesions that were found with significantly greater frequency included fissure tongue, burning tongue and taste disturbance and atrophic glossitis. Fissured tongue, including generalized placation and double fissure running longitudinally along the dorsum of the tongue, has been reported to be more prevalent in persons with DM. The rate in our study (36.2%) was higher to that found in other studies (12.3%), (22.7%). [17, 25] It has been estimated, however, that the prevalence of fissured tongue in the general population can range up to 5%. The pathogenesis of fissured tongue is considered to be genetically determined developmental variant as well as a manifestation of aging changes in the oral environment [26]. In our study, its presence was higher significantly among type 1 diabetes and was related to the subjective complain of dry mouth. Fissured tongue was found to be significantly more prevalent among type 1 diabetic subjects who met the dry mouth criteria. These findings are in agreement with the data reported by Maria et al.[11] who demonstrated that fissured tongue more prevalent in type 1 diabetes.

In the present work, atrophic glossitis was more significantly prevalent among the subjects with diabetes than control. Atrophy of the lingual papillae in patients with IDDM has been previously reported, and Candida mycelia were found in smears from 25% of those patients [27]. In this study, this abnormality was found toward the anterior portion of the tongue and, therefore, resembled nonspecific glossitis rather than atrophic (erythematous) candidiasis, and may be related to similar factors involved in the formation of fissure tongue rather than in candidal infections. Atrophic glossitis was higher in type 1 diabetes than type 2. This is consistent with a previous study by Maria et. al. [11] who found higher prevalence of atrophic glossitis among type 1 diabetes. The differences in the prevalence of mucosal lesions between type 1 and type 2 diabetes could be attributed to the difference in the duration of diabetic status.

Burning tongue was very significant in the present study. This is in accordance with Carrington et al. 2001 [28]. They reported that burning tongue is also often associated with diabetes mellitus, as well as other causes including vitamin B deficiencies, psychic disorders, impaired salivary gland function, hematological change, candida infection and allergies [29].Taste alteration in our study was more prevalent in diabetic patients than control. These findings are in agreement with the data reported by Eyitope et al. 2005 [30], and could be explained due to neuropathic changes in diabetic patients.

This study showed a significant difference in hyposalivation between cases and control. Hyposalivation was present in 33.6% of the cases as opposed to 68% documented by Dodds et al.[31] subjective complain of dry mouth was more clear among type 1 diabetes than type 2. This results in accordance with Moore et. al. [32] who found that salivary flow reduction more prevalent in type 1

than type 2 diabetes. This in not in agreement with Ethope et. al.[30] who reported that dry mouth more common in type 2 diabetes. Although many authors have investigated dry mouth in diabetic patient is difficult to establish comparisons among studies due to the great diversity in patient selection criteria and study design involved. Hyposalivation is said to be very common symptom of the disease and has been linked with dysfunction of the parenchyma of the major salivary glands and with polyuria. The substitution of the functioning tissue by adipose tissue has been suggested to quantitatively and qualitatively modify saliva production, facilitating hyposalivation and burning mouth symptoms [12, 33]. Some studies have failed to show any difference between controls and diabetic patients examined for prevalence of complaints of dry mouth.

We identified only three cases of lichen planus that were equally distributed between the type 1 and type 2 diabetes. The relationship between lichen planus and diabetes has been extensively studied, but the findings conflict. Among the studies found and increased association, one suggested that this may be related to a similar immunologic defect in the 2 diseases.[34] Lichenoid lesions among patients with diabetes may also be attributed to a number of medications that were taken, particularly by older individuals with NIDDM[35]. We suggests that, because IDDM is considered to be an autoimmune disorder and patients with other autoimmune diseases, such as systemic lupus erythematosus or graft-vs-host disease, may manifest lichen planus-like lesions, a similar effect could occur with diabetes. It's believed that most cases of denture stomatitis are candida related. Candida species are part of the usual flora of the mouth and C. albicans has been shown to form on acrylic surfaces [36]. Although denture stomatitis were observed among three patients with diabetes. This cannot be documented due to small sample of denture wearers in our study.

Although studies of oral mucosal lesions in diabetic patients have produced variable results, a correlation between the quality of glycemic control and the oral lesions has not been demonstrated (HbA). There have been conflicting reports regarding a correlation between oral mucosal lesions and glycemic control [37,38].

In the present study we cannot identify any significant differences between the oral mucosal lesions in relation to the metabolic control. These observations in accordance with other previous reports [37], which indicated no differences were found in the oral mucosal lesions in different levels of hyperglycemia and the degree of glycemic control does not significantly affect oral lesions in diabetic patients. However this is not in accordance with Syrjala et al.[38] were found the presence of oral lesions was related to elevated glycosylated hemoglobin. Also they reported that hyperglycemia could contribute to the risk of oral lesions by increasing salivary glucose level which may promote over growth by candida and impair antifungal immunoglobulin in saliva.

However, the comparison between epidemiological surveys is difficult as methodologies have not been uniform. Some authors have examined institutionalized individuals [4, 16, 17], other had the sample size smaller than our samples [4, 6, 7, 16, 19], and finally the diagnosis criteria for describing one or more oral mucosal lesions have not been equally established.

In conclusion, the results of the present study shows that diabetic patient have more oral mucosal lesions than control subjects, thus, need more intense effort regarding oral health care to prevent the development of such lesions. The degree of glycaemic control does not significantly affect incidence of oral mucosal lesions among diabetic patients.

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