

## Frequency of Oral Manifestation in Diabetic Patients in Yazd 2016-2017

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### Abstract

**Objective:** Diabetes Mellitus (DM) is one of the most common endocrine diseases with many systemic complications such as oral manifestations. The present study aimed to compare the oral manifestations frequency in diabetic patients and healthy subjects.

**Materials and Methods:** This cross sectional study was conducted during 2016-17 on subjects came to Yazd Diabetic Research Center. In this study, 181 type 2 diabetic patients (T2DM) and 181 healthy individuals, based on convenient sample method, were included. Two groups were compared for basic information and oral manifestations including candidiasis, oral lichen planus (OLP), periodontitis, xerostomia, delayed oral wound healing, geographic tongue, gingival hyperplasia, fissured tongue, burning mouth and finally at least one of these lesions.

**Results:** The frequency of candidiasis, OLP, periodontitis, delay oral wound healing, geographic tongue, xerostomia and at least one of lesions in diabetics were significantly higher than control group ( $P$ -value< 0.001). After regression analysis and adjusting for confounding factors, candidiasis, periodontitis and xerostomia in diabetics were significantly more prevalent than non-DM patients with odds ratio of 15.16 (1.80-127.57), 9.58 (4.68-19.63) and 78.639 (10.05-615.231) respectively.

**Conclusion:** Xerostomia, candidiasis and periodontitis were significantly more prevalent in T2DM than Non-T2DM persons. Therefore, increasing awareness on oral manifestations in this group is recommended for timely diagnosis and referring to an oral medicine.

**Keywords:** Oral complications, Oral manifestations, Diabetes mellitus. Oral diseases

### Introduction

Diabetes Mellitus (DM) is one of the most common endocrine disease with many systemic complications such as oral manifestation (1). Diabetes is the 5th leading cause of mortality in western societies

and the fourth reason of visiting doctors. Diabetes is a growing threat to world health so that World Health Organization (WHO) has called all the countries to fight against this disease (2).

Oral complications in patients with poorly controlled diabetes include bacterial, viral and fungal infection, delayed oral wound healing, decay, gingival and periodontal disease, peri-apical abscesses and burning mouth syndrome (3). The prevalence and incidence of oral mucosal lesions were found to be higher in diabetics persons compared to healthy controls (4).

Mechanism of periodontal destruction by diabetes is not clear, however, there are many theories such as advanced glycation end products, changes in collagen tissues, and altered immune function that causes impaired polymorphonuclear leukocyte function which may facilitate bacterial persistence and increased secretion of pro-inflammatory cytokines such as tumor necrosis factor- $\alpha$  and prostaglandins. The increase in collagenase activity and reduction in collagen synthesis result in delay wound healing and periodontal tissue destruction (5,6).

Complications of diabetes lead to a decrease in quality of life and an increase in mortality in diabetic patients (7). In recent years, extensive programs have been planned to prevent diabetes, prevent or treat complications and disability of disease. Dentists can play an important role in health care team of diabetics and monitoring of diabetic patients and timely identification and treatment of oral problems in this group (8).

The aim of this study was to investigate the frequency of oral manifestations in type 2 diabetic patients (T2DM) and compare the oral presentations of diabetic and healthy individuals.

## Materials and Methods

In this analytical cross sectional study, 181 T2DM patients and 181 healthy individuals were included during 2016-17. T2DM patients were selected from subjects who came to Yazd diabetic research center based on convenient sampling method. Healthy individuals were selected from T2DM peers. Inclusion criteria in diabetic group consist of known diabetic subjects who had medical file in Yazd

Diabetic Research Center, age between 20 -70. Healthy individuals had fasting blood sugar (FBS) less than 100mg/dl, HbA1c $\leq$  5.7% and no previous history of diabetes. Exclusion criteria of two groups were any systemic diseases, presence of oral cancer or major dental and periodontal disease, previous radiation therapy and any drug consumption in two months ago except anti-glycemic drugs, aspirin, statins, anti-hypertensive and anti-hyper-lipidemic drugs in diabetic group. Demographic and basic information such as age, gender, use of denture, smoking, body mass index (BMI), and familial history of T2DM, systolic and diastolic blood pressure was collected. History taking and physical examination (extra-oral and intra-oral thorough examination) was conducted in two groups by oral medicine specialist. Oral examination was performed in place by adequate light and retracting the lips and cheeks and exploration was conducted in all regions of mouth. Oral manifestations include candidiasis, lichen planus, periodontitis, xerostomia, delayed oral wound healing, geographic tongue, gingival hyperplasia, fissured tongue, burning mouth syndrome and at least one of these lesions that have been recorded. Diagnosis of these lesions was based on patient's history and clinical appearance and in suspicious cases, the final diagnosis was determined by performing a biopsy. Two groups were compared based on frequency of above-mentioned oral manifestations. Finally, data was entered SPSS 20 software and then analyzed by Chi square test, T-test, ANOVA and regression.

## Ethical considerations

Patients were signed an informed consent and the study was approved by the ethics committee of Shahid Sadoughi University of Medical Sciences. (code IR.SSU.REC.1393 .157520).

## Results

In this study, comparison of oral manifestations frequency between 181 T2DM

and 181 non-diabetic patients was performed. The mean age of T2DM patient was significantly higher than control group ( $P$ -value < 0.001). Also, two groups weren't match with respect of gender ( $P$ -value < 0.014).

Among basic variables, BMI, smoking, denture usage, family history of diabetes, systolic blood pressure and diastolic blood pressure in T2DM patients were significantly more than another group (Table-1).

Comparison of oral manifestations frequency between diabetic and control groups reveals that candidiasis; OLP, periodontitis, delay oral wound healing, geographic tongue, xerostomia and at least one of these lesions in T2DM were significantly more than control. However, there were no significant differences between two groups about gingival hyperplasia, fissured tongue and burning mouth (Table-2).

Candidiasis, periodontitis and xerostomia in diabetics were significantly more than control persons with odds ratio of 15.16 (1.80-127.57), 9.58 (4.68-19.63) and 78.639 (10.05-615.231) respectively, after regression analysis and adjusting for age, sex, smoking, BMI and denture wearer. This analysis was not performed for other oral manifestations due to low frequency of lesions (Table-3).

## Discussion

The aim of this study was to evaluate and compare the frequency of oral manifestation in diabetic and healthy subjects in Yazd province.

In this study, the oral manifestations included candidiasis, lichen planus, periodontitis, xerostomia, delayed wound healing, fissured tongue, burning mouth and at least one of these lesions, but tooth decay were not one of

**Table 1. Comparison of basic variables between T2DM and healthy groups**

Variants	Diabetic Group N=181	Control Group N=181	P-value
Mean Age(years)	57.46 ( $\pm$ 10.5)	37.66 ( $\pm$ 13.6)	0.001
BMI ( $\text{kg}/\text{m}^2$ )	27.86 ( $\pm$ 4.1)	25.15 ( $\pm$ 4.3)	0.001
Female % (N)	53.6 (97)	66.3 (120)	0.014
Smoking % (N)	7.7 (14)	0.6 (1)	0.001
Denture wearer % (N)	46.4 (84)	2.2 (4)	0.001
Family history of Diabetes % (N)	66.3 (120)	13.3 (24)	0.001
Systolic Blood Pressure(mmHg)	128.95 ( $\pm$ 18.6)	119.66 ( $\pm$ 14.3)	0.001
Diastolic Blood Pressure(mmHg)	79.41 ( $\pm$ 8.2)	76.21 ( $\pm$ 9.7)	0.001

**Table 2. Comparison of oral manifestations frequency between T2DM and control group**

Oral manifestations	Diabetic patients Percent (Number)	Control Subjects Percent (Number)	P-value <sup>1</sup>
Oral Candidiasis	24.3 (44)	0.6 (1)	0.001
Oral Lichen Planus	96.1 (7)	0 (0)	0.015
Periodontitis	45.3 (82)	10.5 (19)	0.001
Delay wound healing	7.7 (14)	3.9 (7)	0.009
Geographic tongue	11 (20)	3.9 (7)	0.009
Xerostomia	36.5 (66)	0.6 (1)	0.001
Gingival hyperplasia	1.7 (3)	1.7 (3)	1.000
Fissured tongue	2.8 (5)	2.2 (4)	1.000
Burning Mouth	3.9 (7)	1.1 (2)	0.174
At least one of these lesions	89.5 (162)	47 (85)	0.001

1: chi-square

**Table 3. Adjusted odds ratio, confidence interval, and P-value of prevalence of oral manifestations with respect to age, sex, smoking, BMI and denture wearer**

Oral manifestations	Odd ratio	Confidence interval	P-value
Candidiasis	15.165	1.80-127.57	0.012
Periodontitis	9.586	4.68-19.63	<0.001
Xerostomia	78.639	10.05-615.231	<0.001
Geographic Tongue	1.105	0.35-3.45	0.864

the variables. We also compared some of the various risk factors affecting the incidence or prevalence of oral manifestations, including age, sex, BMI, cigarette, use of dentures, familial history, systolic and diastolic pressure in diabetic patients with healthy subjects.

In our study, older age, higher BMI, smoking, denture usage, family history of diabetes in T2DM patients were more prevalent than healthy subjects. Also, systolic and diastolic blood pressure in T2DM was higher than another group. Some of this dis-match between two groups is rational. Prevalence of diabetes increased with advancing age and BMI and family history of T2DM in diabetic persons are higher than healthy persons. Also, diabetes is a component of metabolic syndrome, so it is usual to accompany with increasing systolic and diastolic blood pressure (another component of metabolic syndrome). However future studies with matching factors such as age, sex, BMI, smoking status and denture usage maybe helpful.

The prevalence of oral manifestations was significantly higher among diabetic patients than control subjects in Al-Maweri study (9). Patients with diabetes had a higher prevalence of geographic tongue, denture stomatitis (a form of candidiasis), and angular cheilitis than controls. Overall, diabetic patients with poor metabolic control had a significantly higher prevalence of oral mucosal lesions and xerostomia than patients with moderate and well-controlled disease (9).

Yarahmadi Sh. and colleagues found that candida albicans were the most common fungus in the mouths of both diabetic and control groups, but there was a significant difference between the mean candida colonies of the patients and the control group (10). The mean of colonies with denture usage and cigarette smoking was significantly increased. In addition, poor control of diabetes and low oral hygiene were other factors for colonization. Also, the results showed that the average of the colonies was related to the increase in age and sex (10). In our study, oral candidiasis was higher than in diabetic

compare to control group in baseline and after adjusting for age, sex, smoking, BMI and denture wearer.

Candidiasis, periodontitis and xerostomia in DM patient were significantly more than healthy patients. In addition, candidiasis and periodontitis in denture users were higher than non-denture users in another study (11).

Higher prevalence of xerostomia in DM patients in relation to healthy population, 12.5%-53.5% versus 0-30% were seen in review article by López-Pintor. Also, quantity of saliva in DM population in relation to healthy people reported lower flow rates of saliva in DM than in control group (12).

A recent meta-analysis showed frequency of oral lichen planus in DM was higher compared with control subjects (13).

Diabetes is a risk factor for periodontitis, and the risk of periodontitis is higher in people with poorly controlled diabetes (a two-way relationship) (14-16).

Delay oral wound healing was reported higher in diabetic than control in previous studies (3,8), that is similar to our results.

Diabetes is a risk factor for gingival hyperplasia (17,18) in previous studies due to vitamin C deficiency. It may be possible that people in our research had no vitamin C deficiency.

Fissure tongue due to chronic low salivary flow rate reported with high frequency in both type 1 and 2 DM (19,20). Our results are in contrast with no explanation.

Burning mouth syndrome without other oral pathology were reported equal by T1DM and control subjects in Moore study (21). Presence of other pathologies such as atrophy of the tongue papillae, fissured tongue, denture stomatitis, and candidiasis may increase prevalence of burning mouth syndrome (21).

In the present study, candidiasis, periodontitis and xerostomia were reported with high frequency in DM people after adjusting for age, sex, smoking, BMI and denture wearer. For example, xerostomia was seen with odds ratio of 78.639 in DM people. Also 89.5% of diabetics had at least one of the oral



manifestations. Therefore, dentists should be aware of the rule of diabetes in their oral pathology of people, and various oral conditions are associated with diabetes, including xerostomia, candidiasis and periodontitis. American diabetes association (ADA) in 2003 acknowledged that periodontal disease is often found in people with diabetes (22).

The limitations of this study were small sample size, so studies with a larger sample and a cohort format for future research are recommended. Another limitation of this study was low information about duration of diabetes and type of treatment for hyperglycemia. Also in our study, basic characteristic of two groups such as age and sex was not matched, so future studies with sex and age group match of two group is helpful.

## Conclusions

Xerostomia, candidiasis and periodontitis were significantly more prevalent in T2DM than

Non-T2DM persons. So, increasing awareness of oral manifestations in this group is recommended for early diagnosis and referring to diabetologist as well. Therefore, oral examination should be integrated in people with diabetes as a component of their overall management. Likewise, closer collaboration between diabetologist and oral medicine specialist is necessary for the management of oral problems in diabetic patients.

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## Conflict of Interest

There was no conflict of interest in this research.

## References

1. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *The Lancet*. 2009;373(9677):1773-9.
2. Spinaci S, Crowell V, Currat L, Kehler J, Shetty P, World Health Organization. Tough choices: investing in health for development: experiences from national follow-up to the Commission on Macroeconomics and Health. World Health Organization; 2006.
3. Ambachew S, Eshetie S, Geremew D, Endalamaw A, Melku M. Prevalence of Type 2 Diabetes Mellitus among Hepatitis C Virus-Infected Patients: A Systematic Review and Meta-Analysis. *International Journal of Diabetes and Metabolism*. 2018;21(1-4):29-37.
4. Saini R, Al-Maweri SA, Saini D, Ismail NM, Ismail AR. Oral mucosal lesions in non oral habit diabetic patients and association of diabetes mellitus with oral precancerous lesions. *Diabetes research and clinical practice*. 2010;89(3):320-6.
5. Moore PA, Weyant RJ, Mongelluzzo MB, Myers DE, Rossie K, Guggenheimer J, et al. Type 1 diabetes mellitus and oral health: assessment of periodontal disease. *Journal of periodontology*. 1999;70(4):409-17.
6. Ritchie CS. Mechanistic links between type 2 diabetes and periodontitis. *Journal of dentistry*. 2009;8(37):S578-9.
7. Trikkalinou A, Papazafiropoulou AK, Melidonis A. Type 2 diabetes and quality of life. *World journal of diabetes*. 2017;8(4):120.
8. Al-Maskari AY, Al-Maskari MY, Al-Sudairy S. Oral manifestations and complications of diabetes mellitus: a review. *Sultan Qaboos University Medical Journal*. 2011;11(2):179.
9. Al-MAweri SA, Ismail NM, ISMAIL AR, Al-Ghashm A. Prevalence of oral mucosal lesions in patients with type 2 diabetes attending hospital universiti sains malaysia. *The Malaysian journal of medical sciences: MJMS*. 2013;20(4):39.
10. Yar Ahmadi SH, Khosravi AR, Larijani B, Baiat M, Mahmoudi M, Baradar Jalili R. Assessment of the fungal flora and the

- prevalence of fungal infections in the mouth of diabetics. *Iranian Journal of Endocrinology and Metabolism*. 2002;4(2):105-9.(In persian)
11. do Egito Vasconcelos BC, Novaes M, Sandrini FA, de Albuquerque Maranhão Filho AW, Coimbra LS. Prevalence of oral mucosa lesions in diabetic patients: a preliminary study. *Brazilian journal of otorhinolaryngology*. 2008;74(3):423-8.
  12. Lopez-Pintor RM, Casanas E, Gonzalez-Serrano J, Serrano J, Ramirez L, de Arriba L, et al. Xerostomia, hyposalivation, and salivary flow in diabetes patients. *Journal of diabetes research*. 2016;2016.
  13. Mozaffari HR, Sharifi R, Sadeghi M. Prevalence of oral lichen planus in diabetes mellitus: a meta-analysis study. *Acta Informatica Medica*. 2016;24(6):390.
  14. Preshaw PM, Alba AL, Herrera D, Jepsen S, Konstantinidis A, Makrilakis K, et al. Periodontitis and diabetes: a two-way relationship. *Diabetologia*. 2012;55(1):21-31.
  15. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *The lancet*. 2005;366(9499):1809-20.
  16. Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. *Annals of Periodontology*. 2001;6(1):91-8.
  17. Omori K, Hanayama Y, Naruishi K, Akiyama K, Maeda H, Otsuka F, et al. Gingival overgrowth caused by vitamin C deficiency associated with metabolic syndrome and severe periodontal infection: a case report. *Clinical case reports*. 2014;2(6):286-95.
  18. Agrawal AA. Gingival enlargements: Differential diagnosis and review of literature. *World Journal of Clinical Cases: WJCC*. 2015;3(9):779.
  19. de Souza Bastos A, Leite AR, Spin-Neto R, Nassar PO, Massucato EM, Orrico SR. Diabetes mellitus and oral mucosa alterations: prevalence and risk factors. *Diabetes research and clinical practice*. 2011;92(1):100-5.
  20. Guggenheimer J, Moore PA, Rossie K, Myers D, Mongelluzzo MB, Block HM, et al. Insulin-dependent diabetes mellitus and oral soft tissue pathologies. II. Prevalence and characteristics of Candida and candidal lesions. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2000;89(5):570-6.
  21. Moore PA, Guggenheimer J, Orchard T. Burning mouth syndrome and peripheral neuropathy in patients with type 1 diabetes mellitus. *Journal of diabetes and its complications*. 2007;21(6):397-402.
  22. Genuth S, Alberti KG, bennett P, buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care*. 2003;26:3160-7.