

Comparing the Frequency of Some Oral Lesions in Prediabetic and Healthy Individuals: Is There Any Difference?

Abstract

Background: Diagnosis of prediabetic stage is very important for prevention of diabetes and complications. This stage may be associated with some oral lesions. Only a few studies are available on the oral status of prediabetic patients and incidence of oral lesions in this population. This study aimed to compare some oral complications between prediabetic and healthy control groups. **Methods:** The present two-group cross-sectional study was carried out on 302 prediabetic and non-diabetic (healthy) 20- to 60-year-old subjects. In this study, data on age, gender, educational level, medications use, smoking, and some other variables were extracted through history taking. In addition, orodental examination was carried out by an oral medicine specialist to diagnose oral lesions including candidiasis, lichen planus, periodontitis, gingivitis, xerostomia, delayed wound healing, geographic tongue, fissured tongue, and burning mouth sensation. Data entry and analysis was performed by SPSS version 22 software, and *P* value and odds ratio (OR) were calculated to show statistical relationship between variables. **Results:** The most common oral lesion in prediabetic subjects was periodontitis (27.2%), followed by gingivitis (14.7%) and xerostomia (11.3%). In the control group, gingivitis (20.5%) followed by periodontitis (11.3%) are common oral lesions. Candidiasis (*P* = 0.036), periodontitis (*P* < 0.001), and xerostomia (*P* < 0.001) in prediabetic subjects were higher than control group that is statistically significant. Regression analysis showed that in the prediabetic group, periodontitis [OR = 2.91, confidence interval (CI): 1.54–5.49] and xerostomia (OR = 18.51, CI = 2.42–141.45) were significantly more prevalent than healthy subjects. **Conclusion:** Based on the results, glucose intolerance stage exhibited a significantly higher oral problems such as periodontitis and xerostomia than healthy euglycemic stage.

Keywords: Periodontitis, prediabetes oral lesions, xerostomia

Introduction

Prior to diabetes mellitus, the affected individuals suffer from defective metabolism of glucose. This condition is referred to as prediabetes.^[1] Studies have shown that if the prediabetic state is corrected, progression to type 2 diabetes decreases by up to 60%.^[2,3]

Since diabetes is considered a risk factor for oral diseases, it is necessary to pay attention to this disease and oral complications in the early stages (International Federation of Diabetes^[4] recommends that the primary care for diabetes should consist of annual evaluation of gingival diseases, including bleeding during tooth-brushing and swelling and persuasion for regular check-ups and treatment by a dentist).^[5] The mechanism of connective tissue damage in the oral cavity in hyperglycemia includes decreased

gingival fibroblast synthesis which results in the loss of periodontal fibers and supporting alveolar bone.^[6] In addition, impairment of phagocytic activity of mononuclear and polymorphonuclear cells leading to the presence of aggressive pathogenic subgingival flora was seen.^[7] Therefore, periodontal infection can increase systemic inflammation with induction of chronic state of insulin resistance and amplifying of vicious cycle of hyperglycemia and accumulation of advanced glycation end-product and connective tissue degradation.^[6]

Lamster showed that prediabetic persons demonstrate a level of periodontal destruction between that observed for normoglycemic individuals and persons with overt diabetes.^[8] SHIP Trend Study revealed that periodontitis and edentulous were not associated with prediabetes and well-controlled diabetes.^[9] Since prediabetes

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is a state of mild chronic hyperglycemia, it may be possible that oral lesions were higher than normal glycemic state. Also, a few studies with different results in this field are available on prediabetic patients; this study was set up to evaluate and compare oral lesions in prediabetic and healthy subjects who attended Diabetes Research Center in Yazd.

Methods

Patients

The present two-group cross-sectional study was carried out on 302 prediabetic and nondiabetic (healthy) 20- to 60-year-old subjects referring to Diabetes Research Center in Yazd, a city at the center of Iran, from January to December 2016. The protocol of the study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (No. 17/1/157520) and all participants signed an informed consent before including in the study. In this study, 151 prediabetic subjects were assigned to one group and 151 age- and sex-matched healthy subjects in another group. Prediabetic state was defined as fasting blood Sugar (FBS) in the range of 100–125 mg/dL and HbA1c in the range of 5.7%–6.4% based on laboratory tests. The inclusion criteria for healthy subjects consisted of FBS <100 mg/dL and HbA1c <5.7%.^[10]

Healthy and prediabetic subjects with previous history of diabetes or those who were undergoing drug therapy for diabetes, previous orodental malignancy, or being under treatment for malignancy and using antibiotics, antifungal agents, steroids, or nonsteroidal anti-inflammatory drugs within the past 3 months were excluded from the study. Convenience (consecutive) sampling technique was used to select study subjects.

Demographic data including age, gender, educational level, medication use, smoking or drug abuse, using toothbrush, dental floss, and mouth rinse were extracted from patients through history taking. After that, all the subjects underwent thorough orodental examination by an oral medicine specialist. All oral examinations were carried out by retracting the lips and cheeks under natural light. Almost all lesions were diagnosed based on clinical examination, but those lesions that could not be diagnosed clinically were assessed through biopsy and microscopic examination.

The pathological states of the oral cavity which patients were examined for consisted of candidiasis including different forms of oral candidiasis and related lesions such as denture stomatitis, angular cheilitis, median rhomboid glossitis, and complete atrophy of lingual papilla and others including lichen planus, periodontitis, gingivitis, xerostomia, delayed wound healing, geographic tongue, fissured tongue, and burning mouth sensation. All the information about the type of the lesions and their location (gingiva, lip, tongue, or oral mucosal tissue) were recorded in a data collection form.

Statistical analysis

Data entry and analysis was performed by SPSS version 22 software. In this study, independent sample *T*-test and Chi-square test were, respectively, used to compare quantitative and qualitative variables between groups. In addition, logistic regression was performed on data to evaluate the effect of prediabetes on different oral lesions without the effect of confounders. To do this, grouping variable (prediabetes/healthy) and some important variables for oral lesion including age, sex, having denture, and smoking were included as independent variables and every oral lesion was included as dependent variable in each model. Therefore, we had eight binary logistic regression models at the end. *P* value and odds ratio (OR) were calculated to show statistical relationship between variables. *P* value less than 0.05 was considered statistically significant.

Results

In this study, 151 prediabetic subjects and 151 healthy individuals were included. There was no significant difference in age, sex, smoking, and denture between the two groups. Family history of diabetes, history of hypertension, body mass index, and mean systolic and diastolic blood pressure were statistically significant between the two groups [Tables 1 and 2].

As shown in Table 3, the most common oral lesion in prediabetic subjects was periodontitis (27.2%), followed by gingivitis (14.7%) and xerostomia (11.3%).

Meanwhile, gingivitis and periodontitis were the most common oral lesions in the control group. Candidiasis, periodontitis, and xerostomia in prediabetic subjects were more prevalent in the prediabetic than the control group (*P* < 0.05).

Table 1: Frequency comparison of baseline characteristics between the healthy and prediabetic subjects

	Prediabetic	Healthy	<i>P</i>
Age	43.20	41.19	0.158
Gender, <i>n</i> (%)			
Female	86 (57)	98 (65)	0.157
Male	65 (43)	53 (35)	
Family history of diabetes, <i>n</i> (%)	38 (25)	22 (14.65)	0.021
History of smoking, <i>n</i> (%)	1 (0.7)	1 (0.7)	1.000
Dentures, <i>n</i> (%)	6 (4)	4 (2.6)	0.75
History of hypertension, <i>n</i> (%)	21 (13.9)	10 (6.6)	0.037

Table 2: Mean comparison of baseline characteristics between the healthy and prediabetic subjects

	Prediabetic	Healthy	<i>P</i>
Mean body mass index (kg/m ²)	29.26	25.83	<0.001
Mean systolic blood pressure (mmHg)	125.28	119.86	0.001
Mean diastolic blood pressure (mmHg)	79.76	76.84	0.007

The regression model could be implemented for all oral lesions except for lichen planus and burning mouth sensation, and the results showed that periodontitis (OR = 2.91, $P = 0.001$) and xerostomia (OR = 18.51, $P = 0.005$) were significantly more prevalent in the prediabetic than the healthy subjects [Table 4].

Discussion

Prediabetes is an initial state of hyperglycemia with plasma glucose between normal and diabetes threshold. The diagnosis of this state is very important for prevention of diabetes or at least postponing it.^[10] Since macro- and microvascular complications of diabetes usually occur before the clinical diagnosis of diabetes (at prediabetic stage), and therefore it is very important to reach an early diagnosis of this.^[11]

In this study, baseline characteristics of both the groups are similar; history of hypertension, family history of diabetes, body mass index, mean systolic blood pressure, and diastolic blood pressure were different between the two groups which is the usual phenomenon because prediabetic case may be associated with other components of metabolic syndrome.

Periodontitis, gingivitis, and xerostomia are the common oral lesions in prediabetic subjects, and gingivitis and periodontitis were the common oral lesions in the control group. Candidiasis, periodontitis, and xerostomia in

prediabetic subjects were higher than the control group that is statistically significant. After regression analysis, prediabetic state, itself, causes higher rate of periodontitis and xerostomia than normoglycemic state.

Lamster's study revealed that prediabetic persons demonstrate a level of periodontal problems between normoglycemic individuals and persons with overt diabetes.^[8] Javed *et al.* in 2012 showed that gingival bleeding perceived by the subject and clinical gingival inflammation were higher in subjects with prediabetic condition compared with the control group.^[12] In addition, positive association between impaired glucose tolerance and periodontal disease was seen in other studies.^[13-16]

In contrast to our result, SHIP Trend Study showed that periodontitis and edentulous were not associated with prediabetes and well-controlled diabetes.^[9] Also, no association between prediabetes and periodontitis was seen in epidemiological studies.^[17,18] In our study, FBS and HbA1c were used for definition of prediabetes; but in the mentioned study,^[9,17,18] prediabetes comprised impaired fasting glucose and impaired glucose tolerance test but no HbA1c.

In addition, specific bacterial colonization that contributes to prediabetes development in susceptible individuals maybe low or absent in Kowall *et al.*'s study.^[9] It is possible that periodontitis and prediabetes (or diabetes) may be comorbid conditions due to shared microbial risk factors. Comparison of periodontal bacteria between prediabetic and healthy persons in ORIGINS' study showed higher colonization of specific periodontal bacteria in prediabetic subjects than the other group prior to diabetes development.^[19] ORIGINS' findings show that associations between bacterial measures and prediabetes were consistently stronger than associations between periodontitis and prediabetes.^[19] In this regard, abnormal phagocytic activity of mononuclear and polymorphonuclear cells leading to the presence of aggressive pathogenic subgingival flora was seen.^[7] Hence, periodontal infection can potentiate a vicious cycle of systemic inflammation with induction of insulin resistance and amplifying of hyperglycemia and elevation of advanced glycation end-product and connective tissue degradation.^[6]

Table 3: Comparison of the frequencies of oral diseases between prediabetic and healthy individuals

	Prediabetic (%)	Healthy (%)	P
Candidiasis	8 (5.3)	1 (0.7)	0.036
Lichen planus	3 (2)	0	0.24
Periodontitis	41 (27.2)	17 (11.3)	<0.001
Gingivitis	22 (14.7)	31 (20.5)	0.182
Xerostomia	17 (11.3)	1 (0.7)	<0.001
Delayed wound healing	6 (4)	7 (4.6)	0.777
Geographic tongue	3 (2)	6 (4)	0.501
Fissured tongue	5 (3.3)	3 (2)	0.723
Burning mouth sensation	3 (2)	2 (1.3)	1.000
Presence of at least one of the lesions above	87 (58)	72 (47.7)	0.073

Table 4: Results of logistic regression model to show the effect of prediabetes on different oral lesions

Variables	Crude OR	P	Adjusted OR	P
Candidiasis	8.39 (1.03-67.94)	0.046	8.73 (0.92-82.19)	0.058
Periodontitis	2.91 (1.54-5.49)	0.001	3.00 (1.57-5.70)	0.001
Gingivitis	0.66 (0.36-1.21)	0.183	0.75 (0.40-1.40)	0.374
Delayed wound healing	0.85 (0.27-2.59)	0.777	0.82 (0.26-2.57)	0.738
Geographic tongue	0.49 (0.12-1.99)	0.319	0.42 (0.10-1.80)	0.245
Xerostomia	18.51 (2.42-141.45)	0.005	20.49 (2.44-171.83)	0.005
Fissured tongue	1.68 (0.39-7.19)	0.478	1.71 (0.40-7.34)	0.468
Presence of at least one of the lesions	1.50 (0.94-2.38)	0.086	1.51 (0.96-2.38)	0.074

OR=Odds ratio

In addition, low gingival fibroblast synthesis that results in the loss of periodontal fibers and supporting alveolar bone and connective tissue was seen in hyperglycemia.^[6] Another mechanism of oral complications in chronic mild hyperglycemia maybe increased production and accumulation of reactive oxygen species and inflammatory markers in the body tissues including the periodontium.^[20-23]

In this study, candidiasis was seen in prediabetic cases higher than the control group, but it was not significant after regression analysis. Oral candidiasis was higher in patients with prediabetes than in controls in Javed *et al.*'s study in 2014. Smokers were excluded from this study, and adjustment for denture, xerostomia, and other factors was not discussed.^[24] It seems that other factors such as increasing age, denture, xerostomia, and smoking are important factors for the presence of candidiasis. Therefore, due to mild hyperglycemic nature and younger age of prediabetic populations than diabetic, this disorder was not significant after regression analysis.

In this study, the frequency of xerostomia was higher than healthy subjects that persists after regression analysis (OR = 18.51). Javed *et al.* reported that xerostomia is more frequent in prediabetic patients compared with healthy individuals.^[24] Xerostomia is a subjective complaint of dry mouth, whereas hyposalivation is an objective decrease of salivary flow. Xerostomia is often associated with hyposalivation, but not always. Some cases of xerostomia have been described in patients with a normal salivary flow rate.^[25] Since xerostomia is a common manifestation in patients with chronic hyperglycemia even mild,^[26,27] it seems that other unknown factors beside reduced salivary flow maybe responsible.

Xerostomia in patients with poorly controlled diabetes and prediabetes is important, because it results in a change in salivary composition and an increase in its glucose levels, leading to high rate of smooth surface caries, atrophy of the oral mucosa, and an increase in the incidence of candidiasis.^[28,29]

Other oral lesions and presence of at least one mucosal lesion were not differing between the two groups. It is the first study that evaluates all the oral lesions in prediabetic persons.

Prediabetic stage is associated with periodontitis and xerostomia, indicating an increased inflammatory response and accumulation of reactive oxygen species in the periodontium.^[20-23] Since periodontal problem in such individuals cannot be justified only by accumulation of calculus and dental plaque, early identification of persons with dysglycemia is important to avoid the devastating clinical consequences of diabetes.

This study has several limitations. Small sample size and the absence of diabetic subjects with good and poor

glycemic control are the limitations. In this study, we did not use oral glucose tolerance test for detecting prediabetic from healthy persons. Therefore, it is another limitation. Future studies with large sample size and using oral glucose tolerance test, FBS, and HbA1c all together for definite diagnosis of prediabetes is recommended. Also, sialometry test, an objective method for detection of salivary flow rate, is helpful.

Conclusion

The present findings indicate that subjects with prediabetes are at increased risk of periodontal disease. High frequency of oral presentations in prediabetes supports that oral problems are early clinical manifestations of glucose intolerance. Therefore, oral medicine specialists can play an important role in early identification of at-risk patients.

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Conflicts of interest

There are no conflicts of interest.

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