

## Oral cavity candidiasis as a complication of fungal diseases in diabetic patients in south-East of Iran

Ebrahimzadeh Adel<sup>1</sup>, Saryazdi-pour Khadijed<sup>2</sup>, and Mosavi Mohammad<sup>3</sup>

<sup>1</sup>PhD, associated Professor, Department of Mycology and Parasitology and Membership of Infectious Disease and Tropical Medicine Reseach Center, Zahedan University of Medical Sciences, Zahedan, Iran

<sup>2</sup>MSc Student, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

<sup>3</sup>BS.c in Nursing, Department of Medical Parasitology and Mycology, Zahedan University of Medical Sciences, Zahedan, Iran

---

Copyright © 2016 ISSR Journals. This is an open access article distributed under the **Creative Commons Attribution License**, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**ABSTRACT:** Oral candidiasis is a common opportunistic infection in diabetic patients. *Candida albicans* is colonized on different oral surfaces such as tongue, palate, dental caries and plaques. Different factors like age, sex, denture wears and smoking play role in amount and severity of colonization of this microorganism. Our goal was to determine the relationship between the existences of *Candida Albicans* in oral diabetic patient. This cross - sectional study was performed on 120 diabetic patients. After completing the questionnaire and collect saliva samples and smears from the mouth were cultured directly on sabouraud agar medium containing 0.005% chloramphenicol and for identified use of specific tests. Data were statistically analyzed using Chi-Square, Mann-Whitney, t-test and correlation tests. Overall, in this study from 120 patients, 61 cases (50.8%) had a positive culture for *Candida*. In this study, Based on observations *Candida* infection rates were relatively higher in older patients and in women. Infections among participants who used dentures ( $0.001P <$ ) and have smoking ( $P < 0.038$ ) had significant relationship. The infection in people with type II diabetes is more than subjects with Type I diabetes. *C. Albicans* was the most common isolated *Candida* species in both groups. This study showed a high prevalence of Candidiasis and *Candida* colonization in oral samples of diabetic patients. Our goal was to determine the relationship between the existences of *Candida Albicans* in oral diabetic patient.

**KEYWORDS:** Candidiasis, Diabetic, Oral Infection, South-East, Iran

### 1 INTRODUCTION

Oral infections are caused due to the invasion of different microorganisms. One of these microorganisms is candida yeasts fungus, especially *Candida Albicans*. These organisms are found in the normal flora of the mouth, vagina and intestines and through the budding, yeast forms can be proliferated but the main gathering of them is the place in the posterior region of the tongue in place of cup-shaped papilla. In normal conditions, these fungi are not pathogenic but the local or systemic predisposing factors such as poor oral hygiene, diabetes mellitus, acquired immune deficiency syndrome, using pacifiers in infants, blood group, Shogron's syndrome, use of dentures, smoking, hormonal factors, impairment of PH and those treated with rays are causing the fungus to become pathogenic [1-3]. Mouth fungal infections are the most common opportunistic infections in patients with diabetes [4-6]. Diabetes is a chronic disease due to a disorder in glucose metabolism. The World Health Organization (WHO) referred the diabetes as a hidden epidemic and since 1993 all the world countries is calling to confront this epidemic [7-9]. There are two main forms of diabetes which have been identified as type I diabetes, and type II diabetes. Type I diabetes is usually seen in younger people and caused by an abnormal immune system reactions that damage cells that are insulin-secreting in the pancreas, factors such as viral infections and genetic and also inheritance are involved in this disease. Most of these patients suddenly and during a severe diabetic ketoacidosis syndrome become aware of their disease; these patients are dependent on insulin injections [10-12]. Type II diabetes can be seen over the age of 40

years. The cause of type II has not been determined, but genetic factors and obesity are important in causing this disease. One- third of affected people, have some diabetic dependents. This form of diabetes is characterized by reduced insulin secretion and peripheral resistance than it. Genetic factors predisposing play a stronger role in this type of diabetes [13, 14]. Despite the high concentration of salivary glucose combined with low salivary secretion could be a reason for diabetics that are susceptible to candidiasis [1-3, 14]. Neutrophil function is impaired in this disease, and can help to develop oral candidiasis in diabetic patients [15-16]. The aim of the present study is investigation of the prevalence of oral candidiasis in patients with diabetes admitted to Ali Asghar hospital Diabetes Center in zahedan.

## 2 MATERIALS AND METHOD

This study was a cross - sectional descriptive study. This research was done in hospitals Ali Asghar (AS) Zahedan on 120 patients who were diagnosed with diabetes with blood glucose test. After completing the questionnaire, which included the factors such as: gender, age, cigarette smoking, having or not having dentures, weight, PH saliva, blood group, type of diabetes, history of fungal infection and antibiotics, the oral examination performed on all patients, were asked the patients in fasting situation and without washing the mouth, discarded the primary part of their saliva and then shed the rest of saliva into sterile container with lid. Samples were taken with a sterile swab from the lining of the palate, tongue, gums and saliva, And on Sabouraud agar medium (Sabouraud's agar) containing 0.005 percent chloram-phenicol were cultured, after 6 days of incubation, colony counts were performed on the medium, then colony color, texture, shape and size were examined. Positive cultures samples, direct test of KOH 10% presence of yeast cells was performed. Finally, examples of culture yeast cells in terms of *Candida Albicans* and other species with germ tube testing method (Germ tube) and the ability to produce chlamydo spores on corn meal agar medium Tween 80 (Corn Meal Agar, tween 80) and assimilation test kit by API 120 were detected and identified, and the results were recorded in the form. In addition, to determine the pH, acid paper meter with forceps from sampling areas will be sampled. Data analysis was performed using spss software version 18. And the chi-square test, Mann – Whitney, t test and correlation test was used to evaluate the relationships among the data. Significance level was considered as  $p < 0.05$ .

## 3 RESULTS

The study was included 120 diabetic patients that are attending to diabetes center of Zahedan Ali Asghar hospital(AS), including 38 (31.7%) male and 82 (68.3%) were female. These patients had a between the age of 25 years to 75 years, that the most frequent age group were 46-55 comprised 42 patients (35%) and the lowest rate of 25-35 age group, 4 patients (3/3%). Two groups of patients, according to the type diabetes, were divided into type I diabetes, type II diabetes, that 30 patients (25%) had type I and 90 patients (75%) had type II diabetes. Patients in terms of blood group: O, 40 patients (3/33%), blood group A, 33 patients (5/27%), blood group AB 33 patients (5/27%) and blood group B, 14 patients (7 / 11%). 14 patients (11.7%) had a history of fungal disease. All cultures include *Candida*, were 61 patients (50.8%), of which 54 (88.52%), related to *Candida Albicans* and 5 cases (8.19%), to *Candida Glabrata* and 2 patients (27.3%) were related to other types of *Candida*. The observations were carried out in 61 patients with positive cultures, 20 cases (32.8%), with diabetes mellitus type I and 41 (67.2%) were diagnosed with type II diabetes. From samples taken from 46 patients (3/38%) had antibiotics that the 26 patients (6/42%) of them had positive fungal cultures. Among the subjects studied, 79 subjects with acidic PH, 13 persons with Alkaline pH and 28 patients (23.3%) had PH neutral pH. On whether the from samples taken that used artificial teeth, the results indicate that 40 patients (33.3%) were using dentures. 23 persons (19.2%) were smokers. As can be seen in Table 1 there is a significant relationship between the diabetes, cigarette smoking and use of dentures and oral *Candida* infection (Table 1).

Table 1. Distribution of candidates in terms of the level variables in patients

The variable name		negative culture	Positive culture	p-value
Gender	Male, number (%)	21(35.6)	17(27.9)	<b>0.363</b>
	Female, number (%)	38( 64.4 )	44(72.1)	
Age	25-35	3(5.1)	1(16)	<b>0.793</b>
	36-45	9(15.3)	10(16.4)	
	46-55	22(37.3)	20(32.8)	
	56-65	13(22)	17(27.3)	
	66-75	12(20.3)	13(21.3)	
Smoking	+	16(11.9)	16(26.2)	<b>0.038</b>
	-	52(88.1)	45(73.8)	
PH saliva	acidic	34(57.6)	45(73.8)	<b>0.067</b>
	monoecism	15(25.4)	13(21.3)	
	alkaline	10(16.9)	3(4.9)	
Diabetes	I	10(16.9)	20(32.8)	<b>0.036</b>
	II	49(83.1)	41(67.2)	
Weight	50-60	11(18.6)	13(21.3)	<b>0.991</b>
	61-70	21(31.6)	21(34.4)	
	71-80	13(22)	12(19.7)	
	81-90	10(16.9)	10(16.4)	
	91-100	4(6.8)	5(8.2)	
Antibiotic usage	+	20(33.9)	26(42.6)	<b>0.326</b>
	-	39(66.1)	35(57.4)	
Fungal disease	+	6(10.2)6	8(13.1)	<b>0.615</b>
	-	53(89.8)53	53(86.9)	
Blood group	O	13(22)	27(44.3)	<b>0.068</b>
	A	20(33.9)	13(21.3)	
	AB	19(22.2)	14(23)	
	B	7(11.9)	7(11.5)	
Teeth	Denture wears	8(13.6)	32(52.5)	<b>0.001</b>
	natural	51(86.4)	29(47.5)	

#### 4 DISCUSSION

According to the findings of this study Out of the 120 diabetic patients, 61 cases (50.8%) had a candidate in his mouth. Disturbances such as decreased neutrophil function in diabetic patients, increased epithelial cell receptivity to Candida species, increasing the glucose concentration in saliva and salivary flow decreases with increasing adherence of Candida to epithelial cells, provides the premises of candidates. As a result, people with diabetes are more prone to fungal infections of the mouth [17]. Similar studies by Belazi M and colleagues conducted on 128 patients with diabetes indicate that more than 64% of patients were with Candida. In another study by Martinez, RF took place from 141 patients over a 7/82% were infected with Candida, this is indicative of the high incidence of candidiasis in patients with diabetes. [18,19]. Strains of Candida Albicans and Candida dubliniensis are components of saprophyte gastrointestinal mucosal surfaces, and create conditions for opportunistic infection in people with diabetes are provided. The observations conducted in this study, showed that the most common pathogenic Candida Albicans is the predominant species. And in other studies well as to other species Candida Albicans is the most common [19, 20-22]. It appears that the fungal infection increases with aging. In these research candidates in the age group 46-55 were the most common (32.8%), but there is no significant relationship between them. In other studies which are done by paula.V and Al Mubarak.S and Maria Belazi on diabetes there is not a significant relationship between age group and there candidate. But prevalent in people over 60 years reported more than other groups [20, 23, 18].

In old age due to reduced excitability and plasticity of T lymphocyte proliferation and thus reduce their number and cell-dependent immune mechanism CMI (Cell Mediated Immunity) an increase in oral candidiasis were seen (19). In the present study, women (aged 66-75) are more exposed to infection than men (84.6%) and according to the results obtained using the T-test there was a significant correlation between sex and age (P = 0.001). In a study conducted in 2011 by Arjuna NB Ellepola indicated that the risk of candidiasis in women is more than men [22]. Moalic and colleagues have been reported that

Candida outbreaks in men more frequently than women [24]. And study by the doctor Shahin Yar Mohammad was reported that there is not a significant correlation between age and sex [25]. Several evidence showed that type I diabetic patient are more prone to candida infections than type II, and according to chi-square test, there is a significant relationship ( $P = 0.036$ ). This result is similar to some recently conducted studies [23, 27, 26]. In the study of Dr. T. Rashidi and colleagues infection in people with type I diabetes, most have reported [28]. The prevalence of candidates in diabetic patients depend on several factors including tobacco use, antibiotic use, use of dentures, PH mouth, weight, age, blood group, gender, history of fungal disease and may depend on ..... , And in its prevalence rate [17]. Mouth environment of diabetic patients is acidic. A study by Karaev and colleagues showed that the activity of candidates between 7 to 6.2 to 7 PH is their maximum activities and findings of this study correspond with the results [29]. Patients who had blood group O compared with other blood groups were more sensitive to fungal infection , although there was no statistically significant difference between the candidates, but studies have shown that blood group O than other blood groups is critical to the colonization of Candida in the mouth. [30,31,32]. Factors such as smoking that plays an important role in the increased susceptibility of Candida in the mouth, the quality and how to implement of health behaviors such as brushing and using mouthwash are involved in this association. In this study, the number of people who smoking and had fungal infection were also lower than those who were none smoking , But according to the chi-square test showed a significant relationship between smoking and Candida infection ( $P = 0.038$ ). Studies conducted by Ramon Felip and Arjuna NB Ellepola showed the candidate prevalence in tobacco consumers more than 60% [22, 19]. Also significant associations between antibiotic use and experience with Candida fungal disease and weight have been reported.

## CONCLUSION

Family fungus Candida is part of the normal oral flora form and causes opportunistic infections. It is clear that diabetics are more susceptible to oral candidiasis than non-diabetics. Furthermore, smoking and denture wears are at high risk of being infected. *C. albicans* is by far the most prevalent among all Candida spp. as the cause of oral candidiasis in Iran.

## ACKNOWLEDGEMENTS

Hereby from efforts of Mr. Dr.Ramin Saravani and Mrs. S. Karimi, Seyyed Mohammad Mir Abedini, Research and Cooperation Deputy, due to their lot of work to do in this regard would be thanked.

## REFERENCES

- [1] Krogh P, Hald B, Holmstrup P. Possible mycological etiology of oral mucosal cancer: catalytic potential of infecting *Candida albicans* and other yeasts in production of N-nitrosobenzyl-methylamine. *Carcinogenesis* 1987;8:1543.
- [2] Krogh P, Holmstrup P, Vedtofte P, Pindborg JJ. Yeast organisms associated with human oral leukoplakia. *Acta Derm Venerol Suppl (Stockh)* 1986;121:51–5.
- [3] Barrett AW, Kingsmill UT, Speight PM. The frequency of fungal infection of oral mucosal lesions. *Oral Dis* 1998;4(1):26–31.
- [4] Soysa NS, Samaranayake LP, Ellepola AN. Diabetes mellitus as a contributory factor in oral candidosis. *Diabetic medicine : a journal of the British Diabetic Association*. 2006 May;23(5):455-9.
- [5] Kadir T, Pisiriciler R, Akyuz S, Yarat A, Emekli N, Ipbuker A. Mycological and cytological examination of oral candidal carriage in diabetic patients and non-diabetic control subjects: thorough analysis of local aetiological and systemic factors. *Journal of oral rehabilitation*. 2002 May;29(5):452-7.
- [6] Lotfi-Kamran MH, Jafari AA, Falah-Tafti A, Tavakoli E, Falahzadeh MH. Candida Colonization on the Denture of Diabetic and Non-diabetic Patients. *Dental research journal*. 2009 Spring;6(1):23-7. PubMed PMID: 21528026.
- [7] WHO. The Epidemiology of Diabetes Intervention & complication jamma. 2003;2900(16):2159-2197.
- [8] Behrman R, Kliegman R, Jenson H, Nelson Textbook of pediatrics 17th edition, 2004;2:1793-1803.
- [9] What care to expect. British diabetic association website: [www.Diabetes.org.uk](http://www.Diabetes.org.uk). June 1998.
- [10] DCCT/EDIC Research Group, Intensive diabetes therapy and carotid intima-MediaThickness in Type I Diabetes Mellitus. *New England Journal of Medicine*. 2003;348(23):2294-2303.
- [11] Lindberg U, Bergstrom AL, Carlsson E, Dahlquist G, Sjoblad S, Thalme B: urinary tract infection in children with type I diabetes. *Acta Paediatr Scand* 1985;74:85-88.
- [12] Dunstan DW, Zimmet PZ, Welborn TA, et al. The rising prevalence of diabetes and impaired glucose tolerance: The Australian Diabetes, Obesity and lifestyle study. *Diabetes care* 2002;25:829-834.
- [13] Dorocka-Bobkowska B, Zozulinska-Ziolkiewicz D, Wierusz-Wysocka B, Hedzelek W, Szumala-Kakol A, Budtz-Jorgensen E.

- Candida-associated denture stomatitis in type 2 diabetes mellitus. *Diabetes research and clinical practice*. 2010 Oct;90(1):81-6.
- [14] Ko SH, Song KH, Ahn YB, Yoo SJ, Son HS, Yoon KH, et al. The effect of rosiglitazone on serum lipoprotein(a) levels in Korean patients with type 2 diabetes mellitus. *Metabolism: clinical and experimental*. 2003 Jun;52(6):7314.
- [15] Aly FZ, Blackwell CC, Mackenzie DA, Weir DM, Clarke BF. Factors influencing oral carriage of yeasts among individuals with diabetes mellitus. *Epidemiol Infect*. 1992; 109:507-18.
- [16] Borg Andersson A, Birkhed D, Berntorp K, Lindgarde F, Matsson L. Glucose concentration in parotid saliva after glucose/food intake in individuals with glucose intolerance and diabetes mellitus. *Eur J Oral Sci*. 1998;106:931-7
- [17] Zegarelli DJ. Fungal infections of the oral cavity. *Otolaryngol Clin North Am*. 1993 Dec;26(6):1069-89.
- [18] Belazi M, Velegraki A, Fleva A, Gidarakou I, Papanau L, Baka D, et al. Candidal overgrowth in diabetic patients: potential predisposing factors. *Mycoses*. 2005 May;48(3):192-6.
- [19] Martinez RF, Jaimes-Aveldanez A, Hernandez-Perez F, Arenas R, Miguel GF. Oral Candida spp carriers: its prevalence in patients with type 2 diabetes mellitus. *Anais brasileiros de dermatologia*. 2013 Mar-Apr;88(2):222-5.
- [20] Sanita PV, Pavarina AC, Giampaolo ET, Silva MM, Mima EG, Ribeiro DG, et al. Candida spp. prevalence in well controlled type 2 diabetic patients with denture stomatitis. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*. 2011 Jun;111(6):726-33.
- [21] Muir A, Forrest G, Clarkson J, Wheals A. Detection of Candida albicans DNA from blood samples using a novel electrochemical assay. *Journal of medical microbiology*. 2011 Apr;60(Pt 4):467-71.
- [22] Ellepola AN, Khan ZU, Joseph B, Chandy R, Philip L. Prevalence of Candida dubliniensis among oral Candida isolates in patients attending the Kuwait University Dental Clinic. *Medical principles and practice : international journal of the Kuwait University, Health Science Centre*. 2011;20(3):271-6.
- [23] Al Mubarak S, Robert AA, Baskaradoss JK, Al-Zoman K, Al Sohail A, Alsuwyed A, et al. The prevalence of oral Candida infections in periodontitis patients with type 2 diabetes mellitus. *Journal of infection and public health*. 2013 Aug;6(4):296-301.
- [24] Moalic E, Gestalin A, Quinio D, Gest PE, Zerilli A, Leflohic AM. The extent of oral fungal flora in 273 students and possible relationships with dental caries. *Caries Res* 2001; 13: 125-31.
- [25] Ahmadi sy. Evaluation of oral fungal flora and the prevalence of fungal infections in diabetic patients. *Journal of Endocrinology and Metabolism*. 2002;2:109-5.
- [26] Dorocka-Bobkowska B, Zozulinska-Ziolkiewicz D, Wierusz-Wysocka B, Hedzelek W, Szumala-Kakol A, Budtz-Jorgensen E. Candida-associated denture stomatitis in type 2 diabetes mellitus. *Diabetes research and clinical practice*. 2010 Oct;90(1)
- [27] Soysa NS, Samaranyake LP, Ellepola AN. Diabetes mellitus as a contributory factor in oral candidosis. *Diabetic medicine : a journal of the British Diabetic Association*. 2006 May;23(5):455-9.
- [28] Rashidi t. Skin Infection Candida albicans in patients with diabetes. *Journal of Ardabil University of Medical Sciences*. 2008;3:255-0.
- [29] Karaev ZO, Velichko EV, Bykov VL. Basic characteristics of the process of Candida adhesion to human epitheliocytes. *Zh Mikrobiol Epidemiol Immunobiol* 1986; (7): 59-61.
- [30] Odds. FC. *Candida and Candidosis*, 2nd ed. Bailliere Tindall; 1988; pp.93-104.
- [31] Burford-Mason AP, Weber JC, Willoughby JM. Oral carriage of candida albicans, ABO blood group and secretor status in healthy subjects. *J Med Vet Mycol* 1988 Feb;26(1):49-56.
- [32] Ben-Aryeh H, Blumfield E, Szargel R, Laufer D, Berdicevsky I. Oral candida carriage and blood group antigen secretor status. *Mycoses* 1995 Sep-Oct;38(9-10):355-8.