

Diabetic Control and the Occurrence of Oral Candidiasis

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Abstract

Background: Being diabetic in itself may not place a person at increased risk of fungal infection, unless diabetic control is very poor, as evidenced by glycosylated hemoglobin (HbA1c) concentration of more than 12%.

Aim of Study: Assessment of the value of HbA1c to predict the prevalence of oral yeast infection in diabetic patients in multiple variable analysis including age, sex, smoking and dental histories.

Methods: Occurrence of fungal infection in 51 diabetics was analyzed statistically in relation to different variables including age, sex, smoking, denture wearing and diabetic control.

Results: The prevalence of oral yeast infection in our population was 49%. HbA1c above 12% was strongly associated with oral yeast infection (odd ratio= 13) ($p < 0.001$), risk of oral candidiasis among diabetics wearing dentures was significantly higher than among dentate diabetics (odd ratio=4.78). After controlling for the effect of denture wearing, HbA1c > 12% remained highly predictive of oral yeast infection, particularly among diabetics without dentures.

Key words: Diabetes mellitus, fasting blood sugar, urinary glucose concentration, glycosylated hemoglobin, oral candidiasis.

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Introduction:

Degree of diabetic control, as measured by blood and urinary glucose concentration has previously been associated with the presence of oral yeast and humoral precipitating antibodies to candida albicans in some studies¹. Other investigators have found that blood and urinary glucose concentrations were unrelated to oral candidiasis^{2,15}, even after diabetics and controls were matched for age, sex, smoking and dental state³⁻⁶. Glycosylated hemoglobin (HbA1c) concentrations reflect the degree of diabetic control during the preceding two months. It has been shown that estimation of HbA1c is a better method of measuring diabetic control than the usual criteria of determining fasting blood glucose and glycosuria^{7,8}.

This study assessed the value of using HbA1c to predict the prevalence of oral yeast in 51 diabetics in a multiple variable analysis, including age, sex, smoking and dental histories, blood and urinary glucose concentrations.

Patients and Methods:

The study population comprised 51 consecutive diabetic outpatients attending the outpatient clinic of Ameryia General Hospital in Ameryia, Falluja, Iraq, from June 2010 to September 2010. The palatal mucosa and denture base have been shown to support a high rate of yeast colonization⁹, so specimens for candidiasis were taken from these sites. The prevalence of oral yeast was determined by obtaining fungal cultures from the palatal mucosa and denture base (if any) of each subject by rolling cotton swabs moistened in sterile water along the palatal mucosa or denture base and breaking them into a sterile glass vial containing 2 cc of sterile water for transport to the laboratory.

Samples were streaked, using the four quadrant method with a 2mm wire loop, on saboraud agar plate. After 5-7 days incubation at room temperature, increasing quantities were rated 1+ to 4+.

Three tests were used to assess the degree of diabetic control. The fasting blood sugar (enzymatic colorimetric {GOD-PAP}; Biomaghreb,2006), degree of glycosuria (Cybow strips, DFI Company Ltd. And HbA1c(Stanbio glycohemoglobin {Pre Fil} a colorimetric method by Stanbio Lab.s, these tests were done at the same time the swabs were taken for fungal cultures from each diabetic in our study.

Chandler and Chandler were able to show an increased carriage of *C. albicans* in diabetics with the poorest control, which they defined as persistent fasting sugars above 200 mg/dl, glycosuria equal to or greater than 3%, and past episodes of diabetic ketoacidosis⁶.because of their findings, we analyzed diabetic control by comparing fasting sugars above and below 12 mmol/l and urinary sugars above and below 3+ (7g/dl). The normal range of HbA1c in routine use at the diabetes clinic was 5.5 – 8.2%. In this study patients with poor diabetic control did not show evidence of oral yeast infection until HbA1c was > 12%.

Data was analyzed using the BMDP statistical program. Odds ratios were calculated and Pearson χ^2 tests were used to determine differences in proportions. Stepwise logistic regression analysis was applied to the data to adjust for the effects of extraneous variables.

Results:

The mean age, age range, sex, presence or absence of dentures and smoking history of the 51 diabetics are shown in table 1. 25 diabetics harbored oral yeasts.

There was some variation in the 1+2+ v 3+4+ colony density, determined by four quadrant semi quantitative

streaking of inoculum among subgroups of patients studied (table 2).

Increased density is evident among denture wearers but not among smokers. Significant differences could not be determined due to the small size of the subsample of diabetics with yeast.

Table 1: Characteristics of Sample Population (n = 51)

Mean age	46.4
Age range	19-77
No. of women	30
No. of dentures	25
No. of smokers	16
No. of oral yeast infection	25
Density (1+ - 2+ growth)	13
Density (3+ - 4+ growth)	12

Table2: Density of yeast colonization in subgroups of diabetics with oral yeast infection (n= 25)
Density 3+ to 4+

	n	number	%
Age			
> 50	9	3	33.3
≤ 50	16	9	56.2
Sex			
F	15	7	46.7
M	10	5	50.0
Dentures			
Yes	17	10	58.8
No	8	2	25.0
Smokers			
Yes	8	3	37.5
No	17	9	52.9
HbA1c			
> 12%	13	5	38.5
≤ 12%	12	7	58.3
Urinary sugar			
3+ to 4+	4	2	50.2
0 to 2+	21	10	50.2
Fasting sugar			
> 12mmol/l	12	5	41.7
≤ 12mmol/l	13	7	53.8

Glycosylated hemoglobin concentrations above 12% were significantly associated with oral yeast infection ($P < 0.001$), while fasting glucose concentrations $> 12\text{mmol/l}$ and urinary glucose concentration $> 3+$ were not (table 3). Age, sex, dental and smoking state, HbA1c, urinary and blood glucose concentrations were included in a logistic regression model.

Stepwise analysis showed that dental state and HbA1c concentrations were the only variables to have a significant effect on the risk of oral yeast infection.

The association of HbA1c concentrations with yeast infection was evaluated separately according to dental state (table 4) because the likelihood of oral candidiasis among denture wearers is so high, the predictive potential of HbA1c concentration is most evident among diabetics without dentures.

Table 3 Potential risk factors for yeast infection among diabetics

	No.	No. with yeast infection (%)	Odds ratio	95% Confidence interval
Age				
>50	25	16 (64.0)	3.36 ($P = 0.04$)	(1.06, 10.59)
≤50	26	9 (34.6)		
Sex				
Female	30	15 (50)	1.10 ($P = 0.87$)	(0.36, 3.35)
male	21	10 (47.6)		
Dentures				
Yes	25	17 (68)	4.78 ($P < 0.01$)	(1.46, 15.62)
no	26	8 (30.8)		
Smokers				
Yes	16	8 (50)	1.06 ($P = 0.92$)	(0.32, 3.46)
no	35	17 (48)		
HbA1c				
> 12%	15	13 (86.7)	13.00 ($P < 0.001$)	(2.52, 67.19)
≤ 12%	36	12 (33.3)		
Urinary glucose				
3+ to 4+	9	6 (66.6)	1.27 ($P = 0.78$)	(0.25, 6.42)
0 to 2+	42	22 (52.3)		
Fasting glucose				
> 12 mmol/l	18	12 (66.7)	3.08 ($P = 0.06$)	(0.92, 10.25)
≤ 12 mmol/l	33	13 (39.5)		

Table 4 Stratification of glycosylated hemoglobin concentration by denture state

	No.	Yeast infection %
Among those without dentures	26	
High HbA1c	7/9	77.8
Low HbA1c	1/17	4.9
	$X^2 = 14.28, P=0.0002$	
Among those with dentures	25	
High HbA1c	6/6	100.0
Low HbA1c	11/19	57.9
	$X^2 = 3.72, P=0.0539$	

Discussion

The association between diabetic control and fungal infection was examined by comparing urinary glucose concentrations (which are a poor index of glycaemia).

Fasting blood glucose (which reflects the degree of glycaemia at one point in time), and HbA1c concentrations (which reflect the degree of glycaemia during the preceding two months) among the 51 diabetic outpatients studied. Degree of control as measured by fasting sugars and urinary glucose concentrations was unrelated to prevalence of oral candidiasis, confirming earlier reports^{2,3,15}. HbA1c concentrations above 12% were significantly associated with oral yeast infection, which suggests that fungal infections of mucous membranes may only be significantly associated with diabetes in patients with a longer history of hyperglycemia. Being diabetic in itself may not place a person at increased risk of fungal infection¹⁶, unless diabetic control is very poor, as evidenced by HbA1c concentrations of more than 12% (table 3). Because of the common belief that diabetes of any degree is associated with an increased risk of fungal infection, many people with recurrent genital candidiasis are screened for diabetes mellitus.

Only 15 (10.9%) of 138 men with candidal balanitis were diabetic in an uncontrolled trial of 1% clotrimazol (canestan) cream, and this group was significantly older than the non-diabetic studied¹⁰. In a study of the microbial flora of the vagina in 90 diabetic and non-diabetic women there was no difference between diabetic and non diabetic patients in the isolation of candida albicans¹¹ even when diabetic control was poor. Among 85 women with alleged recurrent vulvovaginal candidiasis, there were no abnormal blood glucose concentrations detected two hours after eating; and among 250 women referred for this disorder, over 80% have been tested by their practitioners for subclinical diabetes and all were found to be normal¹². Similarly, glucose tolerance curves in 72 pregnant women with vaginal candidiasis confirmed by culture did not differ from those of an equal number of matched control¹³.

These studies suggest that in women genital candidiasis is rarely associated with diabetes, while 89% of men with genital candidiasis are also not diabetic.

The same principle may apply in oral candidiasis that is most people with oral yeast are not diabetic; but very poorly controlled diabetics are significantly more likely to have oral candidiasis as this study suggest. Other studies suggest diabetes predisposes to oral candidiasis regardless to diabetic control¹⁷⁻²⁰. Javed *et al* found that oral candidiasis is more among diabetic females than diabetic males²¹.

Tobacco smoking and wearing dentures continuously day and night have been found to be important local factors in chronic oral hyperplastic candidiasis¹⁴. In the present study the presence of dentures and HbA1c concentration were independent predictor of the risk of developing candidiasis. This finding suggests that diabetics are relatively more susceptible to fungal infections in areas of moisture and trauma, but in the absence dentures a high HbA1c concentration is an important risk factor for yeast infection.

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