

VULVOVAGINAL CANDIDIASIS AND ITS RELATED FACTORS IN DIABETIC WOMEN

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SUMMARY

Objective: One of the problems of women with diabetes is resistant vulvovaginitis, which is related to some factors such as hyperglycemia, allergy and atopy. One of the most common pathogens associated with this condition is *Candida albicans*. Thus, most physicians begin antifungal therapy at the patient's first visit, even without para-clinical findings. We aimed to determine the prevalence of *Candida* vulvovaginitis and factors that cause diabetic women to be prone to this infection.

Materials and Methods: This descriptive, analytic cross-sectional study was performed in 160 nonpregnant diabetic women who visited the diabetes clinic of Shariati Hospital in Tehran, Iran from 2002 to 2005. The fasting blood sugar, 2-hour postprandial blood sugar, and glycosylated hemoglobin were measured, and a culture of the vaginal discharge was obtained. Statistical analysis was performed using Fisher's exact test.

Results: Seventy-one percent of the women had clinical vaginitis (fungal or bacterial), and 12.5% (20/160) had *Candida* vaginitis. Microscopic findings for *Candida* were positive in 12 patients, of whom two had *Candida* vaginitis. The prevalence of *Candida* vaginitis together with positive culture was 2.6% (4/160). After including the 10 patients with positive *Candida* culture together with other clinical vaginitis, the overall prevalence of *Candida* vaginitis based on positive culture was 8.8% (14/160). There was a significant statistical difference between either mean fasting blood sugar or educational level and infectious vaginal culture. There were no significant associations between positive culture and age, glycosylated hemoglobin, history of allergy, genital hygiene, occupation, kind of treatment, and type or duration of diabetes.

Conclusion: We suggest that in the case of clinical vaginitis, especially *Candida* vulvovaginitis, culture of vaginal discharge should be warranted even if there is a positive smear. [*Taiwan J Obstet Gynecol* 2007;46(2):399-404]

Key Words: candidiasis, diabetes mellitus, vulvovaginitis

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Introduction

Diabetes mellitus is a chronic, insidious disease that can affect any organ or system of the body. One of the problems associated with this condition is infection.

Although the prevalences of infection among diabetic and non-diabetic subjects are similar, the intensity of infection is being more severe and the response to therapy slow in diabetic patients.

One of the complications experienced by diabetic patients is resistant and recurrent infections. Some believe that the condition is caused by malfunctioning leucocytes, especially in the presence of uncontrolled blood glucose levels [1-3]. Among the infections, vaginal inflammation or infection, especially fungal vaginitis, is more disturbing in severe hyperglycemic conditions [4].

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The most common etiologic agent for this infection is the yeast (fungal) organism, usually *Candida* [5–9]. Therefore, most gynecologists begin antifungal therapy at the patient's first visit, even without a culture of vaginal discharge [5]. Others believe that a specimen should be taken in resistant or recurrent infections for vaginal culture during future visits [5]. In a study by Eckert et al [6], *Candida* was detected in 28% of cultures of vaginal discharge obtained during the initial visit of women with vaginitis; the remaining cultures were for other organisms, such as sexually transmitted organisms. The authors believed that the causes of recurrent disease or resistance to therapy were false diagnosis of the pathogenic organism and unsuitable treatment [6]. On the other hand, even when correct diagnosis had been made, background factors, especially those associated with systemic diseases like diabetes mellitus, caused treatment failure [4,7]. Researchers have stressed the importance of personal hygiene, history of infections and allergic diseases of the upper respiratory tract (nose, sinuses), and atopic dermatitis in the subject or the relative(s) in recurrent diseases or resistance to therapy [8]. They believed that effective steps could be taken to successfully treat this condition by preventing and controlling or eliminating background factors. In this study, we aimed to determine the prevalence of *Candida* vaginitis in Iranian women with diabetes mellitus who attended the diabetes clinic of Shariati Hospital in Tehran during a 3-year period and the relationship between vulvovaginal candidiasis and its influencing factors.

Materials and Methods

This descriptive, analytic cross-sectional study was performed in all diabetic women who visited the diabetes clinic of Shariati Hospital in Tehran from 2002–2005 and were enrolled in the study after signing the informed consent form.

Each participant had to have proven diabetes 3 months previously. Exclusion criteria included lack of desire to participate in the study or pregnancy. All subjects were asked to fill out prepared questionnaires on demographic characteristics, type of diabetes mellitus, duration and type of its treatment, past history of allergy, methods of washing underwear (detergents, heat, etc) and voiding after sexual intercourse, and vaginal examination was done for each participant by a general physician. Also, concentrations of fasting blood sugar, 2-hour postprandial blood sugar and glycosylated hemoglobin were measured, and cultures of vaginal discharge were performed.

Definitions

Vaginitis is the infection or inflammation of the external genital tract (vagina) and is caused by various organisms. Presence of disturbing clinical manifestations, such as burning sensation, itching and vaginal discharge, are inadequate for definite diagnosis of *Candida* vaginitis. In order to determine the organism, especially in recurrent *Candida* vaginitis, it is advisable to obtain a history, perform microscopic examination with 10–20% potassium hydroxide or 10% normal saline, and perform subsequent culture of vaginal discharge [6]. According to some studies, *Candida* was found in only 28% of all cases with positive clinical signs of *Candida* vaginitis. Therefore, the best diagnostic test, on which most researchers, gynecologists and midwives agree on, is culture of vaginal discharge. In this way, it is possible to differentiate between the different infecting organisms, especially those causing sexually transmitted diseases, thereby preventing treatment failure.

Laboratory methods

All vaginal discharge specimens (for assessment with or without 10–20% potassium hydroxide or 10% normal saline and culture of vaginal discharge) were sent to the Noor Laboratory. The culture media used were eosin-methylene blue agar for Gram-negative bacilli, Sabouraud dextrose agar for yeasts, and blood agar for fungi and bacteria. All media were produced by Merck (Darmstadt, Germany). Fasting blood sugar, 2-hour postprandial blood sugar and glycosylated hemoglobin were estimated in the hormone laboratory of the Endocrinology Research Center of Shariati Hospital.

Written consent was obtained from all patients. This study was approved by the Medical Ethics Committee of the Deputy of Research affiliated to the Ministry of Health and Medical Education. After a data bank had been designed, data entered into the computer were analyzed using Fisher's exact test (SPSS version 11.5). A p value of ≤ 0.05 was considered to be statistically significant.

Results

A total of 160 women with diabetes mellitus (mean age, 51 ± 10 years; age range, 16–75 years) were enrolled. Ninety-four percent of the patients had type II diabetes mellitus and the remaining had type I. Seventy-five percent of the participants received oral hypoglycemic drugs, 15% received insulin, and the rest were given combination therapy (tablets plus insulin). The mean duration of diabetes mellitus in these patients

was 9 ± 6 years (range, 0.08–36 years). The duration of diabetes based on median and quantitative distribution was ≤ 7.5 years in 50.6% of them and > 7.5 years in the remaining. Mean fasting blood sugar level was 176 ± 56 mg/dL (range, 73–326 mg/dL), 2-hour postprandial blood sugar level was 246 ± 91 mg/dL (range, 52–553 mg/dL) and mean glycosylated hemoglobin level was $8.9\% \pm 2\%$ (range, 3.2–16%). Regarding educational

level, 61.9% of our patients were illiterate or had incomplete primary school education, and 38.1% were educated. The subjects were mainly housewives (92.5%), and the rest were working women. There was sexual activity in 86.3% of the cases, and none in 13.7% of the cases. Twenty-one percent of our patients had a history of allergy (rhinitis, sinusitis or atopic dermatitis) (Table 1).

Table 1. Frequency distribution of clinical vaginitis, infectious culture, *Candida* culture among 160 diabetic women based on influencing factors

Variable	Total	Clinical vaginitis, <i>n</i> (%)	Infectious culture, <i>n</i> (%)	Positive <i>Candida</i> culture, <i>n</i> (%)
Age				
≤ 45 years	42	31 (73.8)	16 (38.1)	5 (11.9)
> 45 years	118	82 (69.5)	33 (28)	9 (7.6)
Occupation				
Working	12	10 (83.3)	5 (41.7)	3 (25)
Housewife	148	103 (69.6)	44 (29.7)	11 (7.4)
Education				
Illiterate, incomplete primary school	99	71 (71.7)	24 (24.2)*	5 (5.1)*
Literate	61	42 (68.9)	25 (41)	9 (14.8)
Diabetes mellitus				
Type II	151	106 (70.2)	45 (29.8)	13 (8.6)
Type I	9	7 (77.8)	4 (44.4)	1 (11.1)
Duration of diabetes mellitus				
≤ 7.5 years	81	60 (74.1)	31 (38.3)*	9 (11.1)
> 7.5 years	79	53 (67.1)	18 (22.8)	5 (6.3)
Treatment				
Insulin	24	17 (70.8)	9 (37.5)	3 (12.5)
Oral hypoglycemic drug or combination therapy	136	96 (70.6)	40 (29.4)	11 (8.1)
Fasting blood sugar				
< 200 mg/dL	115	80 (69.6)	29 (25.2)*	7 (6.1)
≥ 200 mg/dL	45	33 (73.3)	20 (44.4)	7 (15.6)
Glycosylated hemoglobin				
$< 7\%$	27	20 (74.1)	9 (33.3)	2 (7.4)
$\geq 7\%$	113	83 (73.5)	34 (30.1)	8 (7.1)
History of allergy				
Yes	34	23 (67.6)	4 (11.8)*	3 (8.8)
No	126	90 (71.4)	45 (35.7)	11 (8.7)
Genital hygiene				
Satisfactory	131	93 (71)	38 (29)	13 (9.9)
Moderate or unsatisfactory	29	20 (69)	11 (37.9)	1 (3.4)
Sexual relationship				
Yes	138	102 (73.9)*	37 (26.8)*	13 (9.4)
No	22	11 (50)	12 (54.5)	1 (4.5)

* $p \leq 0.05$ by Fisher's exact test.

The Figure shows the relationship between fasting blood sugar and prevalence of vaginitis and positive culture. Clinical vaginitis and *Candida* vaginitis were positive in 71% (113/160) and 12.5% (20/160) of the patients, respectively.

In total, microscopic findings for *Candida* were positive in 12 patients, of whom two had *Candida* vaginitis. There were no significant statistical differences between them ($p=0.648$). Vaginal culture was positive for *Candida* in two patients who had positive smear for *Candida* ($p=0.000$). The prevalence of *Candida* vaginitis together with positive culture was 2.6% (4/160). After including the 10 patients with positive *Candida* culture together with other clinical vaginitis, overall prevalence of *Candida* vaginitis based on culture was 8.8% (14/160) (Table 2). Genital hygiene (cleanliness, evacuation of the bladder after intercourse, and drying the genital region after intercourse) was satisfactory, moderate and poor in 82%, 17% and 1% of the patients, respectively (Table 1).

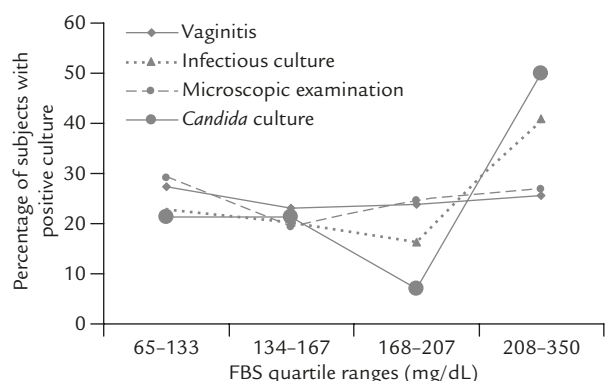


Figure. Relationship between fasting blood sugar (FBS) quartile ranges and percentage of subjects with vaginitis, microscopic findings of *Candida*, and positive vaginal culture for *Candida* species.

Discussion

In the present study, we did not find a significant statistical difference or relationship between positive vaginal *Candida* culture and type of diabetes mellitus, age, glycosylated hemoglobin, duration of diabetes mellitus, history of allergy, occupation, genital hygiene and vaginal intercourse. Diabetes mellitus has long been considered as one of the factors causing *Candida* vaginitis [10,11]. Different studies showed that symptomatic infection is more common in women with diabetes than in the normal population [10,11]. The prevalence ranged from around 7% to more than 50% [12-14], and most of which was attributed to *Candida albicans* [15,16]. In our study, the prevalences of *Candida* vaginitis based on clinical findings and culture were 12.5% and 8.8%, respectively. Culture of vaginal discharge revealed that the *Candida* group was responsible for 2.6% and 8.8% of *Candida* vaginitis and total vaginitis, respectively. In other words, *Candida* was shown after culture of vaginal discharge from patients who had colonization of *Candida* but did not have *Candida* vaginitis and *Candida* on microscopic examination (Table 2). Nonetheless, during the last decade, there have been reports on increasing non-*albicans* species [17]. Two specialized clinics reported that the prevalence of vulvovaginitis caused by non-*albicans* species is around 10-20%, with *Candida glabrata* dominating [18,19]. Sobel et al [17] stated that the probable causes of higher non-*albicans* species: the short duration of use for oral or local anti-*Candida* regimens; widespread use of over-the-counter antifungal agents, most of which are used incorrectly or inadequately; and the prolonged use of antifungal compounds for the prevention of recurrent vulvovaginitis, which further intensifies the problem.

There is the basic problem of vulvovaginitis in women with uncontrolled blood glucose levels. The control of

Table 2. Frequency distribution of culture for *Candida* from vaginal discharge based on presence of vaginitis and microscopic examination

Variable	Positive <i>Candida</i> culture, n (%)	Negative <i>Candida</i> culture, n (%)	Total, n (%)	p
Clinical <i>Candida</i> vaginitis with positive smear for <i>Candida</i>	2 (100)	0 (0)	2 (1.3)	0.007
Clinical <i>Candida</i> vaginitis with negative smear for <i>Candida</i>	2 (11.1)	16 (88.9)	18 (11.3)	0.660
Negative clinical <i>Candida</i> vaginitis with positive smear for <i>Candida</i>	5 (50)	5 (50)	10 (6.3)	0.000
Negative clinical <i>Candida</i> vaginitis with negative smear for <i>Candida</i>	5 (3.8)	125 (96.2)	130 (81.3)	0.000

blood glucose levels and a suitable antifungal therapy play an important role in controlling vaginal *Candida* infection in diabetic women [12]. In a study of 241 diabetic women, a significant statistical relationship existed between overall prevalence of vaginal infections (bacterial and fungal) and mean blood glucose level [20]. Also, it was suggested that glucose levels be maintained below 200 mg/dL to avoid dehydration, caloric loss and glycosuria and to reduce the risk of infection [21]. We also found a significant statistical difference between mean fasting blood sugar and infectious culture of vaginal discharge ($p=0.016$) (Table 1 and Figure). We did not find a significant statistical difference between glycosylated hemoglobin and infectious vaginitis, because acute infections such as vaginitis often occur during the hyperglycemic state, but glycosylated hemoglobin reflects the mean blood glucose level over the previous 3 months.

Similar to the study by Mas Martin [22], we also found that most of the patients with positive vaginal *Candida* culture (64%) were older than 45 years. Regarding the high prevalence of *Candida* vaginitis in reproductive ages [18,23] and our lack of knowledge about the prevalence of this condition in non-diabetic women with similar age groups (16–75 years), it is suggested that further evaluation be conducted to determine the cause. In any case, the incidence of symptomatic infection is high among reproductive ages (18–44 years) [24]. Although it was reported that allergic rhinitis and recurrent *Candida* vaginitis were present concurrently in 70% of patients [8], we did not find any relationship between *Candida* or non-*Candida* vaginitis and past history of allergy (sinusitis, rhinitis or atopic dermatitis).

According to our results, there was significant statistical difference between educational level and infectious or positive vaginal *Candida* culture. Based on previous studies [25–28], it is possible that educated women have knowledge about vaginal conditions or have had past experience of vaginal symptoms with or without a gynecologic examination, resulting in their self-diagnosis or self-treatment. Other factors involved in the pathogenesis of *Candida* vulvovaginitis include lifestyle factors. Although vulvovaginal candidiasis is more frequent among sexually active women (during the second decade of life) [24], it is not considered as a sexually transmitted disease [17]. *Candida* accounts for 20–50% of the normal vaginal flora of asymptomatic healthy women [29], and *Candida* vaginitis can even occur in single women. Naturally, *Candida* is transmitted through vaginal sexual intercourse, as well as other modes of sexual contact [19,30].

There is controversy about the frequency of sexual intercourse as a risk factor of vaginitis [19,24]. However,

some studies showed that oral sex increases the incidence of vulvovaginal candidiasis [24,31,32] and that vaginal intercourse alone cannot change the *Candida* colonization rates in the vagina [33].

To conclude, our study showed that fungi were not the cause of infection in more than 50% of the samples examined in the laboratory. On the other hand, definite diagnosis would be defined by positive culture. So, antifungal therapy should be withdrawn in patients with positive culture for vaginitis, with or without presenting signs of *Candida* vaginitis, especially in those with risk factors such as diabetes mellitus. It is important, because less attention to that may lead to vulvovaginitis [34–38]. We suggest the use of microscopic examination plus culture of vaginal discharge to diagnose vulvovaginal candidiasis, especially in hyperglycemic women. Considering the various factors involved in *Candida* vaginitis, such as oral contraceptive pill, synthetic underwear and our study limitations, our results would have been more reliable if the study had been performed on a larger scale and for a longer duration.

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