

The Epidemiology of *Candida* Species Isolated From Urinary Tract Infections

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Abstract

Background: *Candida* spp. are members of a genus, including closely related fungal species that cause a variety of infections.

Objectives: The aim of this study was the isolation of various *Candida* species from vulvovaginitis and urethra of patients in Neyshabur, Northeast Iran from 2013 to 2015.

Methods: This descriptive-analytical and cross-sectional study was performed to identify *Candida* spp. causing vulvovaginitis and Urinary Tract Infection (UTI) at a referral laboratory in Neyshabur district, Khorasan Razavi Province. A total of 451 vaginal and mid-stream urine samples were collected. Ten micro-liters of each specimen was cultured on CHROM agar plates and then incubated at 37°C for 24 to 48 hours, aerobically. *Candida* species were identified based on colony morphology, germ tube production and micro-morphology on corn meal agar including 1% Tween 80.

Results: The mean age of the patients was 34.7 ± 16.3 . *Candida albicans* was the predominant species isolated. Moreover, age groups of 21 to 30 and 0 to 1 years were the most and the least infected individuals. Moreover, *Candida* spp. were significantly more common in females compared to males (P value < 0.001). It was demonstrated that the prevalence of *C. albicans* had significantly declined from 2013-2014 to 2015. Furthermore, the prevalence of *C. tropicalis* was significantly higher in 2014 compared to 2013 and 2015. Moreover, all the species had a colony count of $> 10^3$.

Conclusions: In this study, *C. albicans* was the most common species isolated from patients with vulvovaginitis and UTI, and significantly more common amongst females compared to males. The prevalence of *candida* spp. had significantly declined from 2013 to 2015. Moreover, the *candida* spp. counts were mostly higher than 10^3 cfu/mL.

Keywords: *Candida* Species, Urinary Tract Infections, Neyshabur, Iran

1. Background

Candida spp. are members of a genus, including closely related fungal species, such as *Candida albicans* (*C. albicans*), *C. tropicalis* and *C. parapsilosis*, and in addition, distantly related organisms including *C. glabrata* and *C. krusei* (1, 2). *Candida* spp. are among common causative agents of nosocomial infections in the United States, Europe and other parts of the world (3). *Candida albicans* remains the predominant species in related infections, although recent studies suggest an increase in the proportion of species other than *C. albicans*, such as *C. glabrata*, *C. tropicalis*, *C. parapsilosis* and *C. krusei* (4, 5). *Candida* spp. commonly colonize the gut, oral and vaginal cavity

in healthy individuals. However, they are also capable of causing disease under circumstances that prosper their overgrowth and damage of the host (6). The range of diseases caused by the species varies from superficial and benign infections of the mucosae, such as oropharyngeal or vulvovaginal candidiasis, to severe life-threatening conditions of disseminated or invasive candidiasis; especially in immune-compromised patients (7-10). The most important factors predisposing individuals to mucosal related infections include Human Immunodeficiency Virus (HIV) infection, diabetes, antibiotic consumption and use of immunosuppressive drugs and extremes of age (11-13). Vulvovaginal candidiasis is common in certain conditions, even in otherwise healthy females (14). Risk factors for UTIs in

clude female gender, age of 65 years or older, deficiency of immune system, and urinary catheters (15). Although candiduria is often associated with a benign outcome (16), several large studies of hospitalized patients have demonstrated decreased survival of patients with candiduria in comparison with respective control populations (17, 18). Candiduria leads to systemic infection or candidemia only in 0 - 8% of the cases (19-21). Therefore, it remains unclear if candiduria leads directly to mortality or alternatively merely constitutes a surrogate marker.

2. Objectives

The aim of this study was the assessment of prevalence of candiduria and vulvovaginitis candidiasis among patients attending a referral laboratory in Neyshabur during 2013 - 2015.

3. Methods

3.1. Patients and Collection of Fungal Species

This cross-sectional epidemiologic study was carried out in Neyshabur and countryside rural areas between 2013 and 2015 to determine the prevalence of candiduria in Neyshabur district. A total of 421 vulvovaginitis samples were collected in this study. Patients of all ages, all ethnicities and from both rural and urban areas were included. Patients from other cities were excluded. Moreover, *Candida* spp. from other infection sites other than UTI were excluded.

Samples were collected from patients complaining of urinary tract pains, dysuria or discharge and pus secretions.

3.2. Identification Procedures

Briefly, 10 μ L of each un-centrifuged sample was cultured on CHROM agar plates and incubated at 37°C for 24 to 48 hours, aerobically. *Candida* species were identified based on colony morphology on CHROM agar (CHROM agar Candida®, France), germ tube production and micro-morphology on corn meal agar including 1% Tween 80.

The materials and methods were tested for quality and confirmation was achieved with the following approaches: the micro tubes had been sterile, samplers had been calibrated, the CHROM agar medium was prepared from a valid corporation, and the culture of samples was conducted under sterile conditions and using 70% ethanol for disinfection. Furthermore, a valid microscope was employed for morphology diagnosis.

Support for this study was obtained from the research and technology deputy of ACECR, Mashhad Branch.

Several variables were assessed such as age, gender, years and months and living in rural or urban places. These criteria were considered in some previous published studies found in our literature search (22-24). However, some of variables may not specifically or certainly be related to the predisposition of candiduria.

3.3. Data Analysis

Data were analyzed with the SPSS software version 20 (IBM SPSS statistics for windows, version 20, Armonk, NY, IBM Corp.), using the chi-square and one-way analysis of variance (ANOVA) tests. P values < 0.05 were considered statistically significant. T- and F-tests were employed when needed (between two groups or amongst more, respectively).

3.4. Ethical Approval

This work was supported by ACECR and ethical approval was provided by this center.

The patients provided consent for this study, and no animal model was examined here.

4. Results

The mean age of the patients was 34.7 ± 16.3 . From Table 1 and Figure 1, it is obvious that *C. albicans* was the predominant species isolated. Moreover, age groups of 21 to 30 and 0 to 1 years were the most and the least infected individuals. Moreover, *Candida* spp. were significantly more common in female than male patients (P value < 0.001, Table 2).

It was demonstrated that the prevalence of *C. albicans* was significantly declined from 2013-2014 to 2015. Furthermore, the prevalence of *C. tropicalis* was significantly higher in 2014 compared to 2013 and 2015 (Table 3 and Figure 2). Fifteen patients showed mixed infection of *C. albicans*, *E. coli* and *Enterobacter aerogenes* isolates. Moreover, all species had a colony count of $> 10^3$ (Table 4).

5. Discussion

To the best of our knowledge, this was the first study assessing the prevalence of *Candida* spp. in patients from Neyshabur, North-east of Iran. In the current study, the mean age of patients was 34.7 ± 16.3 . From Table 1 and Figure 1, it is obvious that *C. albicans* was the predominant species isolated. This result is similar to a study from south of Iran, in which *C. albicans* was predominant (48%) followed by *C. krusei* (16.1%), *C. glabrata* (13.5%), *C. kefyr* (7.4%), *C. parapsilosis* (4.8%), *C. tropicalis* (1.7%) and other species (8.5%) (25). Moreover, age groups of 21 to 30 and 0 to 1 years

Table 1. The Prevalence of *Candida* spp. Among Various Age Groups

	<i>C. albicans</i>	<i>C. glabrata</i>	<i>C. krusei</i>	<i>C. spp.</i>	<i>C. tropicalis</i>	Total	P Value
Age							
0 -10	3	0	0	0	0	3	0.12
11 -20	33	4	1	0	6	44	0.001
21 -30	147	8	4	2	17	178	0.001
31 -40	75	5	1	3	8	92	< 0.001
41 -50	21	3	1	1	8	34	0.033
51 -60	22	2	2	0	9	35	0.012
> 60	25	1	3	0	6	35	0.003
Total	326 (77.4)	23 (5.46)	12 (2.85)	6 (1.42)	54 (12.8)	421 (100)	

Table 2. The *Candida* spp. Distribution Between Male and Female Patients

	<i>C. albicans</i>	<i>C. glabrata</i>	<i>C. krusei</i>	<i>C. spp.</i>	<i>C. tropicalis</i>	Odds ratio	Total	P value
Female	321	23	12	6	51	4.46	413	< 0.0001
Male	5	0	0	0	3	1.33	8	
Total	326 (77.4)	23 (5.46)	12 (2.85)	6 (1.42)	54 (12.8)		421 (100)	

Table 3. The Incidence of *Candida* spp. According to Year

Year	<i>C. albicans</i>	<i>C. glabrata</i>	<i>C. krusei</i>	<i>Candida spp.</i>	<i>C. tropicalis</i>	Total
2013	138	4	2	2	4	150
2014	174	15	8	3	47	247
2015	14	4	2	1	3	24
P value	< 0.001	0.011	0.276	0.412	0.0012	0.044
Total	326 (77.4)	23 (5.46)	12 (2.85)	6 (1.42)	54 (12.8)	421 (100)

Table 4. The Colony Counts of *Candida* spp. and the Prevalence in Each Count

Colony Count (CFU)	< 1000	1001 - 5000	5001 - 10000	> 10000	Total (%)
<i>C. albicans</i>	59	39	79	149	326 (77.4)
<i>C. glabrata</i>	2	9	1	11	23 (5.46)
<i>C. krusei</i>	2	3	0	7	12 (2.85)
<i>C.spp.</i>	1	0	0	5	6 (1.42)
<i>C. tropicalis</i>	9	1	18	26	54 (12.8)
Total (%)	73 (17.3)	52 (12.4)	98 (23.3)	198 (47)	421 (100)

were the most and the least infected individuals. One of reasons for more urethral infection among young adults compared to children and other ages, may be because of higher sexual activities. Moreover, *Candida* spp. exhibited significantly higher rates amongst female than male patients (P value < 0.001), indicating the greater vulner-

ability of females to candida UTI. In this study, *C. albicans* was the most common species (77.4%) followed by *C. tropicalis* (12.8%), *C. glabrata* (5.46%), *C. krusei* (2.85%) and other *Candida* spp. (1.42%) remaining unspecified. In agreement with our results, a study by Shokohi showed that *C. albicans* was the predominant species (77.5%), followed by *C.*

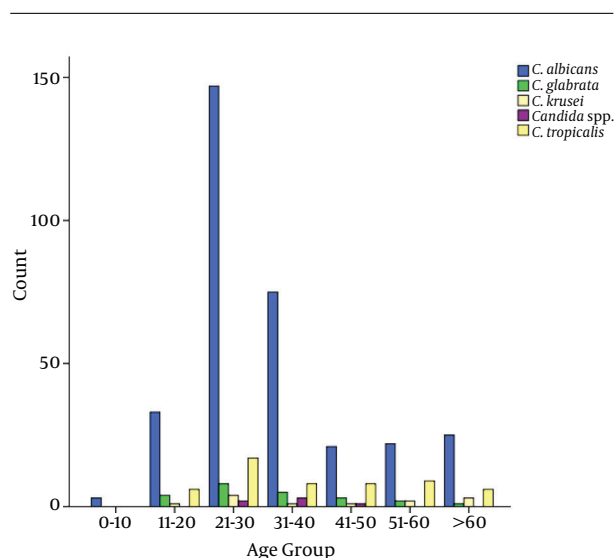


Figure 1. The Schematic Representation of Age Groups Infected With *Candida* spp.

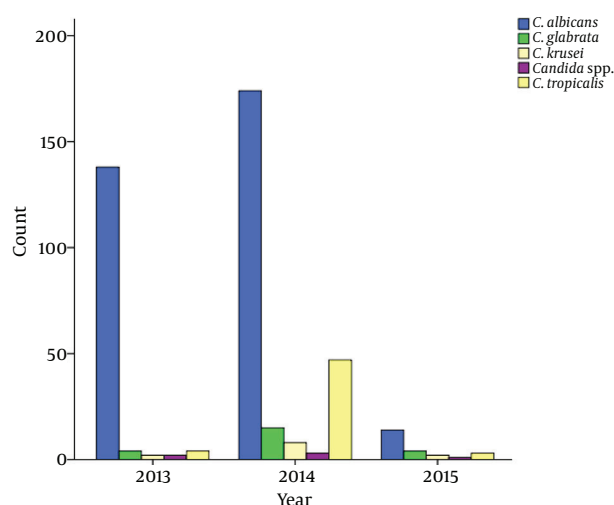


Figure 2. The Frequency of *Candida* spp. According to Year

glabrata (15%), *C. tropicalis* (5%) and *C. krusei* (2.5%) by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) (26). In another study by Zarei Mahmoudabadi, the prevalence of *Candida* spp. among 300 females was determined as 49%. On the other hand, recurrent and acute vaginal candidiasis was 48.3% and 51.7%, respectively. In addition, *C. albicans* was the most prevalent species among the isolates followed by *C. glabrata*, *C. dubliniensis* and other *Candida* species (27). Rad's study demonstrated that *C. albicans* was the most common (67%) species amongst single and mixed infections and other

identified species included: *C. glabrata* (18.3%) followed by *C. tropicalis* (6.8%), *C. krusei* (5.8%), *C. parapsilosis* (1.6%) and *C. guilliermondii* (0.5%) (28). These studies revealed that *C. albicans* is the most common candida in vulvovaginitis. In another study, it was confirmed that *C. albicans* and *C. glabrata* were the predominant species isolated from the specimens. However, the difference amongst previous studies and the present study includes epidemiological differences, different years on which the study was conducted, different sample sizes and sources of infections, ages and gender of patients.

The mixed infection of *C. albicans* and *C. glabrata* was demonstrated among 29 patients, while mixed infection of *C. albicans*, *Escherichia coli* and *Enterobacter aerogenes* isolates was observed among 15 patients. In a study by Mohammadi, a mix of *C. glabrata* and *C. albicans* was the most usual mixed infection from a total of 855 yeast strains isolated from different clinical specimens (29).

It was demonstrated that the prevalence of *C. albicans* has significantly declined from 2013-2014 to 2015. Furthermore, the prevalence of *C. tropicalis* was significantly higher in 2014 compared to 2013 and 2015. Moreover, all the species had a colony count of $> 10^3$. The weak points of the current study were lack of molecular method for the identification of species, narrow area of study, lack of antibiotic susceptibility test of species, and vagueness in the education level and economic status of patients. The strong points include the relatively high number of isolates collected from the study area for three years.

In this study, the most common mixed infection was the combination of *C. albicans* and *C. glabrata*. Individuals, who were sexually active and those with urogenital sex were more likely to have recurrent vulvovaginal and urethral candidiasis.

5.1. Conclusion

In this study, *C. albicans* was the most common species isolated from vulvovaginitis and urethral infection. The prevalence of *Candida* spp. was significantly declined from 2013 to 2015. Moreover, the *Candida* spp. counts were mostly higher than 10^3 cfu/mL. The mixed infection of *C. albicans*, *C. glabrata*, *Escherichia coli* and *E. aerogenes* was observed among several patients.

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Footnotes

Authors' Contribution: Mohammad Salehi, Abdolmajid Ghasemian and Seyyed Khalil Shokouhi Mostafavi performed the study and managed the manuscript preparation; Farshad Nojoomi and Hassan Rajabi Vardanjani were the advisors of this research and performed the data analysis.

Conflict of Interest: The authors declare no conflict of interest for the study.

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