Research Article

Clinical Characteristics of Turkish Women with Candida krusei Vaginitis and Antifungal Susceptibility of the C. krusei Isolates

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Received 30 July 2013; Accepted 4 November 2013

Academic Editor: Harold Wiesenfeld

1. Introduction

Vulvovaginal candidiasis (VVC) is a common illness attributed to an overgrowth of Candida species, and it is estimated that 75% of all women will experience an episode of VVC in their lifetimes. C. albicans accounts for 80–95% of all episodes of VVC worldwide [1, 2]. The prevalence of VVC due to non-C. albicans Candida species previously ranged from 5 to 20%; however, the number of reported cases has increased sharply over the last two decades, particularly for cases of C. glabrata [3, 4]. Therefore, the possibility of antifungal resistant strains of non-C. albicans Candida species in Candida vaginitis should be considered in clinics. The emergence of resistance may be attributed to the following factors (i) the widespread use of over-the-counter (OTC) medications; (ii) long-term use of suppressive azoles; and (iii) the frequent use of courses of antifungal medications [1, 3] or (iv) the increase use of vaginal cultures for reliable diagnoses [2, 5]. There is no evidence to suggest the followings: (i) certain women may be more susceptible to infection by particular Candida species over other species, or (ii) there are epidemiologic factors that may predispose women to acute VVC (AVVC) versus recurrent VVC (RVVC) [1, 2].

VVC is also, albeit infrequently, caused by C. parapsilosis, C. tropicalis, and C. krusei [1, 6, 7]. The decreased susceptibility of bloodstream C. krusei isolates to amphotericin B and 5-flucytosine as determined using the broth microdilution method is well documented [8]. However, in vitro susceptibility testing has not been used to evaluate the clinical response of C. krusei vaginitis [9]. In addition, little is known about vaginal C. krusei infections because they are relatively rare. However, C. krusei is known to
be inherently resistant to one of the most commonly used antifungal drugs, fluconazole. The signs and symptoms of \textit{C. krusei} vaginitis appear to be indistinguishable from the signs and symptoms of VVC cases caused by other \textit{Candida} species [6, 10]. Although rare, \textit{C. krusei} is an intractable cause of RVVC. Furthermore, most institutions have had limited experience with \textit{C. krusei} vaginitis [6]. Thus, the present study aims to fill this gap in the literature. Here, we retrospectively analyzed the epidemiological characteristics of 28 vaginal \textit{C. krusei} isolates, including host and risk factors. In addition, we investigated the antifungal susceptibility profiles of these isolates to 10 antifungal drugs to determine the most appropriate therapeutic choice(s) in women with \textit{C. krusei} vaginitis.

2. Materials and Methods

2.1. Vaginal \textit{C. krusei} Isolates. We examined 1,543 vaginal samples from unrelated women, of which 560 (36.3%) were culture-positive and 983 (63.7%) were culture-negative for \textit{Candida} yeasts, and the medical records of these cases were reviewed. Among the 560 vaginal yeast isolates, \textit{C. albicans} was the most common species and identified in 242 (43.2%) patients, followed by \textit{C. glabrata} in 155 (27.7%), \textit{C. krusei} in 28 (5.0%), \textit{C. kefyr} in 20 (3.6%), and in 115 (20.5%) representing several species of \textit{Candida}. Women who had \textit{C. krusei} in their vagina were included in the study. The definitions of the clinical presentations of VVC for each group were as follows: AVVC (group 1), currently asymptomatic women with initial or sporadic episodes of symptomatic vaginitis, that is, occurring fewer than four times per year (\(n = 8\)); RVVC (group 2), symptomatic patients with a history of four or more clinical episodes of VVC per year (\(n = 13\)) and controls (group 3), women who incidentally carried a normal level of \textit{C. krusei} in their vaginal culture without vaginitis, who were completely asymptomatic and had no history of RVVC (\(n = 7\)). The control group included a mixed group of asymptomatic women who had no history of RVVC and women who had positive cultures. All participants took part in a short interview, which included questions regarding lifestyle and medical, gynecological, and sexual history. This study was reviewed and approved by the Institutional Review Board at the University of Çukurova, Adana, Turkey. The Declaration of Helsinki protocols were followed, and the patients provided written informed consent.

2.2. Identification of \textit{C. krusei}. The \textit{C. krusei} isolates were recovered on CHROMagar Candida (Becton Dickinson, Heidelberg, Germany) and appeared as dull, flat, light mauve to mauve, and colonies with a whitish border. The criteria for the identification of \textit{C. krusei} were the absence of germ tube production in human serum at 37°C at 2 hours, the production of abundant pseudohyphae with some moderate branching on cornmeal-Tween 80 agar (Difco, Detroit, MI, USA), and weak or absent urease activity. These isolates were verified by their assimilation patterns using the API 20C AUX method (bioMérieux, Marcy l’Étoile, France) [11]. \textit{C. krusei} ATCC 6258 was used as a positive control.

2.3. Antifungal Susceptibility Testing. Antifungal testing was conducted at the Department of Microbiology, Faculty of Medicine, Gazi University, Ankara, using a broth microdilution method and according to the guidelines of the M27-A3 document of the Clinical and Laboratory Standards Institute (CLSI). Before testing, each isolate was subcultured on Sabouraud glucose agar (SGA; Merck, Darmstadt, Germany) to ensure purity and viability. The interpretation of antifungal susceptibility was guided by criteria derived from the CLSI’s M27-A3 protocol [12]. The following antifungal agents were tested: amphotericin B (0.03–16 \(\mu\)g/mL), 5-flucytosine (0.06–64 \(\mu\)g/mL), caspofungin (0.03–16 \(\mu\)g/mL), fluconazole (0.12–128 \(\mu\)g/mL), itraconazole (0.03–16 \(\mu\)g/mL), voriconazole (0.008–16 \(\mu\)g/mL), econazole (0.007–8 \(\mu\)g/mL), ketoconazole (0.007–8 \(\mu\)g/mL), miconazole (0.007–8 \(\mu\)g/mL), and sulconazole (0.03–16 \(\mu\)g/mL).

The minimal inhibitory concentrations (MICs) were determined for each antifungal agent and used to classify the susceptibility of the isolates as follows: (i) amphotericin B, MIC \(\leq 1 \text{ (} \mu\)g/mL), susceptible (S); (ii) 5-flucytosine, MIC \(\leq 4 \text{ (} \mu\)g/mL) S, MIC between 8 and 16 (\(\mu\)g/mL) intermediate (I), MIC \(\geq 32 \text{ (} \mu\)g/mL) resistant (R); (iii) caspofungin, MIC \(\geq 2 \text{ (} \mu\)g/mL) R; (iv) fluconazole, MIC \(\leq 8 \text{ (} \mu\)g/mL) S, MIC between 16 and 32 (\(\mu\)g/mL) susceptible dose dependent (S- DD), MIC \(\geq 64 \text{ (} \mu\)g/mL) R; (v) itraconazole, MIC \(\leq 0.125 \text{ (} \mu\)g/mL) S, MIC between 0.25 and 0.5 (\(\mu\)g/mL) S-DD, MIC \(\geq 1 \text{ (} \mu\)g/mL) R; (vi) voriconazole, \(\leq 1 \text{ (} \mu\)g/mL) S, MIC = 2 (\(\mu\)g/mL) S-DD, MIC \(\geq 4 \text{ (} \mu\)g/mL) R; (vii) ketoconazole, MIC \(\geq 16 \text{ (} \mu\)g/mL) R; and (viii) miconazole, MIC \(\geq 4 \text{ (} \mu\)g/mL) R [12]. Currently, there are no published criteria for defining econazole and sulconazole susceptibility [13]. These results were expressed in terms of the MIC range and the MIC\(_{50}\), and MIC\(_{90}\) values for each antifungal agent. All \textit{C. krusei} isolates were declared resistant to fluconazole. \textit{C. krusei} ATCC 6258 and \textit{C. parapsilosis} ATCC 22019 were used as controls, as recommended by the CLSI [12, 14].

2.4. Statistical Analysis. Data were analyzed using IBM SPSS version 19. Continuous variables, such as age and body mass index, were first divided into bins: <30, 30–39, 40–49, and >50 years of age and <25 (under or normal weight) and >25 (overweight or obese) for body mass index. Then, all categorical variables were cross classified by \textit{C. krusei} infection or carrier status to descriptively summarize the association between the variables using the chi-squared test and to measure the degree of association using the odds ratio with a 95% confidence interval. For the multivariate analysis, logistic regression modeling of the binary data (\textit{C. krusei} infected, carrier, or neither) was used to determine the significant predictors of \textit{C. krusei} infection, after adjusting for other factors in the models. Factors with significance levels <0.30 were entered into the multivariate logistic model to determine the significant effect of each factor simultaneously on the prediction of \textit{C. krusei} infection. None of the other factors contributed significantly to the prediction of \textit{C. krusei} infection.
Table 1: Basic demographic characteristics of women with vaginal complaints in this study.

| Variables         | Present | Absent (%) | Total | P |
|-------------------|---------|------------|-------|---|
| **C. krusei n (%)** |         |            |       |   |
| **Variables**     |         |            |       |   |
| Education status  |         |            |       |   |
| Illiterate        | 4 (1.7) | 226 (98.3) | 230   |   |
| Primary school    | 14 (1.9)| 709 (98.1) | 723   | 0.96 |
| Secondary school  | 2 (1.7) | 119 (98.3) | 121   |   |
| High school       | 5 (1.5) | 338 (98.5) | 343   |   |
| College           | 3 (2.4) | 122 (97.6) | 125   |   |
| Marital status    |         |            |       |   |
| Single            | 0 (0.0) | 17 (100.0) | 17    | 0.77 |
| Married           | 26 (1.8)| 1,418 (98.2)| 1,444 |   |
| Widowed-Divorced  | 2 (2.5) | 79 (97.5)  | 81    |   |
| Tobacco use       |         |            |       |   |
| Yes               | 6 (1.8) | 328 (98.2) | 334   | 0.6 |
| No                | 22 (1.8)| 1,185 (98.2)| 1,207 |   |
| Alcohol use       |         |            |       |   |
| Yes               | 0 (0.0) | 35 (100.0) | 35    | 0.52 |
| No                | 28 (1.9)| 1,479 (98.1)| 1,507 |   |

Mean ± Standard Deviation

| Variable | Mean ± SD |
|----------|-----------|
| Age      | 40.3 ± 10.4 | 35.3 ± 10.8 | 35.4 ± 10.8 | 0.01 |
| Gravida  | 3.4 ± 1.9  | 2.9 ± 2.1   | 2.9 ± 2.0   | 0.2  |

3. Results

*C. krusei* isolates were recovered from non pregnant patients without diabetes mellitus (*n* = 9), pregnant patients (*n* = 6), diabetes mellitus patients (*n* = 6), and contraceptive user’s (*n* = 7) with no previous history of immunodeficiency who visited the Faculty of Medicine Department of Obstetrics and Gynecology at Çukurova University from 2009 until 2012. Of the *C. krusei* isolates, 24 (85.7%) were the only species on plates and four (14.3%) were part of mixed cultures, which were always included by *C. albicans*. In our group, 24 (85.7%) women were in premenopausal and four (14.3%) in postmenopausal period who had also exposed hormone replacement therapy. The mean age of the women was 40.3 ± 10.4 years (range, 21 to 59 years old).

The basic demographic and clinical characteristics of women with vaginal *C. krusei* isolates are presented in Tables 1 and 2. Perineal laceration is significantly higher (*P* = 0.006) in the *C. krusei* group compared with the non-*C. krusei* group (Table 2). As revealed by multivariate analysis, existence of perineal laceration (*P* = 0.009) and an age of over 50 years (*P* = 0.02) were significant predictors of *C. krusei* vaginitis or carrier status (Table 3).

The MIC results for the control strains of *C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019 were within the acceptable range. All the *C. krusei* isolates were susceptible to amphotericin B, caspofungin, ketoconazole, and miconazole, and 10 of the 28 isolates (35.7%) were defined as S-DD for 5-flucytosine. High MIC rates were observed for fluconazole, of which 42.9% of the isolates were S-DD and 57.1% were R. Remarkably, only 42.9% and 67.9% of the isolates were susceptible to itraconazole (six S-DD and 10 R) and voriconazole (four S-DD and five R), respectively. We also observed low MIC levels for econazole and sulconazole. The antifungal susceptibilities of *C. krusei* isolated from patients with AVVC and RVVC did not differ significantly from those isolated from the group of women without symptoms of vaginitis (*P* > 0.05; Table 4).

4. Discussion

To the best of our knowledge, this study is the largest series to exclusively investigate the prevalence of, host and risk factors for, and antifungal susceptibility of the minor isolate *C. krusei*. We also briefly summarized the baseline and demographic characteristics of women who had *C. krusei* present in their vaginal samples (Tables 1 and 2). Our data suggest that the prevalence of *C. krusei* is relatively high (5.0%) in this population, displayed no specific host preferences, and was most often associated with RVVC. Perineal laceration and increased age (>50 years) were significant predictors of *C. krusei* vaginitis (Tables 2 and 3). An important limitation of the present study is the lack of data regarding *in vivo* therapeutic drug choices and outcomes in *C. krusei* vaginitis. In addition, the number of women with *C. krusei* is very small, so, for some of the other factors we examined, the study may not have had sufficient power to detect a difference (Tables 1–3).

The presence of mixed cultures may affect the choice of treatment strategy. In our previous study, using chromogenic
Table 2: Basic clinical characteristics of women with vaginal complaints in the study.

| Variables                                      | Present       | Absent (%)   | Total     | \( p \) |
|------------------------------------------------|---------------|--------------|-----------|---------|
| Diabetes mellitus                              |               | C. krusei    |           |         |
| Absent                                         | 21 (1.7)      | 1,250 (98.3) | 1,271     | 0.21    |
| Present                                        | 7 (2.6)       | 265 (97.4)   | 272       |         |
| Hypothyroidism                                 |               | C. krusei    |           |         |
| Absent                                         | 26 (1.8)      | 1,452 (98.2) | 1,478     | 0.31    |
| Present                                        | 2 (3.2)       | 60 (96.8)    | 62        |         |
| Hyperthyroidism                                |               | C. krusei    |           |         |
| Absent                                         | 26 (1.7)      | 1,478 (98.3) | 1,504     | 0.15    |
| Present                                        | 2 (5.3)       | 36 (94.7)    | 38        |         |
| Other chronic diseases                         |               | C. krusei    |           |         |
| Absent                                         | 19 (1.7)      | 1,127 (98.3) | 1,146     | 0.28    |
| Present                                        | 9 (2.3)       | 387 (97.7)   | 396       |         |
| Medication other than antibiotics              |               | C. krusei    |           |         |
| Absent                                         | 22 (2.0)      | 1,056 (98.0) | 1,078     | 0.22    |
| Present                                        | 6 (1.3)       | 458 (98.7)   | 464       |         |
| Use of local steroid in the last 4 weeks       |               | C. krusei    |           |         |
| Absent                                         | 27 (1.8)      | 1,492 (98.2) | 1,519     | 0.35    |
| Present                                        | 1 (4.3)       | 22 (95.7)    | 23        |         |
| Use of systemic steroid in the last 4 weeks    |               | C. krusei    |           |         |
| Absent                                         | 28 (1.9)      | 1,482 (98.1) | 1,510     | 0.57    |
| Present                                        | 0 (0.0)       | 30 (100.0)   | 30        |         |
| Perineal laceration                            |               | C. krusei    |           |         |
| Absent                                         | 15 (1.3)      | 1,163 (98.7) | 1,178     | 0.006   |
| Present                                        | 13 (3.6)      | 351 (96.4)   | 364       |         |
| Contraception                                  |               | C. krusei    |           |         |
| None                                           | 9 (1.4)       | 637 (98.6)   | 646       |         |
| OC                                             | 1 (1.0)       | 103 (99.0)   | 104       |         |
| IUD                                            | 8 (2.9)       | 268 (97.1)   | 276       | 0.49    |
| Condom                                         | 4 (1.5)       | 258 (98.5)   | 262       |         |
| Others                                         | 6 (2.4)       | 248 (97.6)   | 254       |         |
| Personal allergic history                      |               | C. krusei    |           |         |
| Absent                                         | 24 (1.8)      | 1,316 (98.2) | 1,340     | 0.51    |
| Present                                        | 4 (2.0)       | 197 (98.0)   | 201       |         |
| History of sexual intercourse in the last 4 weeks|           | C. krusei    |           |         |
| Present                                        | 8 (2.8)       | 279 (97.2)   | 287       | 0.13    |
| Absent                                         | 20 (1.6)      | 1,235 (98.4) | 1,255     |         |
| Antibiotic use in the last 4 weeks             |               | C. krusei    |           |         |
| Absent                                         | 27 (2.1)      | 1,260 (97.9) | 1,287     | 0.07    |
| Present                                        | 1 (0.4)       | 254 (99.6)   | 255       |         |
| Body mass index                                |               | C. krusei    |           |         |
| \( \leq 19 \)                                  | 1 (2.3)       | 42 (97.7)    | 43        |         |
| 19–24                                          | 4 (1.1)       | 369 (98.9)   | 373       | 0.4     |
| 24–29                                          | 9 (1.6)       | 561 (98.4)   | 570       |         |
| \( > 29 \)                                     | 14 (2.5)      | 540 (97.5)   | 554       |         |

OC: oral contraceptive; IUD: intrauterine device.
In this investigation, amphotericin B, caspofungin, ketoconazole, and miconazole were observed to be active against all *C. krusei* isolates (Table 4). In contrast to the findings of Singh et al. [6], but in line with those of Richter et al. [16], itraconazole exhibited high S-DD and R rates, 35.7% and 21.4%, respectively. Although the new broad-spectrum oral antifungal voriconazole is rarely used in patients with VVC, we observed that 67.9% of the isolates were susceptible to voriconazole. Pfaller et al. [8] reported a higher rate, stating that 81.5% of 426 genital *C. krusei* isolates were susceptible to voriconazole using the CLSI M44-A disk diffusion method. In contrast to our findings, Lyon et al. [17] reported that fluconazole resistance rates were highly predictive of resistance to voriconazole. Although specific clinical cutoff points have not yet been assigned for econazole and sulconazole susceptibility, we observed low MIC values for both drugs. Nystatin suppositories and boric acid could be therapies of choice for *C. krusei* vaginitis [6].

This study is the largest to date to investigate the antifungal drug-resistance profile of *C. krusei* vaginal isolates and the epidemiologic risk factors of infection. In this investigation, perineal laceration and increasing age (>50 years) were important predictive factors for *C. krusei* vaginitis or carrier status (Table 3). This study also revealed that the topical imidazoles (ketoconazole and miconazole), which can be prescribed safely in routine practice, were effective against all *C. krusei* isolates. In addition, the vaginal *C. krusei* isolates were less susceptible to itraconazole (42.9%) and voriconazole (67.9%) than to other antifungal therapeutics. These findings may have implications for the *in vivo* therapeutic treatment of *C. krusei* vaginitis (Table 4). Thus, the identification of *C. krusei* in vaginal samples and *in vitro* antifungal testing will assist in the selection of appropriate antifungal agents and therapy duration. Future clinical trials to determine the *in vivo* efficacy of the current drugs for women with *C. krusei* vaginitis are required.

### Table 3: Analysis of predictive factors for *Candida krusei* infection using univariate and multivariate logistic analyses.

| Predictors                  | Univariate analysis | Multivariate analysis |
|-----------------------------|---------------------|-----------------------|
| Age                         | OR      | 95 CI         | OR    | 95 CI         |
| <30                         | 1.0     | —             | 1.2   | 0.8–1.6       |
| 30–39                       | 2.56    | 0.87–7.55     | 2.4   | 0.8–7.16      |
| 40–49                       | 2.48    | 0.75–8        | 2.7   | 0.79–9.3      |
| ≥50                         | 5.39    | 1.69–17.2     | 7.9   | 1.34–46.7     |
| Body mass index             | 1.72    | 0.65–4.57     | 1.28  | 0.46–3.57     |
| Diabetes mellitus           | 1.57    | 0.66–3.74     | 0.26  | 0.11          |
| Hyperthyroidism             | 3.2     | 0.72–13.8     | 3.92  | 0.84–18.3     |
| Medication other than antibiotics | 0.63 | 0.25–1.56     | 0.56  | 0.21–1.46     |
| Use of local steroid        | 2.5     | 0.32–19.1     | 3.11  | 0.38–26.2     |
| Perineal laceration         | 2.87    | 1.25–6.1      | 3.25  | 0.38–1.48     |
| Antibiotics (last 4-weeks)  | 0.18    | 0.025–1.3     | 0.19  | 0.03–1.48     |

### Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.
Table 4: Antifungal susceptibility of 28 vaginal *Candida krusei* isolates stratified according to clinical forms.

| Antifungals         | Acute VVC (*n* = 7) | Recurrent VVC (*n* = 13) | Control (*n* = 8) |
|---------------------|----------------------|---------------------------|------------------|
| **Amphotericin B (μg/mL)** |                      |                           |                  |
| MIC range           | 0.03–0.25            | 0.03–0.5                  | 0.06–0.5         |
| MIC<sub>50</sub>    | 0.03                 | 0.25                      | 0.25             |
| MIC<sub>90</sub>    | 0.25                 | 0.25                      | 0.25             |
| R<sub>, ≥2 μg/mL</sub> | n (%)                |                           |                  |
|                     | —                    | —                         | —                |
| **5-Flucytosine (μg/mL)** |                      |                           |                  |
| MIC range           | 0.125–8              | 0.125–8                   | 0.125–16         |
| MIC<sub>50</sub>    | 2                    | 2                         | 8                |
| MIC<sub>90</sub>    | 8                    | 8                         | 16               |
| R<sub>, ≥32 μg/mL</sub> | n (%)                |                           |                  |
|                     | —                    | —                         | —                |
| **Caspofungin (μg/mL)** |                      |                           |                  |
| MIC range           | 0.03–0.06            | 0.03–0.06                 | 0.03–0.06        |
| MIC<sub>50</sub>    | 0.03                 | 0.03                      | 0.03             |
| MIC<sub>90</sub>    | 0.06                 | 0.03                      | 0.06             |
| R<sub>, ≥2 μg/mL</sub> | n (%)                |                           |                  |
|                     | —                    | —                         | —                |
| **Fluconazole (μg/mL)** |                      |                           |                  |
| MIC range           | 16–128               | 16–128                    | 16–128           |
| MIC<sub>50</sub>    | 128                  | 64                        | 32               |
| MIC<sub>90</sub>    | 128                  | 128                       | 128              |
| R<sub>, ≥64 μg/mL</sub> | n (%)                |                           |                  |
|                     | 4                    | 9                         | 3                |
| **S-DD, 16–32 μg/mL** | n (%)                |                           |                  |
|                     | 3                    | 4                         | 5                |
| **Itraconazole (μg/mL)** |                      |                           |                  |
| MIC range           | 0.125–16             | 0.125–16                  | 0.125–8          |
| MIC<sub>50</sub>    | 0.25                 | 0.25                      | 0.125            |
| MIC<sub>90</sub>    | 4                    | 4                         | 2                |
| R<sub>, ≥1 μg/mL</sub> | n (%)                |                           |                  |
|                     | 3                    | 4                         | 3                |
| **Voriconazole (μg/mL)** |                      |                           |                  |
| MIC range           | 0.125–8              | 0.125–16                  | 0.25–8           |
| MIC<sub>50</sub>    | 1                    | 0.5                       | 0.5              |
| MIC<sub>90</sub>    | 4                    | 4                         | 2                |
| R<sub>, ≥4 μg/mL</sub> | n (%)                |                           |                  |
|                     | 2                    | 2                         | 1                |
| **Ketoconazole (μg/mL)** |                      |                           |                  |
| MIC range           | 0.125–8              | 0.25–8                    | 0.25–8           |
| MIC<sub>50</sub>    | 0.25                 | 4                         | 0.25             |
| MIC<sub>90</sub>    | 2                    | 8                         | 8                |
| R<sub>, ≥16 μg/mL</sub> | n (%)                |                           |                  |
|                     | —                    | —                         | —                |
| **Econazole (μg/mL)** |                      |                           |                  |
| MIC range           | 0.5–1                | 0.125–2                   | 0.5–1            |
| MIC<sub>50</sub>    | 1                    | 1                         | 1                |
| MIC<sub>90</sub>    | 1                    | 2                         | 1                |
| R<sub>, ND</sub>    | n (%)                |                           |                  |
|                     | —                    | —                         | —                |
### Table 4: Continued.

| Antifungals (μg/mL) | Acute VVC (n = 7) | Recurrent VVC (n = 13) | Control (n = 8) |
|---------------------|-------------------|------------------------|---------------|
|                     | MIC range         |                        |               |
| Miconazole (µg/mL)  | 0.25–0.5          | 0.06–1                 | 0.25–0.5      |
| MIC<sub>50</sub>    | 0.25              | 0.25                   | 0.25          |
| MIC<sub>90</sub>    | 0.5               | 1                      | 0.5           |
| R, ≥4 µg/mL n (%)  | —                 | —                      | —             |
| Sulconazole (µg/mL) |                   |                        |               |
| MIC range           | 1–4               | 0.06–4                 | 1–2           |
| MIC<sub>50</sub>    | 2                 | 1                      | 1             |
| MIC<sub>90</sub>    | 4                 | 4                      | 2             |
| R, ND n (%)         | —                 | —                      | —             |

VVC: vulvovaginal candidiasis; R: resistance; S-DD: susceptible dose dependent; ND: not determined. *All isolates were declared resistant to fluconazole.*

### Acknowledgments

Funding for this study was received from Çukurova University in Adana, Turkey, and Gazi University in Ankara, Turkey.

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