SHORT COMMUNICATION

Determination of antimicotic susceptibility pattern of *Candida* species isolated from patients with symptomatic candiduria

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Background: The present study was conducted to determine antimicotic susceptibility of *Candida* species (sp.) from patients with symptomatic candiduria. **Materials and Methods:** Identification of *Candida* sp. and determination of efficacy of most routine antifungals were done using polymerase chain reaction-restriction fragment length polymorphism method and E-test, respectively. **Results:** The results from susceptibility test reveal that caspofungin and amphotericin B have high antifungal activity against both albicans (100% and 96%, respectively) and nonalbicans (95.11% and 72.72%, respectively) isolates. **Conclusion:** The present study suggests that caspofungin and amphotericin B have the excellent ability to eradicate both *Candida* groups that showed decreased susceptibility to other compounds.

Keywords: Antifungal drugs, *Candida* species, polymerase chain reaction-restriction fragment length polymorphism, symptomatic candiduria

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INTRODUCTION

Candiduria has been considered as a challenging condition for clinicians because of the complex relationship between its colonization and infection. The complication occurs during long-term hospitalization, especially in individuals who are admitted in the intensive care unit setting that may lead to changes in etiologic agent to nonalbicans *Candida* (NAC).[1] This pictorial variation has created a new and serious complication because a broad spectrum of NAC isolates are typically less susceptible to routine antimicotic.[2] Clinically, amphotericin B and fluconazole were prescribed as the superior choice for the treatment of candiduria.[3] On the other side, a serious concern remains due to the intrinsic resistance of *Candida glabrata* and *Candida krusei* isolates to fluconazole.[4]

In the present study, we aimed to determine the *in vitro* antifungal susceptibility profile of *Candida* sp. from patients with symptomatic candiduria against amphotericin B, fluconazole, itraconazole, voriconazole, and caspofungin.

MATERIALS AND METHODS

Subjects

The experimental study was conducted in 2017. The patients who were suspected of sepsis, candiduria,

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and the presence of pyuria were enrolled for this study. Therefore, 500 midstream of first-void urine and indwelling urinary catheter were collected.

Identification of *Candida* sp.

Identification of *Candida* sp. was performed based on direct examination, colony color, and yeast counts superior to 10^5 UFC/mL on CHROM Agar *Candida* medium (CHROM agar, France) at 35°C for 24 h.

The polymerase chain reaction-restriction fragment length polymorphism (RFLP) was performed based on the amplification of ITS1-5.8SrDNA-ITS2 region and *MspI* (Fermentas, USA) restriction enzyme. Restriction fragments were separated by 2% agarose gel electrophoresis.

Antimicotic susceptibility assay

The susceptibility of amphotericin B, fluconazole, itraconazole, voriconazole, and caspofungin was performed using RPMI 1640 agar-based E-test method (BioMeriéux, Sweden).[5] *Candida albicans* ATCC 24433 was used as the reference control.

RESULTS

Totally, 89 (17.8%) urine samples were positive for *Candida* species which collected from 43 (48.3%) male and 46 (51.6%) female individuals were positive for symptomatic candiduria. The mean age of participants in this study was 57.66 ± 22.30. Fever experience was recorded in 70.8% of patients while other clinical manifestations such as abdominal pain, renal pain, and dysuria were observed in 12.4%, 5.6%, and 6.7% of cases, respectively.

RFLP fingerprint analysis revealed that *C. albicans* (*n* = 56; 63%) is the predominant causative agent isolated from urine followed by *Candida tropicalis* (*n* = 24; 27%), *Candida parapsilosis* (5; 5.6%), *C. glabrata* (*n* = 2; 2.2%), and *C. krusei* (*n* = 2; 2.2%) [Figure 1].

The results from antimycotic susceptibility tests are presented in Table 1.

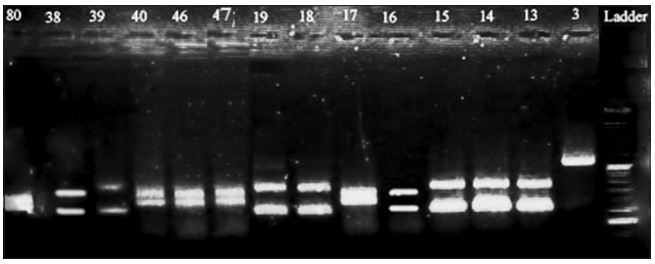

Figure 1: Polymerase chain reaction-restriction fragment length polymorphism fingerprint with MspI restriction enzyme: *Candida* albicans: 80, 40, 46, 47, 17; *Candida* tropicalis: 38, 39, 19, 18, 13, 14, 15; *Candida* parapsilosis: 3; *Candida* krusei: 16

Table 1: A head-to-head comparison of five antifungal susceptibilities profile in *Candida* sp.

Species (*n*)	Antifungals	E-test		
		S	I	R
Candida albicans (56)	AMB	96	0	4
	VCZ	92	8	0
	ICZ	77.82	16	6.8
	FCZ	90	10	0
	CAS	100	0	0
Candida tropicalis (24)	AMB	83.33	16.66	8.33
	VCZ	70.80	20	9.2
	ICZ	66.6	68.33	16.66
	FCZ	75	25	8.33
	CAS	95.11	0	5.89
Candida parapsilosis (5)	AMB	90	8	2
	VCZ	60	40	0
	ICZ	40	0	0
	FCZ	40	60	0
	CAS	100	0	0
Candida krusei (2)	AMB	100	0	0
	VCZ	100	0	0
	ICZ	0	100	0
	FCZ	0	60	40
	CAS	100	0	0
Candida glabrata (2)	AMB	100	0	0
	VCZ	100	0	0
	ICZ	0	50	50
	FCZ	0	0	100
	CAS	100	0	0

AMB=Amphotericin B; FCZ=Fluconazole; ICZ=Itraconazole; VCZ=Voriconazole; CAS=Caspofungin; S=Susceptible; I=Intermediate; R=Resistance

DISCUSSION

In line with previous studies regardless of asymptomatic and symptomatic candiduria,[6-8] the current results based on RFLP pattern revealed that *C. albicans* (63%) is still the predominant causative agent isolated from urine followed by *C. tropicalis* (27%), *C. parapsilosis* (5.6%), *C. glabrata,* and *C. krusei* (2.2%).

An overall look through the results from susceptibility test reveals that caspofungin and amphotericin B have high antimicotic activity against both albicans (100%–96%, respectively) and non albicans (95.11% and 72.72%, respectively) isolates. In line with other investigations,[8-11] the present finding suggests that caspofungin and amphotericin B are suitable alternatives in all cases of *Candida* sp. that showed resistance to azolic compounds.

It has been well established that *C. albicans* is intrinsically sensitive to a broad range of antimicotic classes and resistance must be acquired.[8-10] In concordance with this finding, results in this study show that *C. albicans* is largely susceptible to all antimicotic agents that were used here

except itraconazole. In practice, itraconazole is normally more effective than fluconazole, and it should be prescribed for cases with fluconazole-resistant isolates. Here, emerging resistant isolates were probably associated with previous exposure to fluconazole.

Regarding susceptibility results, decreased susceptibility to voriconazole was exclusively limited to *C. tropicalis*. In several studies, voriconazole-resistant *C. tropicalis* were clinically isolated.[12] In contrast with the present findings, recent investigations in candiuria indicated that no resistance was found among *C. tropicalis*.[8,10]

The rate of resistance to itraconazole varies between NAC isolates; here, the highest rate of resistance to itraconazole was found in *C. tropicalis and C. parapsilosis* species. The resistance to itraconazole has been reported in *C. tropicalis* and *C. glabrata* isolated from urine specimen.[1]

Similar to previous findings in the current investigation, *C. glabrata* and *C. krusei* showed the decreased sensitivity against fluconazole.[1,8] Interestingly, the high fluconazole resistance was determined for *C. tropicalis* and *C. parapsilosis*. Decreased fluconazole sensitivity to *C. tropicalis* was reported.[1,8,10,13] Since, multiple treatment guidelines recommend fluconazole as a first-line antifungal for candiduria emerging resistance to fluconazole in NAC has complicated treatment and is a warning for clinicians and public health authorities.

Finally, the present study suggests that caspofungin and amphotericin B have the excellent ability to eradicate both *Candida* groups that showed decreased susceptibility to other compounds. Taken together, widespread use of antimicotic, emerging new pathogens in addition to misidentification of fungal agents, may lead to poorer clinical outcomes and difficulty of treatment and is an alarm for clinician and public health authorities.

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Conflicts of interest

There are no conflicts of interest.

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