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Spectrum of Antimycotic Activity at Different Loci in Men against *Candida* Fungi

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Abstract

Fungal infections can pose a serious health threat. *Candida* fungi are the leading cause of fungal infections in hospitalized patients, significantly contributing to morbidity and mortality. This article presents the results of antifungal activity against *Candida* spp. in men (n = 85) undergoing to hospital or ambulatory treatment from January 1, 2024, to August 1, 2025. Antifungal susceptibility profiling assessed using the disk-diffusion method at various loci where *Candida* fungi detected. Susceptibility levels were assessed as susceptible (s), moderately susceptible (i), and resistant (r). The results obtained from the biological material revealed that in patients with *Candida* spp. the highest resistance was observed against fluconazole (selective susceptibility 17% (n = 8), resistance 49% (n = 23)). In addition, majority of fluconazole-resistant strains detected in sputum: 10.3% (n = 3) were selectively susceptible, while 48.3% (n = 14) were resistant. The most susceptible *Candida* species, nystatin (95.8%, n = 46) and clotrimazole (87.8%, n = 72), lack a systemic form, making sputum inaccessible. This fact should be considered when prescribing antifungal therapy.

Keywords: *Antifungals; Fluconazole; Susceptibility; Resistance; Men*

Introduction

Fungal infections can pose a serious health threat. Various forms of invasive candidiasis primarily affect immunosuppressed or critically ill patients. Mucocutaneous forms of candidiasis, such as oral and vulvovaginal candidiasis can occur in healthy individuals. Mucocutaneous forms of candidiasis are generally not life-threatening but can cause discomfort, recurrent infections, and complications, especially in patients with comorbidities such as diabetes mellitus or in patients receiving immunosuppressive therapy [1,2]. *Candida* species are the leading cause of fungal infections in hospitalized patients, significantly contributing to morbidity and mortality. Candidiasis caused by *Candida* species is an opportunistic infection that poses a significant health risk, exacerbated by the development of antifungal resistance. The pathogenicity of *Candida* spp. depends on the secretion of aspartic proteinase (Sap), as it is associated with adhesion, invasion, and tissue damage. Isolates of *C. tropicalis*, *C. krusei*, and *C. utilis* also produce phytase, while *C. tropicalis* produces esterases. Proteinase production is encoded by 10 genes known as type A serine proteases (SAPs). The expression of these genes influenced by environmental conditions, which typically results in a higher invasive potential of fungi. Nonpathogenic *Candida* spp. typically have fewer SAP genes, which not necessarily expressed in the genome. All *Candida* isolates adhere to abiotic surfaces and form biofilm on polystyrene, produce aspartic proteinase, and exhibit hemolytic activity, which are considered hallmarks of fungal virulence [1,2,4,5].

Exposure to subinhibitory concentrations of antifungal drugs promotes the development of resistant strains with increased SAP gene expression. In general, *Candida* spp. isolates resistant to antifungal drugs exhibit higher SAP secretion than susceptible isolates. *C. tropicalis* isolates showed resistance to azoles and susceptibility to amphotericin B, flucytosine, and caspofungin. *C. krusei* isolates were resistant to fluconazole, caspofungin, and itraconazole, with 42.8% resistance to flucytosine, in addition to susceptibility to voriconazole and amphotericin B. Fluconazole-resistant pathogens such as *Candida auris* and *Candida parapsilosis* pose a serious threat to public health worldwide. Invasive infections caused by *Candida* species have undergone significant epidemiological, pathophysiological, and clinical changes in recent decades, including a shift toward non-albicans species and an increase in infection rates from candidemia to a range of highly invasive and life-threatening clinical syndromes [1,4,5]. Recent taxonomic revisions have resulted in the reclassification of several *Candida* species, potentially creating confusion in clinical practice. Current treatment guidelines are limited in scope and insufficiently address emerging pathogens and new treatments [2,3]. Preventing the development of resistance is an urgent task aimed at improving treatment effectiveness and reducing healthcare costs.

Aim of the Study

The aim of this study was to determine the susceptibility of antifungal agents to *Candida* spp. at various loci in men.

Materials and Methods

Antifungal susceptibility profiles used as the object of observation. Susceptibility to antifungal agents was assessed using the disk diffusion method in hospitalized and outpatients (n = 85) treated between January 1, 2024, and August 1, 2025, in whom *Candida* spp. was detected at various loci. Susceptibility levels were assessed as sensitive (s), selectively(partially) sensitive (i), or resistant (r).

Results and Discussion

The sensitivity of *Candida* spp. studied in 85 patients at different sites: sputum (n = 52), pharynx (n = 22), wound surface (n = 2), external auditory canal (n = 5), urine (n = 2), tongue (n = 1), oral cavity (n = 1). The sensitivity of *Candida* spp. to fluconazole was 34% (n = 16), 17% (n = 8) were selectively sensitive, 49% (n = 23) were resistant.

Depending on the site: in sputum, 41.4% (n = 12) were sensitive, 10.3% (n = 3) were selectively sensitive, 48.3% (n = 14) were resistant; in the pharynx - 23.1% (n = 3) were sensitive, 15.4% (n = 2) were selectively sensitive, 61.5% (n = 8) were resistant; In the external auditory canal, 100% (n = 3) are selectively sensitive; on the surface of the tongue (n = 1) and the wound surface (n = 1), 100% are sensitive.

The sensitivity of *Candida* spp. to nystatin was 95.8% (n = 46), 4.2% (n = 2) were resistant. Depending on the locus: in sputum, 97.7% (n = 29) were sensitive, 3.3% (n = 1) were resistant; in the pharynx - 92.3% (n = 12) were sensitive, 7.7% (n = 1) were resistant; in the wound surface (n = 1), on the surface of the tongue (n = 1) and in the external auditory canal (n = 3) the sensitivity was 100%. The sensitivity of *Candida* spp. to clotrimazole was 87.8% (n = 72), 12.2% (n = 10) were resistant.

Depending on the locus: in sputum, 88% (n = 44) were sensitive, 12% (n = 6) were resistant; In the pharynx, 90.9% (n = 20) were sensitive and 9.1% (n = 2) were resistant; in the external auditory canal, 80% (n = 4) were sensitive and 20% (n = 1) were resistant; in urine, 50% (n = 1) were sensitive and 50% (n = 1) were resistant; in the wound surface (n = 2) and oral cavity (n = 1), sensitivity was 100%. The sensitivity of *Candida* spp. to amphotericin B was 72.7% (n = 8), and 27.3% (n = 3) were resistant. Depending on the locus: in sputum, 75% (n = 3) were sensitive and 25% (n = 1) were resistant; in the pharynx, 60% (n = 3) were sensitive and 40% (n = 2) were resistant; in the wound surface (n = 1) and external auditory canal (n = 1) the sensitivity was 100% (Table 1).

No.	Antimycotic drug	Patients (n)	Sensitivity (s)		Resistance (r)	
			n	%	n	%
1	Fluconazole	47	16	34	23	49
2	Nystatin	48	46	95,8	2	4,2
3	Clotrimazole	82	72	87,8	10	12,2
4	Amphotericin B	11	8	72,7	3	27,3

Table 1: *Indices of sensitivity and resistance of Candida spp. to antifungal drugs in men.*

We found selective susceptibility to fluconazole of 17% (n = 8). *Candida* spp. demonstrated the highest resistance to fluconazole (49% (n = 23)), while high susceptibility remained to three drugs (nystatin, clotrimazole, and amphotericin B). The highest susceptibility of *Candida* spp. was observed to nystatin (95.8% (n = 46)) and clotrimazole (87.8% (n = 72)); however, it is important to consider the lack of systemic action and the possibility of only topical administration of these drugs.

Conclusion

Analyzing the obtained results of the study of biological material from men treated in inpatient and outpatient settings from January 1, 2024, to August 1, 2025, it concluded that in patients with isolated *Candida* spp. As a causative agent or coinfection, the highest resistance was observed against fluconazole (selective susceptibility 17% (n = 8), resistance 49% (n = 23)). It noted that the majority of fluconazole-resistant strains were detected in sputum: 10.3% (n = 3) were selectively susceptible, while 48.3% (n = 14) were resistant. Patients with the highest sensitivity of *Candida* spp. to nystatin (95.8% (n = 46)) and clotrimazole (87.8% (n = 72)) lacked systemic drug delivery, making sputum an inaccessible targeting site. When prescribing antifungal therapy, it is necessary to consider the targeting site, susceptibility, and resistance of individual antifungal agents to *Candida* spp. to prevent the development of resistance in these fungi to antifungal drugs. For lesions accessible to topical formulations, it is rational to use existing topical antifungal agents (nystatin, clotrimazole), which will reduce the frequency of fluconazole use and prevent the development of resistance to this drug.

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