

## Studies Regarding Antifungal Resistance of *Candida* Species

ILIE Marina-Ionela<sup>1</sup>, RĂDUȚ Teodora<sup>1</sup>, ARSENE Andreea Letiția<sup>1</sup>

<sup>1</sup> “Carol Davila”, Bucharest University of Medicine and Pharmacy, Faculty of Pharmacy, (ROMANIA)  
Emails: marinaxilie@gmail.com, teodora.radut@gmail.com, microbiologiefarmaceutica@gmail.com

### Abstract

Immune imbalance, as a result of different pathologies, of certain physiological states or as a result of certain medicine administration, favors mycotic infection development, especially those determined by *Candida spp.* The purpose of this study was to test the sensitivity or resistance of *Candida* species from several pathologic products, to some antifungal medicines. The study included 180 patients hospitalized at Slatina Municipal Hospital, during March 2017-February 2018. Out of the patients, 69.44% were female and 30.56% were male. The following pathological products were used: vaginal secretion, wound secretion, spit and urine. The patients were distributed in 2 groups, based on the method used for testing the sensibility of the *Candida* species. Samples derived from the first group were processed with the Vitek device, testing the species' resistance to the following drugs: fluconazole, voriconazole, caspofungin, amphotericin B, flucytosine. For the second group, the fungigrama was performed manually, testing the species resistance to fluconazole, amphotericin B, nystatin, clotrimazole, intraconazole, ketoconazole, miconazole. For the two testing methods, the first group developed a sensitivity of 86.87% against fluconazole and 89.90% against amphotericin B, while for the second group, the sensitivity varied as follows: 29.63% against fluconazole and 74.07% against amphotericin B. The study results proved an important variability of *Candida* strains from different pathologic products against different antifungal medicines.

Keywords: *Candida*, antifungal medicines

### 1. Introduction

The predominant nosocomial fungal pathogens include *Candida spp.*, *Aspergillus spp.*, *Mucor spp.*, *Rhizopus spp.*, *Fusarium spp.*, and other molds, including *Scedosporium spp.*

Immune imbalance, as a result of different pathologies, of certain physiological states or as a result of certain medicine administration, favors mycotic infection development, especially those determined by *Candida spp.* [1-3].

Invasive candidosis and candidemia are severe complications in the intensive care units (ICU) and also important causes of morbidity and mortality (37-75%), especially in patients with severe sepsis.

Factors contributing to fungal infections are, among others, hospitalization (particularly in ICU lasting for more than 21 days), the severity of the patient's condition, therapy (steroids, broad spectrum antibiotics, especially a few antibiotics at the same time or repeated rotation of antibiotics), factors impairing tissue integrity or the integrity of mucocutaneous barriers, the extent of surgical procedures as well as colonization of more than one site or extensive colonization of one place [4-6].

The help of the laboratory in the choice of therapy is decisive in determining the susceptibility of the *Candida spp.* strains to the antifungal used [7, 8].

The purpose of this study was testing the sensitivity or resistance to some antifungal medicine, of *Candida* species from certain pathologic products.

## 2. Methods

The study was performed on 180 patients hospitalised at the Slatina Municipal Hospital, Romania, during March 2017- February 2018, from which 69.44% were female and 30.56% were male, divided into 3 main age categories: between 18 and 60 years old (54.15%), over 60 years old (approximately 42%), and under 18 years old.

Patients were distributed in 2 groups, based on the method used for testing the sensibility of the *Candida* species. Samples derived from the first group (99 patients) were processed with the Vitek device, testing the species' resistance to the following drugs: fluconazole, voriconazole, caspofungin, amphotericin B, flucytosine. For the second group (81 patients), the fungigrama was performed manually, testing the species resistance to fluconazole, amphotericin B, nystatin, clotrimazole, intraconazole, ketoconazole, miconazole.

All pathological products used for the analyses were vaginal secretions, wound secretions, spit and urine, collected from all the hospital wards. 33.33% of patients from both groups were pregnant women.



**Fig. 1.** Group 1 patient repartition (99 patients) based on the ward they were hospitalised, and the biologic product from which *Candida* was isolated



**Fig. 2.** Group 2 patient repartition (81 patients) based on the ward they were hospitalised, and the biologic product from which *Candida* was isolated

## 3. Results

More than 200 species of *Candida* are known, but only a small number of them create clinical problems. There are at least 15 distinct *Candida* species that cause human diseases, but more than 90% of invasions are caused by the five most common pathogens: *C. albicans*, *C. glabrata*, *C. tropicalis* and *C. krusei*.

In both patient groups, the most frequent isolated species was *C. albicans*.

**Table I.** *Candida* species frequency isolated in the first group

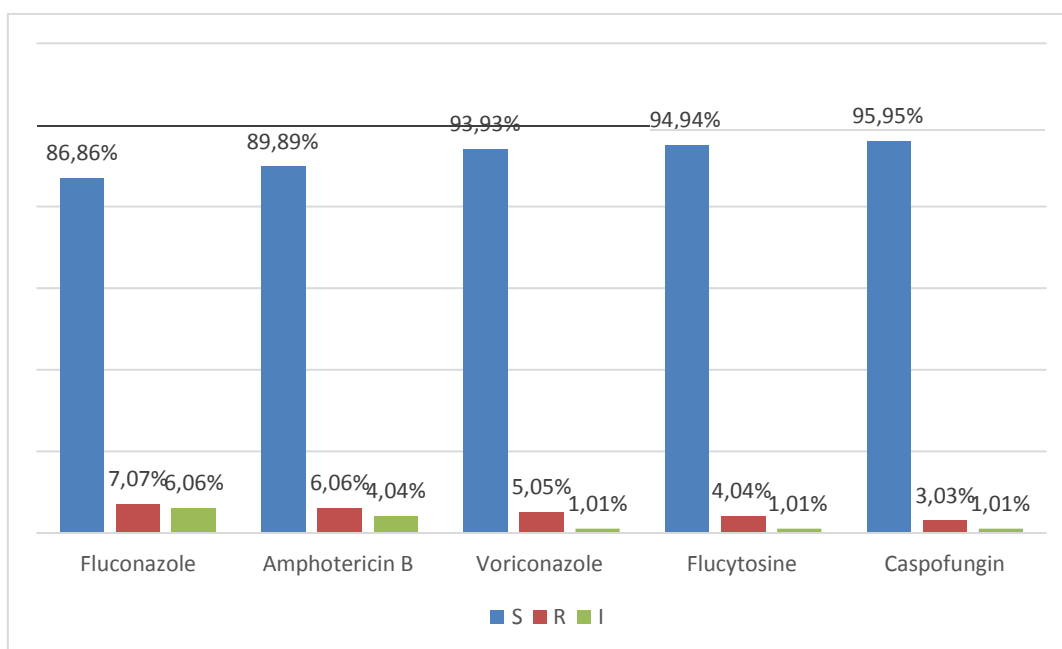
Tested species	Number of stains	Species frequency (%)
<i>C. albicans</i>	92	92.92%
<i>C. krusei</i>	3	3.03%
<i>C. intermedia</i>	1	1.01%
<i>C. rugosa</i>	1	1.01%
<i>C. tropicalis</i>	1	1.01%
<i>C. glabatra</i>	1	1.01%

**Table 2.** *Candida* species frequency isolated in the second group

Tested species	Number of stains	Species frequency (%)
<i>C. albicans</i>	79	97.53%
<i>C. krusei</i>	2	2.46%

*Antifungal sensitivity testing and antifungal sensibility profile comparison of the Candida strains isolated in the 2 groups*

Samples derived from the first group were processed with the Vitek device, testing the species' resistance to the following drugs: fluconazole, voriconazole, caspofungin, amphotericin B, flucytosine. *C. albicans* resistance profile to these antifungals is highlighted in the graph below.



**Fig. 3.** *C. albicans* resistance to the drugs tested

Two out of three *C. krusei* strains are resistant to fluconazole and flucytosine.

*C. intermedia* showed resistance to fluconazole, voriconazole and amphotericin B, and the *C. glabatra*, *C. intermedia* si *C. tropicalis* did not exhibit resistances to any of the tested antifungals.

For the second group, the fungigrama was performed manually, testing the species' resistance to fluconazole, amphotericin B, nystatin, clotrimazole, intraconazole, ketoconazole, miconazole.

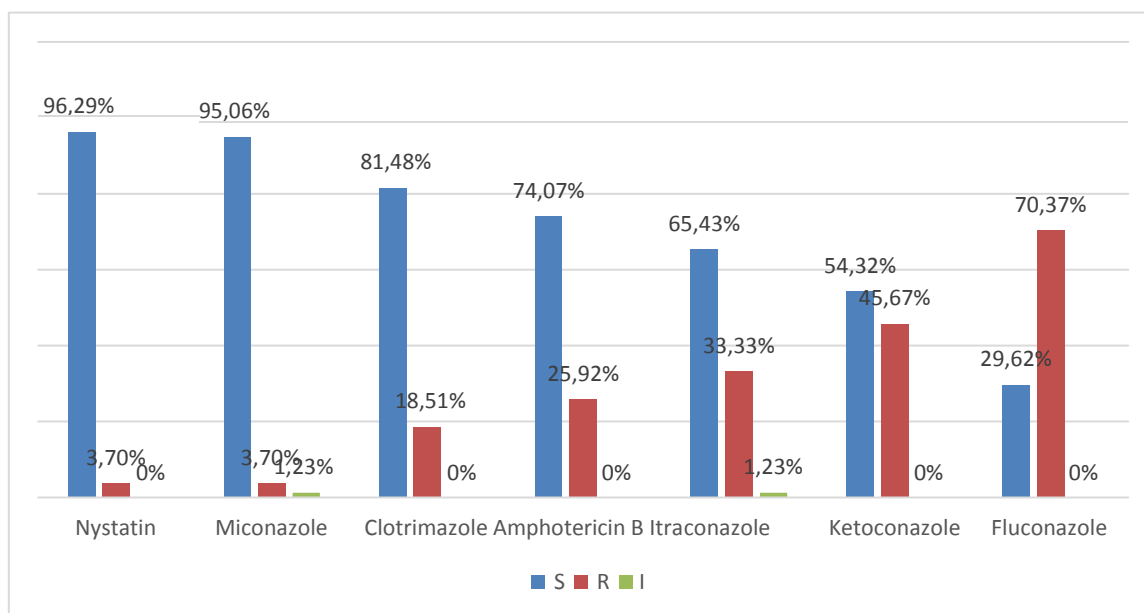


Fig. 4. *Candida* resistance in the second group

One out of the two *C. krusei* strains isolated in the second group was resistant to fluconazole si ketoconazole.

In the case of common antifungals, a major difference can be observed in the *C. albicans* strains' resistances to fluconazole and amphotericin B. This difference can be explained by using different concentrations of medicine for the two fungigramas, and also human error, which could intervene while interpreting the second group's manual fungigrama results.

#### 4. Conclusions

The study results proved an important variability of *Candida* strains from different pathologic products against different antifungal medicines.

The major population which developed candidiases were pregnant women, and the main pathogen agent was *C. albicans*.

Compared to the other tested medicines, a higher resistance to fluconazole and amphotericin B was observed for both groups.

The most efficient antifungals proved to be caspofungin, flucytosine, fluconazole, voriconazole, nistatin, miconazole, clotrimazole.

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