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# COMPARATIVE ASSESSMENT OF CANDIDA SPP. SUSCEPTIBILITY AND RESISTANCE TO ANTIFUNGAL AGENTS BY BIOLOGICAL MATERIAL TYPE

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**Abstract**

**Background:** Invasive fungal infections caused by *Candida* species remain a significant global health concern, particularly in immunocompromised individuals. Effective treatment requires precise knowledge of antifungal susceptibility patterns, which may vary depending on the biological source of isolation.

**Objective:** This study aims to evaluate and compare the susceptibility and resistance profiles of *Candida* spp. to five major antifungal agents across different types of biological materials providing clinically relevant insights for antifungal stewardship and infectious disease management.

**Materials and Methods:** A retrospective, observational, and descriptive study was conducted using 1,220 clinical isolates of *Candida* spp., collected from sputum (n=893), ENT organs (n=277), and cerebrospinal canal (n=50). Identification was carried out using conventional culture and microscopy. Susceptibility to anidulafungin, micafungin, voriconazole, caspofungin, and fluconazole was assessed using the broth microdilution method according to CLSI M27 and EUCAST guidelines. Minimum inhibitory concentrations (MICs) were used to determine susceptibility and resistance. Data analysis was performed using Microsoft Excel and IBM SPSS Statistics.

**Results:** Fluconazole demonstrated the highest overall susceptibility across all specimen types, especially in cerebrospinal canal isolates (80.0%) and sputum (78.6%). Among echinocandins, anidulafungin and micafungin showed strong activity, particularly in CNS and respiratory isolates. Voriconazole consistently exhibited the lowest susceptibility and highest resistance, especially in ENT-derived samples. Caspofungin presented moderate efficacy with variable resistance patterns. Resistance was highest in voriconazole (up to 40.4% in ENT samples), followed by caspofungin and micafungin. Fluconazole had the lowest resistance across all groups.

**Conclusion:** The effectiveness of antifungal drugs varies by the source of Candida spp. Fluconazole was most effective, especially in CNS infections. Voriconazole showed lower efficacy and more resistance. Treatment should be based on infection source to improve outcomes and reduce resistance.

***Keywords:*** Candida *spp., antifungal resistance, biological specimens, antifungal susceptibility, clinical isolates*

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**Резюме**

# СРАВНИТЕЛЬНАЯ ОЦЕНКА ЧУВСТВИТЕЛЬНОСТИ И УСТОЙЧИВОСТИ CANDIDA SPP. К ПРОТИВОГРИБКОВЫМ ПРЕПАРАТАМ В ЗАВИСИМОСТИ ОТ ТИПА БИОЛОГИЧЕСКОГО МАТЕРИАЛА

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**Введение:** Инвазивные грибковые инфекции, вызываемые видами *Candida*, остаются серьёзной проблемой здравоохранения во всем мире, особенно среди пациентов с ослабленным иммунитетом. Эффективное лечение требует точного понимания профилей чувствительности к противогрибковым препаратам, которые могут варьироваться в зависимости от биологического материала, из которого выделен возбудитель.

**Цель:** Оценить и сравнить чувствительность и устойчивость *Candida* spp. к пяти основным противогрибковым препаратам в зависимости от типа клинического материала (мокрота, ЛОР-органы и ликвор), с целью предоставления клинически значимой информации для ведения инфекционных заболеваний и антимикотической стратегии.

**Материалы и методы:** Было проведено ретроспективное, описательное, наблюдательное исследование, включающее 1 220 клинических изолятов *Candida* spp., полученных из мокроты (n=893), ЛОР-органов (n=277) и цереброспинальной жидкости (n=50). Видовая идентификация проводилась с использованием стандартных микологических методов (посев, микроскопия). Тестирование чувствительности к анидулафунгину, микафунгину, вориконазолу, каспофунгину и флуконазолу проводилось методом микробульонного разведения в соответствии с рекомендациями CLSI M27 и EUCAST. Анализ данных выполнен с использованием Microsoft Excel и IBM SPSS Statistics.

**Результаты:** Флуконазол продемонстрировал наивысшую общую чувствительность по всем типам образцов, особенно в ликворе (80,0%) и мокроте (78,6%). Среди эхинокандинов наибольшую активность показали анидулафунгин и микафунгин, особенно в изолятах из ЦНС и дыхательных путей. Вориконазол продемонстрировал наименьшую чувствительность и наибольшую устойчивость, особенно в ЛОР-образцах. Каспофунгин показал умеренную активность и переменную устойчивость. Вориконазол продемонстрировал наибольшую устойчивость (до 40,4% в ЛОР-образцах), за ним следовали каспофунгин и микафунгин. Флуконазол имел наименьшие показатели устойчивости.

**Вывод:** Эффективность противогрибковых препаратов зависит от источника выделения Candida spp. Флуконазол был наиболее эффективен, особенно при инфекциях ЦНС. Вориконазол показал меньшую эффективность и большую устойчивость. Терапию следует подбирать с учётом источника инфекции для повышения эффективности и снижения резистентности.

***Ключевые слова:*** *Candida spp., противогрибковая устойчивость, биологический материал, чувствительность, клинические изоляты*

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**Түйіндеме**

# CANDIDA SPP. ЗЕҢДЕРІНЕ ҚАРСЫ ПРЕПАРАТТАРҒА СЕЗІМТАЛДЫҒЫ МЕН ТӨЗІМДІЛІГІНІҢ БИОЛОГИЯЛЫҚ МАТЕРИАЛ ТҮРІНЕ БАЙЛАНЫСТЫ САЛЫСТЫРМАЛЫ БАҒАЛАУ

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**Кіріспе:** Candida түрлерімен шақырылатын инвазивті зең инфекциялары, әсіресе иммунитеті төмен адамдар арасында, жаһандық денсаулық сақтау жүйесі үшін елеулі қауіп болып табылады. Тиімді ем жүргізу үшін зеңге қарсы дәрілерге сезімталдықтың биологиялық материалға байланысты ерекшеліктерін нақты білу қажет.

**Мақсаты:**Клиникалық маңызды ақпарат беру мақсатында, әртүрлі биологиялық материалдардан бөлінген Candida spp. изоляттарының бес негізгі зеңге қарсы препаратқа (анидулафунгин, микафунгин, вориконазол, каспофунгин және флуконазол) сезімталдық және төзімділік деңгейін бағалау және салыстыру.

**Материалдар мен әдістер:** Зерттеу сипаттамалы, ретроспективті және бақылаулық сипатта жүргізілді. Барлығы 1 220 *Candida* spp. клиникалық изоляттары зерттелді: қақырықтан (n=893), ЛОР-мүшелерінен (n=277), жұлын сұйықтығынан (n=50). Идентификация стандартты микологиялық әдістер арқылы жүргізілді. Зеңге қарсы препараттарға сезімталдық CLSI M27 және EUCAST ұсыныстарына сәйкес микробульонды сұйылту әдісімен анықталды. Мәліметтер Microsoft Excel және IBM SPSS Statistics бағдарламаларында өңделді.

**Нәтижелер:** Флуконазол барлық үлгілер арасында ең жоғары сезімталдықты көрсетті, әсіресе жұлын сұйықтығында (80,0%) және қақырықта (78,6%). Эхинокандиндер арасында анидулафунгин мен микафунгин жақсы белсенділік көрсетті. Вориконазол ең төмен сезімталдықты және жоғары төзімділікті көрсетті, әсіресе ЛОР-жинақтарында. Каспофунгин орташа тиімділікке ие болды. Вориконазолдың төзімділігі ең жоғары болды (ЛОР - 40,4%), флуконазол - ең төмен төзімді дәрі.

**Қорытынды:** Candida spp. түрлерінің антимикотикалық дәрі-дәрмектерге тиімділігі олардың алынған биологиялық материалына байланысты өзгереді. Флуконазол ең тиімді болып, әсіресе орталық жүйке жүйесінің инфекцияларында жақсы нәтиже көрсетті. Вориконазол тиімділігі төменірек және резистенттілік жоғары болды. Емдеуді инфекцияның көзіне байланысты таңдау науқастардың жағдайын жақсартуға және дәрі-дәрмекке төзімділікті азайтуға көмектеседі.

***Түйінді сөздер:*** *Candida spp., зеңге қарсы төзімділік, биоматериал, сезімталдық, клиникалық изоляттар.*

***Дәйексөз үшін:***

*Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Лепесбаев М.Н., Смаилова Ж.К., Оразалина А.С., Кожанова С.К., Муканова Д.А., Апбасова С.А., Рахимжанова Ф.С., Ахметжанов О.Н.* Candida spp. Зеңдеріне қарсы препараттарға сезімталдығы мен төзімділігінің биологиялық материал түріне байланысты салыстырмалы бағалау // Ғылым және Денсаулық сақтау. 2025. Vol.27 (5), Б. 95-102. *doi 10.34689/SH.2025.27.5.012*

**Introduction**

Fungal infections, particularly those caused by Candida species, represent an escalating public health concern across both developed and developing regions. Each year, approximately 1,565,000 people worldwide develop invasive candidiasis. This condition primarily affects individuals with weakened immune systems, including critically ill patients in intensive care units, those undergoing prolonged treatment with broad-spectrum antibiotics, and more recently, people experiencing complications from post-COVID-19 syndrome (also known as long COVID). Invasive candidiasis is frequently misdiagnosed and is responsible for about 995,000 deaths annually, accounting for 63.6% of all cases [8].

Traditionally, Candida albicans has been considered the most prevalent species. However, recent studies reveal a marked epidemiological shift toward non-albicans Candida (NAC) species, including C. glabrata, C. parapsilosis, C.

tropicalis, and C. auris [19]. These species often exhibit intrinsic or acquired resistance to standard antifungal agents, posing challenges to effective treatment. In particular, Candida auris has gained global attention due to its multidrug resistance and capacity to cause nosocomial outbreaks [13].

A growing body of evidence indicates that addressing antifungal resistance requires consideration of site-specific factors, particularly the anatomical location from which Candida species are isolated. Clinical samples obtained from mucosal surfaces or catheterized areas frequently exhibit higher resistance levels, often due to biofilm formation and repeated exposure to antifungal agents. These findings highlight the importance of tailoring antifungal strategies based not only on species identification but also on the source of the clinical specimen [7].

Recent ICU-focused guidelines emphasize that the anatomical origin of Candida isolates plays a critical role in determining antifungal susceptibility. Isolates from sterile sites, such as blood or cerebrospinal fluid, tend to display higher susceptibility rates compared to those from non-sterile sites, including the urinary or respiratory tracts. This supports the integration of specimen-type considerations into both empirical antifungal therapy and local stewardship protocols [3].

Analysis of antifungal susceptibility in both environmental and clinical Candida isolates has revealed significant differences depending on the origin of the sample. Resistance to fluconazole was notably higher in isolates obtained from environments with strong anthropogenic influence. These observations support the concept that site-specific environmental pressures play a crucial role in shaping resistance patterns, even among clinically important yeast species [4].

Global surveillance data further highlight the growing concern of antifungal resistance in Candida species. Fluconazole-resistant C. parapsilosis has emerged as a serious clinical issue, particularly in intensive care settings, with resistance rates in certain regions exceeding 35%. This trend poses a direct threat to the efficacy of first-line antifungal treatments and underscores the urgent need for localized susceptibility testing and targeted antifungal stewardship strategies in high-risk hospital environments [6].

The compounding effects of co-infections and immunosuppressive therapies, particularly evident during the COVID-19 pandemic, have been associated with a marked increase in invasive fungal infections, including those caused by Candida spp. Delays in diagnosis and inappropriate use of azole antifungals have contributed to the emergence of resistant strains, especially in respiratory and urogenital samples. These observations highlight the importance of integrating clinical context, including the source of the isolate and the patient's background, into diagnostic and treatment strategies [10].

**Aim** to analyze the susceptibility profile of Candida spp. to five major antifungal agents according to biological specimen type, providing clinically relevant insights for infectious disease management and antifungal stewardship.

**Materials and Methods**

This study was designed as an observational, retrospective, and descriptive analysis. It included data on the susceptibility of 1,220 isolates of Candida spp., obtained from three types of clinical specimens: sputum (n = 893), ENT organs (n = 277), and cerebrospinal canal (n = 50). The analysis focused on five antifungal agents: anidulafungin, micafungin, voriconazole, caspofungin, and fluconazole.

Identification of Candida species was performed using standard mycological techniques, including culture-based methods and microscopic examination.

Antifungal susceptibility testing was conducted using the broth microdilution method, with determination of minimum inhibitory concentrations (MICs), in accordance with the CLSI M27 and EUCAST guidelines. Based on the MIC values obtained, isolates were classified as susceptible (S) or resistant (R).

*Statistical Analysis*

Data were entered into Microsoft Excel for preliminary sorting and calculation of susceptibility and resistance percentages. Statistical analysis was carried out using IBM SPSS Statistics, applying descriptive statistical methods.

To determine the rates of susceptibility and resistance for each biological specimen type, we calculated the percentage of susceptible and resistant *Candida* isolates relative to the total number of isolates from that material. The formulas used were:

- **Susceptibility (%)** = (Number of susceptible isolates / Total number of isolates per material) × 100
- **Resistance (%)** = (Number of resistant isolates / Total number of isolates per material) × 100

To assess overall trends, we also calculated the average susceptibility and resistance rates across all sample types using the following formulas:

- **Average susceptibility (%)** = (Total number of susceptible isolates from all materials / Total number of isolates) × 100
- **Average resistance (%)** = (Total number of resistant isolates from all materials / Total number of isolates) × 100

**Results**

Table 1 presents the susceptibility and resistance of *Candida* isolates to five antifungal agents across three types of clinical specimens: sputum, ENT organs, and cerebrospinal canal. The largest number of isolates was obtained from sputum (n=893), followed by ENT samples (n=277) and cerebrospinal canal specimens (n=50).

*Table 1.*

**Antifungal Susceptibility and Resistance Patterns of Candida Isolates from Different Clinical Specimens.**

| Antifungal Agent | Sputum (n=893) | | ENT Organs (n=277) | | Cerebral Canal (n=50) | |
|---|---|---|---|---|---|---|
| | Sus | Res | Sus | Res | Sus | Res |
| Anidulafungin | 647 (72.5%) | 246 (27.5%) | 174 (62.8%) | 103 (37.2%) | 38 (76.0%) | 12 (24.0%) |
| Micafungin | 649 (72.7%) | 244 (27.3%) | 170 (61.4%) | 107 (38.6%) | 35 (70.0%) | 15 (30.0%) |
| Voriconazole | 587 (65.7%) | 306 (34.3%) | 165 (59.6%) | 112 (40.4%) | 33 (66.0%) | 17 (34.0%) |
| Caspofungin | 640 (71.7%) | 253 (28.3%) | 167 (60.3%) | 110 (39.7%) | 32 (64.0%) | 18 (36.0%) |
| Fluconazole | 702 (78.6%) | 191 (21.4%) | 178 (64.3%) | 99 (35.7%) | 40 (80.0%) | 10 (20.0%) |

Fluconazole showed the highest overall susceptibility, particularly in isolates from sputum (78.6%) and cerebrospinal fluid (80.0%). Among the echinocandins, Anidulafungin and Micafungin demonstrated relatively high activity, especially in cerebrospinal isolates (76.0% and 70.0%, respectively). In contrast, susceptibility to Voriconazole and Caspofungin was moderate across all sample types, with lower rates observed in ENT isolates.

Table 2 offers a side-by-side comparison of the three most effective antifungal agents for each type of clinical specimen. Across all materials, fluconazole consistently emerged as the most active agent. In sputum samples, it reached a sensitivity of 78,6%, closely followed by micafungin (72,7%) and anidulafungin (72,5%). When considering ENT organ isolates, fluconazole again led with 64,3%, then anidulafungin (62,8%), and caspofungin (60,3%) not far behind. What's particularly noteworthy is that isolates from the cerebrospinal canal exhibited the highest overall antifungal susceptibility: fluconazole showed 80,0%, followed by anidulafungin (76,0%) and micafungin (70,0%).

*Table 2.*

**Comparative Analysis of the Most Effective Antifungal Agents by Biological Source of Isolation.**

| Biological Material | 1st Position | 2nd Position | 3rd Position |
|---|---|---|---|
| Sputum (n=893) | Fluconazole (78.6 %) | Micafungin (72.7 %) | Anidulafungin (72.5 %) |
| ENT Organs (n=277) | Fluconazole (64.3 %) | Anidulafungin (62.8 %) | Caspofungin (60.3 %) |
| Cerebral Canal (n=50) | Fluconazole (80.0 %) | Anidulafungin (76.0 %) | Micafungin (70.0 %) |

Table 3 summarizes the three antifungal agents associated with the highest levels of resistance among fungal isolates from different biological materials. The results indicate a notable variability in resistance profiles depending on the source of isolation, although certain agents, particularly voriconazole and caspofungin, consistently demonstrated higher resistance rates across multiple specimen types. In respiratory samples (sputum), voriconazole showed the highest proportion of resistant isolates (34.3%), followed by caspofungin (28.3%) and anidulafungin (27.5%). Among isolates from ENT organs, voriconazole again ranked first (40.4%), with caspofungin (39.7%) and micafungin (38.6%) close behind highlighting a relatively high resistance burden in this localization. Isolates obtained from the cerebrospinal canal demonstrated a slightly different pattern: caspofungin exhibited the highest resistance (36.0%), followed by voriconazole (34.0%) and micafungin (30.0%).

*Table 3.*

**Top Three Antifungal Agents with the Highest Resistance by Biological Source of Isolation.**

| Biological Material | 1st Position | 2nd Position | 3rd Position |
|---|---|---|---|
| Sputum (n=893) | Voriconazole (34.3 %) | Caspofungin (28.3 %) | Anidulafungin (27.5 %) |
| ENT Organs (n=277) | Voriconazole (40.4 %) | Caspofungin (39.7 %) | Micafungin (38.6 %) |
| Cerebral Canal (n=50) | Caspofungin (36.0 %) | Voriconazole (34.0 %) | Micafungin (30.0 %) |

Figure 1 presents a comparative analysis of Candida susceptibility to five antifungal agents across three biological sources: sputum, ENT organs, and cerebrospinal canal. Across all specimen types, fluconazole demonstrated the highest overall effectiveness, with sensitivity rates ranging from 64.3% (ENT) to 80.0% (cerebral canal). This confirms its broad-spectrum activity and continued relevance in empirical antifungal therapy. Among the echinocandins, anidulafungin and micafungin exhibited comparable efficacy. In particular, anidulafungin showed high activity in cerebrospinal isolates (76.0%) and sputum samples (72.5%), while micafungin showed slightly better performance in respiratory isolates (72.7%). Caspofungin displayed moderate activity across all materials, with sensitivity ranging from 60.3% to 71.7%. Voriconazole, though still active, consistently demonstrated the lowest susceptibility rates in all sample types, particularly in ENT-derived isolates (59.6%).

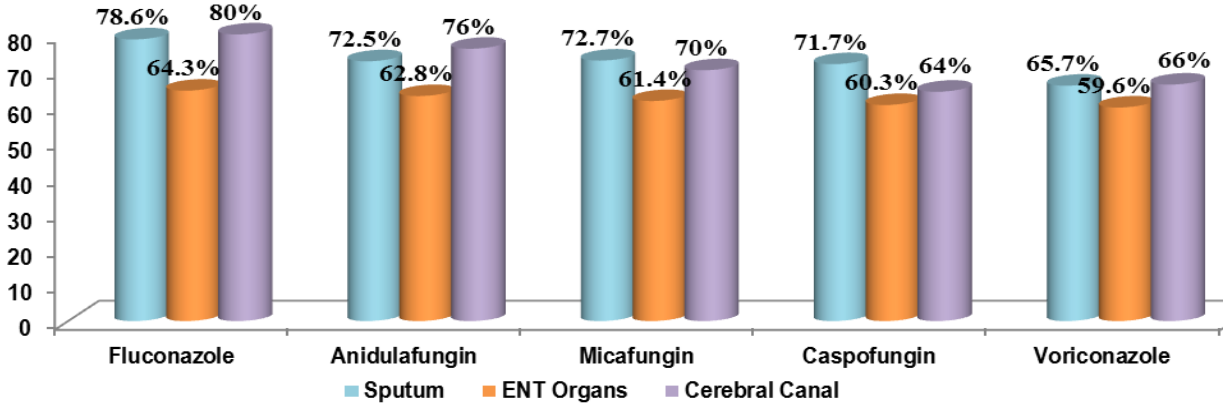


**Figure 1. Comparative Susceptibility of Candida Isolates to Antifungal Agents Across Biological Materials.**

Figure 2 presents the resistance percentages of five antifungal agents across three biological materials: sputum, ENT organs, and the cerebral canal. Voriconazole exhibits the highest resistance rates among the antifungals tested, with 34.3% resistance in sputum samples, 40.4% in ENT organ isolates, and 34% in the cerebral canal. Caspofungin follows closely, showing 28.3% resistance in sputum, 39.7% in ENT organs, and the highest resistance in the cerebral canal at 36%. Micafungin and anidulafungin demonstrate similar resistance profiles. Micafungin's resistance ranges

from 27.3% in sputum to 30% in the cerebral canal, while anidulafungin shows 27.5% resistance in sputum, increasing to 37.2% in ENT organs, but a lower 24% in the cerebral canal. Fluconazole has the lowest resistance rates across all sample types, with 21.4% in sputum, 35.7% in ENT organs, and 20% in the cerebral canal.

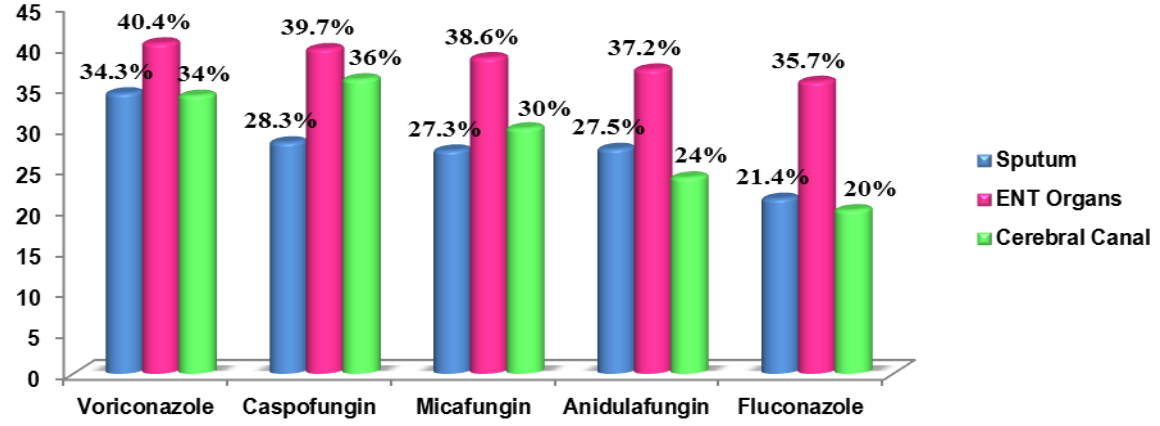


**Figure 2. Antifungal Resistance Rates by Specimen Type.**

Figure 3 shows the average susceptibility and resistance rates of five antifungal drugs based on data from various clinical samples. Fluconazole demonstrated the highest susceptibility at 75.4%, with the lowest resistance rate of 24.6%, indicating strong overall effectiveness. Anidulafungin and micafungin showed similar susceptibility rates of 70.4% and 70%, respectively, with corresponding resistance rates of 29.6% and 30%. Caspofungin had a slightly lower susceptibility at 68.8% and a resistance rate of 31.2%. Voriconazole showed the lowest susceptibility at 64.3% and the highest resistance rate of 35.7%, suggesting reduced effectiveness against Candida compared to the other antifungals.

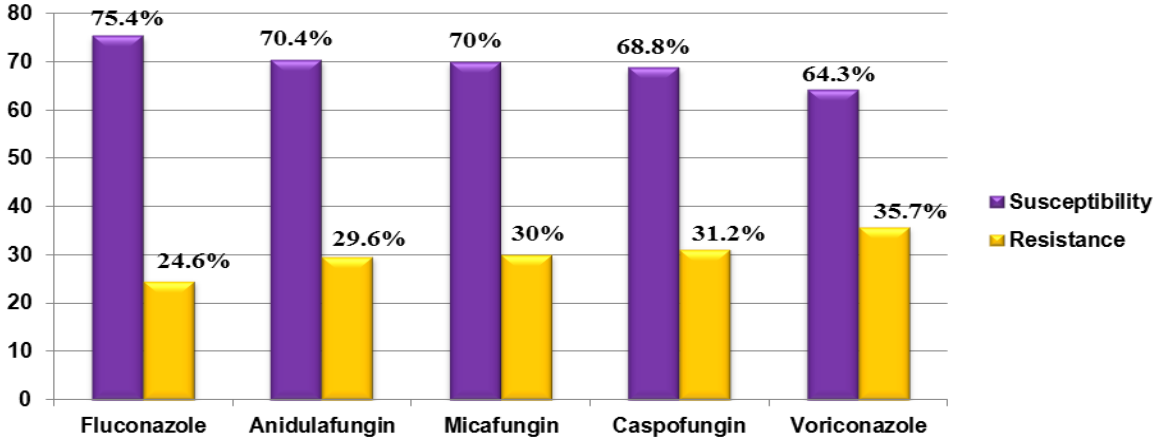


**Figure 3. Average Susceptibility and Resistance Rates of Five Antifungal Agents.**

**Discussion**

Our results confirm that Candida species show different antifungal susceptibility depending on the type of clinical sample. Isolates from cerebrospinal fluid had the highest susceptibility rates, especially to fluconazole (80.0%) and echinocandins like anidulafungin (76.0%) and micafungin (70.0%). On the other hand, samples from the ENT area and respiratory tract showed much higher resistance, particularly to voriconazole and caspofungin. This highlights the importance of considering the sample type when analyzing susceptibility results and choosing the right antifungal treatment.

Our results align with those presented by Parslow and Thornton (2022), who reported that Candida isolates from respiratory samples and non-sterile body sites showed higher resistance rates, especially among non-albicans Candida species [11]. Similarly, CDC surveillance data (*Toda et al.,* 2019) showed that bloodstream isolates were generally more susceptible to antifungals, whereas those from mucosal sites and devices exhibited reduced susceptibility consistent with our findings showing higher resistance in ENT and respiratory specimens [16].

*Fisher et al.* emphasized that antifungal resistance is shaped by site-specific factors such as prior drug exposure, local immune conditions, and the presence of biofilms. This is particularly relevant in ENT and respiratory tracts, where chronic colonization and topical azole use may promote the emergence of resistant strains [7]. Tellapragada et al. also demonstrated intra-species variability: C. albicans isolates from vaginal samples were significantly less susceptible to azoles than those from bloodstream infections [15].

Further evidence is provided by *Turan et al.* (2024), who found that C. albicans strains from the genitourinary tract had higher resistance to fluconazole and miconazole compared to blood-derived isolates [17]. El-Houssaini et al. (2019) reported similar trends in Egypt, where respiratory isolates displayed combined resistance to azoles and echinocandins [5]. These findings corroborate our observations that ENT-derived isolates exhibited the lowest susceptibility rates across all five antifungal agents tested.

*Nett et al.* (2015) provided mechanistic insight into this phenomenon, showing that Candida biofilms associated with catheters and mucosal surfaces confer significant resistance to echinocandins due to protective matrix formation [9]. *Berkow and Lockhart* (2017) further support this, noting that isolates from skin and mucosal tissues were more frequently resistant to fluconazole compared to those from sterile sites [2].

More recent studies continue to support these findings. *Shafiekhani et al.* observed that among solid organ transplant recipients, respiratory isolates contained the highest proportions of rare and multidrug-resistant Candida species [14]. Ashraf et al. showed that urinary catheter and respiratory isolates in India had higher resistance rates than those from CSF and blood, which were generally susceptible [1]. *Velmani et al.* also confirmed that C. auris exhibited the highest levels of resistance in respiratory and urogenital specimens, particularly to azoles. *Likewise [18]. Zhang et al.* found that C. parapsilosis strains from skin and catheter-associated sites were significantly more resistant than bloodstream isolates, which remained broadly susceptible [20].

The clinical source of Candida isolates has increasingly been recognized as a critical factor influencing antifungal susceptibility. Resistance patterns among Candida spp. are not only species-specific but also vary significantly depending on the site of isolation. Mucosal and respiratory tract isolates frequently exhibit higher resistance, while isolates from sterile sites such as bloodstream and cerebrospinal fluid tend to be more susceptible, particularly to echinocandins. These differences are often attributed to local drug exposure and biofilm formation at colonized sites [11].

Recent research on Candida auris has further demonstrated the complexity of antifungal resistance. This species displays clade-specific resistance traits, with less pronounced variation by body site, suggesting a primarily genetic basis for its multidrug-resistant phenotype [12]. Other studies have found that resistance to fluconazole and echinocandins can develop through both natural and acquired mechanisms. This is especially true for isolates from skin and mucous membranes, where biofilm formation creates a protective layer that greatly lowers the effectiveness of antifungal treatments [2].

*Limitations*

This study has several important limitations. First, because it was retrospective, we weren't able to include certain clinical details that could affect antifungal resistance — such as patients' prior use of antifungals, existing medical conditions, or full treatment histories. Second, we did not identify Candida isolates to the species level, which limited our ability to pinpoint species-specific resistance trends. Finally, since all the data were collected from one geographic region, the findings may not fully apply to other areas or diverse patient populations.

*Recommendations*

To better understand patterns of antifungal resistance, future research should use prospective designs and include species-level identification of Candida isolates, along with molecular testing methods. It's also important to track clinical outcomes, so we can link resistance patterns to actual treatment effectiveness. Exploring how infection site, resistance mechanisms, and drug activity interact will help refine treatment guidelines and improve patient care.

**Conclusion**

Our findings show a clear link between antifungal susceptibility and the site from which Candida isolates were obtained. Fluconazole showed the highest effectiveness overall, especially in samples from cerebrospinal fluid reinforcing its value in treating CNS infections. On the other hand, voriconazole had the lowest susceptibility and the highest resistance rates, particularly in ear, nose, and throat (ENT) samples. These results are in line with previous studies and emphasize the need to consider both the infection site and species type when selecting antifungal treatments. This approach can improve treatment accuracy and help reduce antifungal resistance in clinical practice.

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*This material has not been previously submitted for publication in other publications and is not under consideration by other publishers.*

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***References:***

1. *Ashraf A.A., Karnaker V.., Ramanath G., et al.* Frequency and Antifungal Susceptibility Patterns of Candida Species Isolated from Clinical Samples of Patients Attending to a Tertiary Healthcare Setting in Karnataka, India. Journal of Nature and Science of Medicine. 2025. Vol. 8. №. 1. p. 98-106.

2. *Berkow E.L., Lockhart S.R.* Fluconazole resistance in Candida species: a current perspective. Infection and drug resistance. 2017. p. 237-245.

3. *Bhattacharya P.K., Chakrabarti A., Sinha S., et al.* ISCCM position statement on the management of invasive fungal infections in the intensive care unit. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2024. Vol. 28. №. Suppl 2. p. S20.

4. *Caicedo-Bejarano L.D., Osorio-Vanegas L.S., Ramírez-Castrillón M., et al.* Water quality, heavy metals, and antifungal susceptibility to fluconazole of yeasts from water systems. International Journal of Environmental Research and Public Health. 2023. Vol. 20. №. 4. p. 3428.

5. *El-Houssaini H.H., Elnabawy O.M., Nasser H.A., et al.* Correlation between antifungal resistance and virulence factors in Candida albicans recovered from vaginal specimens. Microbial pathogenesis. 2019. Vol. 128. p. 13-19.

6. *Falletta A., Compagnino D.E., Ceccarelli G., et al.* P13. Clinical implications of fluconazole-resistant Candida parapsilosis: the urgent need for enhanced antifungal stewardship (focus project). JAC-Antimicrobial Resistance. 2025. Vol. №. Suppl 2. C. dlaf046. 013.

7. *Fisher M.C., Alastruey-Izquierdo A., Berman J. et al.* Tackling the emerging threat of antifungal resistance to human health. Nature reviews microbiology. 2022. Vol. 20. №. 9. p. 557-571.

8. *Ibe C., Pohl C.H.* Epidemiology and drug resistance among Candida pathogens in Africa: Candida auris could now be leading the pack. The Lancet Microbe. 2025. Т. 6. № 3.

9. *Nett J.E., Zarnowski R., Cabezas-Olcoz J. et al.* Host contributions to construction of three device-associated Candida albicans biofilms. Infection and Immunity. 2015. Vol. 83. №. 12. p. 4630-4638.

10. *Pandey R.P., Dhiman R., Mishra V., et al.* Co-morbidity of COVID 19 and fungal infections. Frontiers in Fungal Biology. 2024. Vol. 5. p. 1462172.

11. *Parslow B.Y., Thornton C.R.* Continuing shifts in epidemiology and antifungal susceptibility highlight the need for improved disease management of invasive candidiasis. Microorganisms. 2022. Vol. 10. №. 6. p. 1208.

12. *Santana D.J., Zhao G., O'Meara T.R.* The many faces of Candida auris: phenotypic and strain variation in an emerging pathogen. PLoS Pathogens. 2024. Vol. 20. №.3. – p. e1012011.

13. *Scipione M. R., Zhao J., Jabbo L., et al.* P-350. Epidemiology of Candida auris isolated from blood cultures at a tertiary care facility in metro Detroit. Open Forum Infectious Diseases. – US : Oxford University Press, 2025. Vol. 12. №. Supplement_1. p. ofae631. 551.

14. *Shafiekhani M., Yazdanpanah S., Zomorodian K., et al.* P. 057: Epidemiology of Candida infection and colonization in solid organ transplant recipients: An observational study. Transplantation. 2024. Vol. 108. №.9S. p. 473

15. *Tellapragada C., Eshwara, V. K., Johar, R., et al.* Antifungal susceptibility patterns, in vitro production of virulence factors, and evaluation of diagnostic modalities for the speciation of pathogenic Candida from blood stream infections and vulvovaginal candidiasis. Journal of pathogens. 2014. Vol. 2014. №. 1. p. 142864.

16. *Toda M.* Population-based active surveillance for culture-confirmed candidemia-four sites, United States, 2012–2016. MMWR. Surveillance Summaries. 2019. Vol.68.

17. *Turan D., Barış A., Kiraz N.* Investigation of Virulence Factors of Candida albicans Species Isolated from Clinical Specimens Phenotypically and Genotypically. Haydarpaşa numune medical journal. 2024. Vol. 64. №. 4. p. 450-455.

18. *Velmani V., Radhakrishnan S., Muppa L., et al.* P-2148. Prospective Study on Microbiological Profile of Fungal Isolates and its Antibiogram in a Tertiary care hospital in South India. Open Forum Infectious Diseases. US: Oxford University Press, 2025. Vol.12. №.Supplement_1. p. ofae631. 2302.

19. *Zhang R., Song Z., Su X., et al.* Molecular epidemiology and antifungal susceptibility of dermatophytes and Candida isolates in superficial fungal infections at a grade A tertiary hospital in Northern China. Medical Mycology. 2024. Vol. 62. №.9. p. myae087.

20. *Zhang W., Zhan M., Wang N., et al.* In vitro Susceptibility Profiles and Clinical Distribution of Candida parapsilosis Species Complex Subtypes from Deep Infections to Nine Antifungal Drugs. Research Perspectives of Microbiology and Biotechnology. 2024. Vol. 8. p. 1-17.

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