**Afghanistan Journal of Infectious Diseases**
**AJID**
https://ajid.ghalib.edu.af/index.php/ajid

2025 Jan 3(1): 39-45

# Sensitivity Pattern of the *Candida* Species Separated from the Blood and Urine of the Patients with Malignancy in Hospital

Farnaz Naderalvojood, *Ebrahim Sadeghi, Mehran Noroozi, Amir Nasimfar

Department of Pediatric Disease, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

**ARTICLE INFO**

**Type: Original Article**
Received: 2024/09/18
Accepted: 2024/12/30

*Corresponding Author:
E-mail:
sadeghi.e@umsu.ac.ir

**To cite this article:** Naderalvojood F, Sadeghi E, Noroozi M, Nasimfar A. Sensitivity Pattern of the *Candida* Species Separated from the Blood and Urine of the Patients with Malignancy in Hospital.

Afghanistan Journal of Infectious Diseases. 2025 Jan 3(1): 39-45.
https://doi.org/10.60141/ajid.77

**ABSTRACT**

**Background:** Infection with Candida species has been increased globally during the past decade. This can be due to the increase in the number of patients with immunodeficiency problems like cancer, HIV AIDs, organ transplantation and hospitalization in ICUs. We aimed to investigate the prevalence rate of the fungal colonization and related species in chemotherapy-subjected children with malignancy.

**Methods:** Present analytical-applied research was conducted on 128 chemotherapy-subjected children with malignancy. Blood and urine samples were collected from all the patients; afterwards, the urine samples were cultivated on Saborrads Dextrose Agar and the blood samples in ordinary culture bottles (monophasic culture method and blood culturing). Then, the developed fungi were separated from the culture medium and subjected to identification tests.

**Results:** There was no significant relationship between the age group and infection with fungus ($P$=0.998) but there was a significant relationship between gender and fungus infection ($P$=0.049) in such a way that fungus infection was found more prevalent amongst the females. Overall, 28 individuals (58.33%) were found infected with C. albicans; 9 (18.75%) with C. tropicalis; 5 (10.42%) with C. glabrata; 3 (6.25%) with C. kefir; 2 (4.116%) with C. krusei and 1 (2.09%) with C. parapsilosis.

**Conclusion:** C. albicans is the most common species in this geographical area. The best treatment for these infectious diseases is voriconazole.

**Keywords:** Fungal infection; Chemotherapy; Children; *Candida*

## Introduction

*Candida* species are yeasts that are present in various levels in different body organs as normal microbial flora (1). The infection with *Candida* species in the world has been increased globally during the past decade for an average percentage of 50 (2) and this can be due to the increase in the number of patients with immunodeficiency problems in patients with cancer, HIV AIDs, organ transplantation and hospitalization in ICUs (3).

Currently, 8% to 10% of the hospitalized nosocomial blood stream infections pertain to *Candida* species (4) recognized as the second cause of death resulting from sepsis in children (5). The expression rate of invasive candidiasis (Candidemia or Candidiasis of deep organ) differs from 0.3 to 5 individuals per every 1000 individuals admitted to the hospitals but, on the contrary, it causes 35% to 80% of the mortalities in critically-ill patients with

immunodeficiency (6). Due to the same reason, the hospitalization duration has been prolonged and a lot of treatment costs are imposed on the treatment-healthcare system (7).

At least, there are 15 various *Candida* species that can cause infections in the humans with the most common of them being *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. tropicalis* and *C. krusei* (8); amongst these, *C. albicans* is the most common (9). However, infections with non-*Albicans* species have been increased recently due to the increase in the number of patients with immunity system weakness as well as increase in the rate of using azoles (10). Very premature infants with birth weights below 1500g, organ or stem cells' transplantation, neutropenia, hematological malignancies and hospitalization in ICUs and taking of a wide spectrum of antibiotics and undergoing chemotherapy and with parenteral nutrition and primary or acquired immunodeficiency, as candidemia's risk factors, are most exposed to the infection (11,12).

Although, fluconazole is used as the first medication for treating *Candida*-induced infections, its effects have reduced nowadays due to the prevalence of azoles-resistant species (13). Consequently, the recent guidelines recommend echinocandin as the first-line medication for treating *Candida* (13). The immunity system's performance following chemotherapy and the combined binaries leads to different clinical responses in the patients to the antifungal treatments (14). Due to the same reason, the selection of the appropriate antifungal drug depends on the patient's conditions and the type of the infection with *Candida* (15) and the most important and most effective factor in regard of the fungal infections' treatment is the fast diagnosis and correct choice of the treatment (11). The prevention and treatment of the invasive fungal infections are the most important and most challenging problems for the children with cancer (12).

We aimed at investigating the prevalence rate of fungal colonies in chemotherapy-subjected children as well as the distribution of various species causing fungal infection in children undergoing chemotherapy so that the proper treatment pattern can be offered for the children with post-chemotherapy fungal infections through the exact identification of the factors causing such infections.

## Materials and Methods

The present analytical-applied research was conducted on 128 chemotherapy-subjected children with malignancy. Blood (3cc) and urine samples were collected from all the patients following which the urine samples were cultured on Saborrads Dextrose Agar and the blood samples were cultured in ordinary culture bottles (monophasic culture method and blood culturing). Then, the developed fungi were separated from the culture environment and subjected to identification tests. The prevalence rate of the various *Candida* species and the sensitivity to various antifungal drugs were tested and the prevalence rates were explored based on gender, age, history of taking antibiotics and presence of neutropenia, mucositis, urinary catheter and peripheral venous catheter.

In order to statistically analyze the data, SPSS software, ver. 19 (IBM Corp., Armonk, NY, USA) was used. To investigate the correlation between two variables, logistic regression statistical model was utilized. The *P*-value was set at below 0.05 for considering data as significant and meaningful.

### *Ethical considerations*

This project has been approved by Urmia University of Medical Sciences with Code of Ethics IR.UMSU.REC.1398.203.

Written consent letters were acquired from all the patients before entering the study and the participants were ensured that the study would not be harmful to them and it

will not also incur them with any expenses. In all of the stages, no work procedure was implemented without the patients' consent and they were allowed to withdraw from the study at any stage even after signing the written consent letter.

## Results

Overall, 128 chemotherapy-subjected children with malignancy were randomly selected.

Eighty four children (64.6%) had ALL type of malignancy; 13 children (10.2%) had AML type of malignancy; 5 children (3.9%) had Hodgkin's lymphoma malignancy, 1 child (0.8%) had optic glioma malignancy, 4 children (3.1%) had neuroblastoma malignancy; 3 children (2.3%) had burkitt lymphoma malignancy; 3 children had rabdomyosarcoma malignancy; 2 children (1.6%) had LCH type of malignancy; 3 children (2.3%) had wilms malignancy; 2 children (1.6%) had PNET type of malignancy; 2 children (1.6%) had lymphoma type of malignancy; 1 child (0.8%) had HLH type of malignancy; 3 children (2.3%) had retinoblastoma type of malignancy and, finally, 2 children (1.6%) had medulloblastoma type of malignancy. Considering the results obtained from Fisher's exact test, the frequency distribution of the malignancy type in the patients with fungal colonization and the patients with negative fungal colonization was identical but it was not statistically significant ($P$=0.6) (Tables 1-3).

**Table 1:** Age range of the patients with and without fungal infections

| ***Variable*** | | ***Culture (%) number*** | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| Age group(yr) | 0-6 | 24 (0.1) | 39 (0.9%) | 63 |
| | 7-12 | 16 (0.2) | 27 (0.8%) | 43 |
| | >=13 | 8 (0.4) | 14 (0.6%) | 22 |
| Gender | Male | 24 (0.8) | 54 (0.2%) | 78 |
| | Female | 24 (48) | 26 (52%) | 50 |

**Table 2:** Concomitant frequency distribution of the blood and urine tests' results for the studied children

| ***Test type and result*** | | ***Urine*** | |
|---|---|---|---|
| | | Positive | Negative |
| Blood | Positive | 4 | 24 |
| | Negative | 24 | 76 |

**Table 3:** Absolute and relative frequency rates of the resistance to antifungal medication studied herein based on the fungus type

| ***Fungus type*** | ***Resistance to antifungal medication N(%)*** | | | | | |
|---|---|---|---|---|---|---|
| | Amphotericin B | Fluconazole | Itraconazole | Voriconazole | Posaconazole | Ketoconazole |
| *C. albicans* | 4 (9.52) | 9 (21.43) | 13 (30.95) | 1 (2.4) | 1 (2.4) | 14 (33.3) |
| *C. glabrata* | 1 (16.7) | 1 (16.7) | 2 (33.2) | 1 (16.7) | 0 | 1 (16.7) |
| *C. tropicalis* | 1 (12.5) | 1 (12.5) | 4 (50) | 0 | 1 (12.5) | 1 (12.5) |
| *C.parapsilosis* | 0 | 1 (100) | 0 | 0 | 0 | 0 |
| *C. krusei* | 0 | 0 | 1 (33.33) | 0 | 1 (33.33) | 1 (33.33) |
| *C. kefir* | 0 | 1 (33.33) | 1 (33.33) | 0 | 0 | 1 (33.33) |

Considering the results obtained from Chi-Square test, there was no significant relationship between the age group and fungal infection ($P$=0.998) but a significant relationship was found between gender and fungal infection ($P$=0.049) in such a way that fungal infection was found more common amongst the females.

The infections with fungus species are showed in Table 4.

Using Kruskal-Wallis test, the effect of the six kinds of antifungal medications was significant only on *C. albicans* ($P$<0.01) and that there was no significant difference for the rest of the fungi in terms of the antifungal drug's effect (Table 5).

**Table 4:** Frequency and percentage distribution of *Candida* infections based on gender and age of the studied children

| ***Variable*** | | ***albicans*** | ***tropicalis*** | ***glabrata*** | ***kefir*** | ***krusei*** | ***parapsilosis*** | ***P*** |
|---|---|---|---|---|---|---|---|---|
| Gender | Male | 12 (50) | 6 (25) | 3 (12.5) | 2 (8.3) | 1 (4.2) | 0 | |
| | Female | 16 (66.7) | 3 (12.5) | 2 (8.3) | 1 (4.2) | 1 (4.2) | 1 (4.2) | 0.811 |
| Age | 0-6 | 14 (58.3) | 5 (20.8) | 2 (8.3) | 2 (8.3) | 1 (4.2) | 0 | 0.986 |
| | 7-12 | 9 (56.3) | 2 (12.5) | 2 (12.5) | 1 (6.3) | 1 (6.3) | 1 (6.3) | |
| | >=12 | 5 (62.5) | 2 (25) | 1 (12.5) | 0 | 0 | 0 | |

**Table 5:** Frequency distributions of the types of sensitivity in various *Candida* species to the antifungal treatments in this study

| ***Variable*** | | ***Frequency*** | ***Percentage*** |
|---|---|---|---|
| Amphotericin B | Sensitive | 37 | 77.1 |
| | Intermediate | 5 | 10.4 |
| | Resistant | 6 | 12.5 |
| Ketoconazole | Sensitive | 18 | 37.5 |
| | Intermediate | 12 | 25 |
| | Resistant | 18 | 37.5 |
| Fluconazole | Sensitive | 23 | 47.9 |
| | Intermediate | 12 | 25 |
| | Resistant | 13 | 27.1 |
| Itraconazole | Sensitive | 20 | 41.7 |
| | Intermediate | 12 | 25 |
| | Resistant | 16 | 33.3 |
| Posaconazole | Sensitive | 41 | 85.4 |
| | Intermediate | 4 | 8.3 |
| | Resistant | 3 | 6.3 |
| Voriconazole | Sensitive | 45 | 93.7 |
| | Intermediate | 1 | 2.1 |
| | Resistant | 2 | 4.2 |

As for *C. albicans*, the antifungal effects of amphotericin B and ketoconazole ($P$=0.01), fluconazole and voriconazole ($P$=0.01), itraconazole and voriconazole ($P$<0.01), itraconazole and posaconazole ($P$<0.01) and in the end, voriconazole and ketoconazole ($P$<0.01) was reported significant. The sensitivity of the various fungus species to voriconazole was in its highest level followed by posaconazole, amphotericin B, fluconazole, itraconazole and ketoconazole, respectively.

None of the children participating in this study were found with a past history of fungal infection. Fourteen children (10.9%) were found with neutropenia, 46 children (35.9%) with mucositis, 5 children (3.9%) with urinary catheter and all of them with

peripheral venous catheter which are all amongst the risk factors giving rise to the emergence of *Candida* infections. Only mucositis was found having an effect on the result of fungus culturing (*P*:0.29). Moreover, all of the studied children had a history of taking antibiotics.

Considering the results obtained from Fisher's exact test, the distribution of the fungus species is identical in regard of the gender and age for the chemotherapy-subjected children hence no significant difference has been evidenced.

## Discussion

Candidemia (blood's infection with various *Candida* species) is one of the five common hospitals' infections amongst the risk factors of which malignancy, prematurity and surgery during postnatal period can be pointed out (16,17). The prevalence rate of the invasive fungal infections ranges from 1% to 38% in the children with malignancy and it is more prevalent in the blood-related malignancies with *Candida* fungi being the most common (18). *C. albicans* was the most common species of invasive *Candida* in children and this is consistent with what has been found herein but the highest mortality rate has been justified for *C. parapsilosis* (19). Recently, the prevalence of non-albicans species has also increased (20,21).

The blood infection with non-*albicans Candida* species in patients with hematological malignancy and neutropenia for over 7 d after chemotherapy is considered as an independent risk factor for the creation of the systemic *Candida* infections (22). Furthermore, prescription of steroids in high dosages, as well, can cause an increase in the risk of invasive fungal infection (23). However, mucositis was proved herein as the only factor contributing to the development of fungal infections in the patients.

Due to the high mortality rate of the invasive fungal infections, the patients with high infliction rate should be prescribed with prophylactic antifungal medications (24). In this study, voriconazole was found having the highest effect on the treatment of invasive candidiasis. Due to the same reason, this drug can be possibly used as saving treatment in resistant cases (25). This is while, itraconazole was found with the highest effect on *Candida* species (26). *C. albicans* and *C. parapsilosis* are resistant to fluconazole and voriconazole for less than 6% whereas the resistance rate was higher in *C. tropicalis* and *C. glabrata* and it was also found increasing with the passage of time (27). The amount of drug resistance has been higher in non-*albicans Candida* species in contrast to *C. albicans* in such a manner that it has been less than 1% in *C. albicans* and between 2% and 4% in *C. glabrata* (28). One of the risk factors can be the prior use of azoles (29,30). The treatment of non-*albicans* species with azoles might take a longer time and be less successful. The prescription of echinocandins in prophylactic form for these patients may cause decrease in the rate of invasive *Candida* infections' expression (31).

## Conclusion

The most common *Candida* species was *C. albicans* and voriconazole is the best and most effective medication for the treating of these infections in the studied patients; however, the prevalence of the various species and their sensitivity to the antifungal drugs differ in various regions.

## Acknowledgements

No financial support was received for this study.

## Conflict of interest

The authors declare that there is no conflict of interests.

## References


1. Mundula T, Ricci F, Barbetta B, Baccini M, Amedei A. Effect of Probiotics on Oral Candidiasis: A Systematic Review and Meta-Analysis. Nutrients. 2019; 11(10).
2. Ejaz H, Ramzan M. Determination of minimum inhibitory concentrations of various antifungal agents in clinical isolates of *Candida* species. J Pak Med Assoc. 2019; 69(8):1131-1135.
3. Sganga G, Wang M, Capparella MR, Tawadrous M, Yan JL, Aram JA, et al. Evaluation of anidulafungin in the treatment of intra-abdominal candidiasis: a pooled analysis of patient-level data from 5 prospective studies. Eur J Clin Microbiol Infect Dis. 2019; 38(10):1849-1856.
4. Poissy J, Damonti L, Bignon A, Khanna N, Von Kietzell M, Boggian K, et al. Risk factors for candidemia: a prospective matched case-control study. Crit Care. 2020 18; 24(1):109.
5. Altintop YA, Ergul AB, Koc AN, Atalay MA. Evaluation of *Candida* colonization and use of the *Candida* Colonization Index in a paediatric Intensive Care Unit: a prospective observational study. Infez Med. 2019;27(2):159-167.
6. Zeng ZR, Tian G, Ding YH, Yang K, Liu JB, Deng J. Surveillance study of the prevalence, species distribution, antifungal susceptibility, risk factors and mortality of invasive candidiasis in a tertiary teaching hospital in Southwest China. BMC Infect Dis. 2019 Nov 7; 19(1):939.
7. Zhang W, Song X, Wu H, Zheng R.Epidemiology, risk factors and outcomes of *Candida albicans* vs. non-*albicans* candidaemia in adult patients in Northeast China. Epidemiol Infect. 2019 Sep 25; 147:e277.
8. Medeiros MAP, Melo APV, Bento AO, Souza LBFC, Neto FAB, Garcia JB, et al. Epidemiology and prognostic factors of nosocomial candidemia in Northeast Brazil: A six-year retrospective study. PLoS One. 2019 Aug 22; 14(8):e0221033.
9. Aldardeer NF, Albar H, Al-Attas M, Eldali A, Qutub M, Hassanien A, et al. Antifungal resistance in patients with Candidaemia: a retrospective cohort study. BMC Infect Dis. 2020 Jan 17;20(1):55.
10. Corcione S, D'Avolio A, Pasero D, Trentalange A, Pagani N, Sanguinetti M, et al. Acquisition of FKS2 mutation after echinocandin treatment of infective endocarditis by *Candida glabrata*. Infez Med. 2019 Sep 1; 27(3):328-331.
11. Ramos JT, Romero CA, Belda S, Candel FJ, Carazo Gallego B, Fernández-Polo A, et al. Clinical practice update of antifungal prophylaxis in immunocompromised children. Rev Esp Quimioter. 2019 Oct;32(5):410-425.
12. Hamzavi SS, Amanati A, Badiee P, Kadivar MR, Jafarian H, Ghasemi F, et al. Changing face of *Candida* colonization pattern in Pediatric patients with hematological malignancy during repeated hospitalizations, results of a prospective observational study (2016-2017) in shiraz, Iran. BMC Infect Dis. 2019 Aug 30;19(1):759.
13. Brunetti G, Navazio AS, Giuliani A, Giordano A, Proli EM, Antonelli G, et al. *Candida* blood stream infections observed between 2011 and 2016 in a large Italian University Hospital: A time-based retrospective analysis on epidemiology, biofilm production, antifungal agents consumption and drug-susceptibility. PLoS One. 2019 Nov 7; 14(11):e0224678.
14. Rodrigues LS, Motta FA, Picharski GL, Vasconcelos TM, Riccieri MC, Dalla-Costa LM. Invasive candidiasis: Risk factor for mortality in a pediatric tertiary care hospital in south of Brazil. Medicine (Baltimore). 2019 Jun; 98(23):e15933.
15. Mroczyńska M, Brillowska-Dabrowska A. First report on echinocandin resistant Polish *Candida* isolates. Acta Biochim Pol. 2019 Sep 12; 66(3):361-364.
16. Keighley C, Chen SC, Marriott D, Pope A, Chapman B, et al. Candidaemia and a risk predictive model for overall mortality: a prospective multicentre study. BMC Infect Dis. 2019 May 21;19(1):445.
17. Benedict K, Roy M, Kabbani S, Anderson EJ, Farley MM, Harb S, et al. Neonatal and Pediatric Candidemia: Results From Population-Based Active Laboratory Surveillance in Four US Locations, 2009-2015. J Pediatric Infect Dis Soc. 2018 Aug 17;7(3):e78-e85.
18. Ruijters VJ, Oosterom N, Wolfs TFW, van den Heuvel-Eibrink MM, van Grotel M.

Frequency and Determinants of Invasive Fungal Infections in Children With Solid and Hematologic Malignancies in a Nonallogeneic Stem Cell Transplantation Setting: A Narrative Review. J Pediatr Hematol Oncol. 2019 Jul;41(5):345-354.

19. Almooosa Z, Ahmed GY, Omran A, AlSarheed A, Alturki A, Alaqeel A, et al. Invasive Candidiasis in pediatric patients at King Fahad Medical City in Central Saudi Arabia. A 5-year retrospective study. Saudi Med J. 2017 Nov; 38(11):1118-1124.
20. Kishimoto K, Kasai M, Kawamura N, Ito Y, Yoshida M, Hasegawa D, et al.Clinical features in proven and probable invasive fungal disease in children and adolescents at a pediatric referral center: a 5-year experience. World J Pediatr. 2019 Jun;15(3):270-275.
21. Widmer AF, Kern WV, Roth JA, Dettenkofer M, Goetting T, Bertz H, et al. Early versus late onset bloodstream infection during neutropenia after high-dose chemotherapy for hematologic malignancy. Infection. 2019 Oct;47(5):837-845.
22. He YZ, Guo XJ, Lin XY, Zhu HB. [Analysis of Risk Factors Affecting the Chemotherapy-related Infections in Patients with ALL]. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2019 Dec;27(6):1825-1830.
23. Fisher BT, Robinson PD, Lehrnbecher T, Steinbach WJ, Zaoutis TE, Phillips B, et al.Risk Factors for Invasive Fungal Disease in Pediatric Cancer and Hematopoietic Stem Cell Transplantation: A Systematic Review. J Pediatric Infect Dis Soc. 2018 Aug 17;7(3):191-198.
24. Linke C, Tragiannidis A, Ahlmann M, Fröhlich B, Wältermann M, Burkhardt B, et al. Epidemiology and management burden of invasive fungal infections after autologous hematopoietic stem cell transplantation: 10-year experience at a European Pediatric Cancer Center. Mycoses. 2019 Oct;62(10):954-960.
25. Lin GL, Chang HH, Lu CY, Chen CM, Lu MY, Lee PI,et al. Clinical characteristics and outcome of invasive fungal infections in pediatric acute myeloid leukemia patients in a medical center in Taiwan. J Microbiol Immunol Infect. 2018 Apr;51(2):251-259.
26. Giamarellos-Bourboulis EJ, Stamou A, Maraki S, Solomonidi N, Belesiotou E, Pistiki A, et al. Susceptibility profiles and clinical efficacy of antifungals against *Candida* bloodstream isolates from critically ill patients: Focus on intravenous itraconazole. Int J Antimicrob Agents. 2019 Oct;54(4):471-477.
27. Xiao M, Sun ZY, Kang M, Guo DW, Liao K, Chen SC, et al.Five-Year National Surveillance of Invasive Candidiasis: Species Distribution and Azole Susceptibility from the China Hospital Invasive Fungal Surveillance Net (CHIF-NET) Study. J Clin Microbiol. 2018 Jun 25;56(7). pii: e00577-18.
28. Gamaletsou MN, Walsh TJ, Sipsas NV. Invasive Fungal Infections in Patients with Hematological Malignancies: Emergence of Resistant Pathogens and New Antifungal Therapies. Turk J Haematol. 2018 Mar 1;35(1):1-11.
29. Hirano R, Minakawa S, Kitazawa J, Saito N, Kayaba H. Impact on Antifungal Susceptibility Patterns of Previous vs. Revised Clinical and Laboratory Standards Institute Breakpoints for *Candida* Species Isolated from Candidemia: Experience of Two Tertiary Care Institutions in Japan. Clin Lab. 2019 Jul 1;65(7).
30. Tsai MH, Hsu JF, Yang LY, Pan YB, Lai MY, Chu SM, et al.Candidemia due to uncommon *Candida* species in children: new threat and impacts on outcomes. Sci Rep. 2018 Oct 15;8(1):15239.
31. Epstein DJ, Seo SK, Brown JM, Papanicolaou GA. Echinocandin prophylaxis in patients undergoing haematopoietic cell transplantation and other treatments for haematological malignancies. J Antimicrob Chemother. 2018 Jan 1;73(suppl_1):i60-i72.