



# Frequency of Candidemia and Associated Factors According to a Sample of Children Admitted to a Pediatric Medical Center in Iran

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## Abstract:

**Background:** The prevalence of candidemia and candiduria has been steadily increasing in medical centers, largely due to the rising use of antibiotics and advancements in medical technology.

**Aim:** This study aims to survey the frequency of candidiasis, focusing specifically on candidemia in children, associated risk factors, species distribution, and antifungal therapies.

**Method:** This cross-sectional [descriptive-analytical] study analyzed positive blood cultures from patients diagnosed with candidiasis. This cross-sectional study was conducted on children admitted to the Children's Medical Center Hospital diagnosed with candidemia from May 2021 to March 2022. All cases with positive blood cultures for *Candida* were included, ultimately examining 59 patients and assessing treatment responses.

**Results:** A total of 68 cases were initially reviewed; however, 9 samples were excluded due to data deficiencies, leaving 59 patients for analysis. During this period, the laboratory reported a total of 2,230 positive cultures, with 68 cases identified as candidemia, accounting for 3.2% of positive cultures. *Candida albicans* was identified in 59.3% of cases compared to 40.7% for non-*albicans* species.

**Conclusion:** Candidemia represents one of many complications examined in this study, and its association with complex therapeutic interventions and mortality highlights the need for careful management to minimize unnecessary procedures and pharmacotherapies.

**Keywords:** Candidemia, Children, Treatment response, Risk factors.

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## 1. INTRODUCTION

Today, due to the increasing prevalence of antibiotic use in medical centers and advances in medical science, the prevalence of candidiasis and candiduria has increased day by day. *Candida* can be seen in 3 morphological forms: 1) Blastospores or round or oval yeast cells [3-6 mm in diameter], 2) double-walled chlamydia spores [7-17 mm in diameter], which are usually seen at the end of the pseudohyphae, and 3) pseudomycelium, which shows an accumulation of pseudo-hyphae and tissue phase of *Candida*.

*Candida albicans* is the cause of many human infections, but *C. parapsilosis*, *C. tropicalis*, *C. krusei*, *C. lusitaniae*, *C. glabrata*, and several other species are increasingly reported as pathogens [1].

During the last two decades, the incidence of candidemia in hospitalized patients has increased, and the risk factors have been clearly described. Treatment costs are especially high in sick and immunocompromised children [2, 3].

*Candida albicans* is the most dominant species of candidemia in adults, although non-*albicans* species, such as *glabrata*, are also increasing [4].

In the pediatric population, the predominant species is *Candida parapsilosis* [5]. The most invasive fungal infections occur in hospitalized children and are often with *Candida* species [6]. A prospective study on hospital-acquired bloodstream infections [BSIs] states that *Candida* species are the third most common microorganism. It is the most common cause of BSIs in general and the most common cause of fungal infection of BSIs [7].

The most common cause of BSI is bacteria [coagulase-negative staph 43.3% and enterococci 9.4%]. Anatomical and physiological differences between adults and children cause differences in the sensitivity and therapeutic response of *Candida* species to different therapeutic and antifungal methods, including those related to drug toxicity, pharmacokinetics, and drug dosage. On the other hand, the information available to make a decision regarding cases of invasive fungal infections in children is far less than in adults [7].

Although the sensitivity to fluconazole has been constant for nearly a decade [8-11], the increase in the MIC of specific *Candida* species [*glabrata*, *parapsilosis*] to fluconazole has been reported [12, 13]. Hence, this study focused on the increasing tendency to use fluconazole as prophylaxis in ELBW [Birth weight < 1000gr] infants [9, 10].

There is some information about the changes in the epidemiology of candidemia in children, as well as the change in the drug sensitivity of antifungal agents in *Candida* isolates, especially with new antifungal drugs, such as Caspofungin [11, 12].

Further, this general review study was conducted regarding invasive candidiasis, especially candidemia in children, and risk factors, species distribution, and antifungal treatment.

## 2. METHODS

This study was a cross-sectional study [descriptive] conducted on children who were admitted to the Children's Medical Center Hospital with the diagnosis of candidemia from May 2021 to March 6th, 2022.

In this study, all cases whose blood cultures were positive for *Candida* were examined. After the blood culture was positive, the resident responsible for the project came to the patient's bedside, and while ensuring the correct sampling by the department personnel, appropriate treatment was started for the patients, and then the patients were examined in terms of underlying factors and risk factors. If the sampling was not done correctly before starting the treatment, the sampling was done again, and then the treatment was started. Finally, the treatment response in all patients was checked.

Pre-designed questionnaire, including age and gender demographic variables as well as hospitalization department, underlying disease, type of drugs used, having or not having a urinary catheter, having or not having a central catheter, *Candida* colony, type of antibiotic used and treatment or not with antifungal drugs was completed for each patient. All patients with candidemia admitted to the pediatric medical center during the period of one and a half years were included in the study and were investigated.

Twenty-thirty patients were examined in terms of candidemia and clean samples were taken according to the recommendations of the references. Patient information was recorded after obtaining consent from the parents. The questionnaires were anonymous and coded, and the findings of the study were reported in general.

The data were entered into SPSS-22v statistical software and analyzed using descriptive statistical tests [Mean, Standard Deviation for quantitative variables and Frequency, Frequency percent for qualitative variables].

## 3. RESULTS

In this study, a total of 68 cases were investigated, of which 9 cases were excluded from the study due to the problems of the files and data deficiencies, and the remaining 59 patients were examined. In this period of time, a total of 2,230 positive blood cultures were reported by the laboratory, and Candidemia cultures account for approximately 3.05% of all positive cultures. Non-candidemia cultures account for about 96.95% of all positive cultures Table 1.

**Table 1. Frequency distribution of patients based on positive *Candida* culture.**

Positive culture	Frequency	Frequency%
Candidate	68	3.05
Non-candidemia cultures	2163	96.95
Total	2230	100%

Table 2 shows the distribution of patients with candidemia by gender; 31 patients are boys, accounting for 52.5% of the total.

**Table 2. Frequency distribution of patients based on gender.**

Gender	Frequency	Frequency%
Boy	31	52.5%
Girl	28	47.5%
Total	59	100%

Table 3 provides insights into the age distribution of patients with candidemia; this indicates a wide range of ages among the patients, with a significant variability as suggested by the large standard deviation. The median age is lower than the average, indicating that the distribution is skewed towards younger ages. The presence of very young patients [as young as 10 days] and older children [up to 8 years] highlights the need for age-specific considerations in managing candidemia in pediatric populations.

**Table 3. Central indicators and distribution of patients' age.**

Average	30.87
Middle	23
Standard deviation	28.69
Maximum	96
Minimum	0.33

The age distribution of patients with candidemia in our study showed a wide range, from as young as 10 days to approximately 8 years, with an average age of 30.87 months and a median of 23 months. This variability underscores the importance of tailoring treatment strategies to the specific age-related needs of pediatric patients. The skewness towards younger ages suggests that neonates and infants may be particularly vulnerable to candidemia, emphasizing the need for vigilant monitoring and early intervention in these high-risk groups.

Table 4 provides information about the distribution of two types of Candida species in a sample.

**Table 4. Frequency distribution of patients based on Candida type.**

Candidate	Frequency	Frequency%
Albicans	35	59.3%
Non albicans	24	40.07%
Total	59	100%

*Candida albicans* is a common species of Candida. It is present in 35 cases out of the total, which accounts for 59.3% of the sample. There are 24 cases of non-albicans Candida, making up 40.07% of the sample.

Table 5 provides an overview of the distribution of candidates across various inpatient departments within a healthcare setting. The focus is on non-albicans infections or conditions, which suggests that the data might be related to a study or survey on these types of infections. Each department has a specific number of candidates

associated with it. For instance, the NICU has 3 candidates, while the PICU has 6. The EICU has the highest number, with 7 candidates, followed by the CICU with 4. The blood department and Romano and Imno each have 3 candidates. The surgery and urology department, as well as dialysis, have no candidates listed. The digestion department has 5 candidates. Overall, there are 35 candidates in one category and 24 in another, indicating a total of 59 candidates across all departments.

**Table 5. Frequency distribution of patients according to the inpatient department.**

Inpatient department	Candidate	
	Albicans	Non albicans
NICU	3	0
PICU	1	6
EICU	7	3
CICU	2	4
Blood	3	3
Romano and Imno	2	3
Surgery and urology	5	0
Digestion	1	5
Dialysis	1	0
Total	35	24

Table 6 reveals that while both types of infections have notable mortality rates, patients with non-Candida albicans infections exhibit a slightly higher survival rate. Specifically, the survival rate for non-Candida albicans infections was 86%, compared to 79% for Candida albicans infections. The overall mortality rate was 17%, with 10 deaths distributed equally between the two infection types. These findings suggest differences in clinical outcomes that could inform treatment strategies and healthcare management practices for patients with Candida infections.

**Table 6. Frequency distribution of patients based on Candida type and mortality.**

		Mortality				Total	Percent
		Have not	Percent	Have	Percent		
Candidate	Albicans	19	47	5	20	24	40
	Non albicans	30	85	5	14	35	50
Total		49	83	10	17	59	100

Table 7 shows the mortality rates among patients who were intubated versus those who were not. The analysis reveals that intubated patients had a significantly higher mortality rate, with 47% of intubated patients dying compared to 2.5% of non-intubated patients. The overall mortality rate was 17%, with 9 out of 10 deaths occurring in the intubated group. These findings suggest that intubation is associated with increased mortality, potentially due to the severity of underlying conditions or complications related to the procedure. Further research is needed to explore underlying factors contributing to these differences in mortality rates.

**Table 7. Frequency distribution of patients based on intubation and mortality.**

		Mortality				Total	Percent
		Have not	Percent	Have	Percent		
Intubation	Have not	39	97	1	2.5	40	67
	Have	10	52	9	47	19	33
Total		49	83	10	17	59	100

Table 8 examines the mortality rates among patients with and without neutropenia. The analysis reveals that patients with neutropenia have a significantly higher mortality rate, with 43% of neutropenic patients dying compared to 9% of non-neutropenic patients. The overall mortality rate was 17%, with 6 out of 10 deaths occurring in the neutropenic group. These findings suggest that neutropenia is associated with increased mortality, potentially due to the severity of underlying conditions or complications related to neutropenia itself.

**Table 8. Frequency distribution of patients based on neutropenia and death.**

		Mortality				Total	Percent
		Have not	Percent	Have	Percent		
Neutropenia	Have not	41	91	4	9	45	76
	Have	8	57	6	43	14	23
Total		49	83	10	17	59	100

#### 4. DISCUSSION

Candidemia poses a significant challenge in medical centers, contributing substantially to mortality and morbidity. Its epidemiology varies widely, making it a complex issue in modern medicine. Despite advancements in medical science, the need for a more detailed examination of candidemia remains pressing. In a recent study, 98 cases were initially considered, but after excluding 9 samples, a total of 59 patients were analyzed. The demographic breakdown showed that 52.5% of the patients were male and 47.5% were female. This contrasts with a study by Natalie *et al.* at Columbia University, where 53 patients were male and 20 were female. During the study period, a total of 2,230 positive cultures were reported, with 48 of these being *Candida*. This represents a fraction of the overall positive cultures, highlighting the importance of targeted surveillance. In comparison, Nelson's book cites a statistic of 0.3, which underscores the variability in reported rates of *Candida* infections across different studies [1]. The average age of 30 patients in this study is 30 months, with a standard deviation of 28.69 months. In the study by Tali *et al.*, this average is equal to a 45-month prevalence [13-20] and 59.30% *Candida albicans* against 4067% of patients. In the study by David *et al.*, this amount was 54.4, and 45 *albicans* in the study by Selby *et al.* and Gand [16].

*Yedda albicans* was the dominant species studied [18], which reflects the results of this study. In the study by Arnold *et al.*, *albicans* was the most common species of Bord [21]. According to these results, *albicans* is the most

common species.

On the other hand, the size of the *Candida* colony could not be compared and checked due to the lack of necessary facilities in this center to count *Candida* colonies.

In this study, death was statistically significantly higher in patients who were intubated. On the other hand, neutropenia was significantly more common in patients who died.

In a study conducted by Selbi in Turkey, mechanical ventilation was significantly higher in deceased patients [17]. In the study conducted by Peter at the University of Alabama, death was significantly higher in patients with intubation and osteopathic patients. In this study, 508 TPN patients were included, and 22 patients had underlying diseases.

About 94.9 patients had venous deafness, and 16.9% of patients had DEVICE [Shaldon internal pacemaker, micronephrostomy]. Regarding the number of patients who did not have an intravenous catheter, they were related to the patients in the blood department who had a port. In general, in all the studies related to the presence of foreign bodies in these patients, whether through different ways in the body or other embedded tools, it is considered a risk factor in these patients.

In these patients, 55.9% of the patients had a stay in the hospital of more than one month, which is significantly higher in these patients. Among the patients, 44 [74.5] patients were treated with antibiotics more than 10 times. They found that these compounds were mainly compounds, including ceftriaxone and vancomycin, ceftazidime and vancomycin, meropenem and vancomycin, ampicillin and safer taxim, and cefotaxim and vancomycin.

According to the above findings, it seems that due to the progress of medical science and the chronicity of hospitalized patients and diseases, the prevalence of candidemia is increasing, and the pattern of the disease is changing.

Among the patients, only 45 had culture after treatment, and the rest could not be evaluated due to a lack of file information. Among these patients, 4 had positive cultures again. These patients included a urology department patient with bladder exstrophy and an immunodeficiency patient.

In the study by Hater, the most common inpatient department in terms of the prevalence of disseminated candidemia was the ICU, followed by the heart and blood, oncology, and gastroenterology departments, while in the study by Priya *et al.*, oncology and the lung department were common [13]. The presence of patients with candidemia was clearly higher in the NICU than in the ECU distribution, which was probably due to the longer presence and chronicity of more patients in the PICU. The general reason for the higher number of patients in the ICU department is the transfer of sick patients in this center to the ICU department. According to the number of hospitalizations in the special ward, the distribution of

patients was similar to the study by Priya [13].

Among the patients, 10 cases, equal to 16.9 patients, died, of which 5 were patients with *Candida albicans* culture and the rest were non-*albicans*. The mortality rate in the non-*albicans* group was equal to 2008, and in the *Albicans* group, it was equal to 14.2%. While the mortality rate in the non-*Albicans* group was lower in the study of de Poyd *et al.* [16], in the patients of this study, the amount of *Candida albicans* and non-*albicans* had the same distribution.

The findings of this study highlight the importance of candidemia as a significant complication in pediatric patients, particularly those with prolonged hospital stays and exposure to invasive medical devices. The prevalence of *Candida albicans* and non-*albicans* species underscores the need for tailored antifungal therapies based on species identification. The association between intubation, neutropenia, and higher mortality rates emphasizes the critical role of these factors in patient outcomes. Furthermore, the increasing use of antibiotics and advancements in medical technology contribute to the rising incidence of candidemia, necessitating vigilant infection control practices and judicious use of antifungal prophylaxis. The limitations of the study, such as data collection from parents and the lack of comprehensive follow-up cultures, suggest areas for improvement in future research. Future studies should focus on developing evidence-based guidelines for the prevention and management of candidemia in pediatric settings, incorporating insights from diverse healthcare contexts, especially in low- and middle-income countries. Additionally, exploring the cost-effectiveness of antifungal treatments and their impact on healthcare resource utilization could inform policy decisions aimed at optimizing care for children with candidemia. Ultimately, addressing the complex interplay of risk factors and treatment strategies for candidemia requires a collaborative approach that integrates clinical expertise, epidemiological insights, and economic considerations to improve outcomes for vulnerable pediatric populations.

## CONCLUSION

According to this study and other studies, it seems that as instrumental interventions and drug therapy become more advanced, despite the fact that the survival of patients improves, the complications that patients face increase, including candidemia. This issue is clearly evident from the ratio between the length of stay of the patient and the broadening of the range of antibiotics, and the increase in the prevalence of candidemia. In fact, the increasing number of complex patients, who may have been considered ill-health and low survival until a few years ago have today joined the ranks of patients with good health. This has been implemented under the shadow of these many medical and drug interventions, but at the cost of increasing complications, such as candidemia. Another point is that candidemia was only one of the many complications of Shababeh in this study, and so on. It was evident in the results of our study, especially in the cases

of financial and complex pharmacotherapy. Further, its correlation with mortality is another proof of the need for attention and precision, and reducing unnecessary medical interventions and drug treatments. Another one of the important topics is sufficient accuracy regarding the stay of patients in medical centers. It is very clear that not only from the financial point of view, but also from the point of view of the risk of suffering from complications, such as sedation and its consequences, a stricter point of view should be applied to the standards governing the stay and discharge of patients in medical centers.

## LIMITATIONS OF THE STUDY

The limitations of the study, such as data collection from parents and the lack of comprehensive follow-up cultures, suggest areas for improvement in future research.

## AUTHORS' CONTRIBUTIONS

Study conception and design were contributed by SM and BSM; data collection was done by MRM; analysis and interpretation of results were performed by BSM, AR, and AD; and the draft manuscript was prepared by AG and SD. All authors reviewed the results and approved the final version of the manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study received ethical approval from the Research Ethics Committee in the Qazvin University of Medical Sciences, Iran, with Ethical code of IR.QUMS.RES.1400.456.

## HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committee and with the 1975 Declaration of Helsinki, as revised in 2013.

## CONSENT FOR PUBLICATION

Patient information was recorded after obtaining consent from the parents.

## AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## STANDARDS OF REPORTING

STROBE guidelines have been followed.

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## CONFLICT OF INTERESTS

The authors declare no conflict of interest, financial or otherwise.

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