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Invasive candidiasis in a pediatric tertiary hospital: Epidemiology, antifungal susceptibility, and mortality rates

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Abstract

Invasive infections caused by non-albicans *Candida* are increasing worldwide. However, there is still a lack of information on invasive candidiasis (IC) in the pediatric setting, including susceptibility profiles and clonal studies. We investigated the clinical, epidemiologic, and laboratory characteristics of IC, possible changes in antifungal susceptibility profiles over time, and the occurrence of clonality in our tertiary children's hospital. We analyzed 123 non-duplicate *Candida* isolates from sterile sites of pediatric patients in a tertiary hospital in southern Brazil, between 2016 and 2021. Data on demographics, comorbidities, and clinical outcomes were collected. *Candida* species distribution, antifungal susceptibility profiles, biofilm production, and molecular epidemiology of isolates were assessed using reference methods. The range of IC incidence was 0.88–1.55 cases/1000 hospitalized patients/year, and the IC-related mortality rate was 20.3%. Of the total IC cases, 42.3% were in patients aged < 13 months. Mechanical ventilation, parenteral nutrition, and intensive care unit (ICU) admission were common in this group. In addition, ICU admission was identified as a risk factor for IC-related mortality. The main site of *Candida* spp. isolation was blood, and non-albicans *Candida* species were predominant (70.8%). No significant clonal spread was observed among isolates of the three most commonly isolated species, and 99.1% of all isolates were biofilm producers. Non-albicans *Candida* species were predominant in this study. Notably, clonal expansion and emergence of antifungal drug resistance were not observed in our pediatric setting.

Lay summary

The epidemiology of invasive candidiasis has changed over time and there is still a lack of information in the pediatric setting. Non-albicans *Candida* species predominated in this study, clonal expansion and emergence of antifungal drug resistance were not observed in our pediatric setting.

Key words: *Candida* spp., candidemia, pediatric patients, hospital-acquired infections, epidemiological trends.

Introduction

Invasive fungal diseases (IFDs) pose a substantial public health challenge and are associated with high morbidity and mortality rates.[1] A broad spectrum of pediatric patients is vulnerable to IFDs, with candidemia being the leading cause of IFD among hospitalized individuals worldwide.[2,3] This scenario has implications for the length of patient stays and additional healthcare costs. Among several pediatric patient populations, the highest rates of candidemia are observed in neonates and infants aged under 1 year, especially in critically ill patients admitted to intensive care units (ICUs). Notably, candidemia in pediatric patients is associated with better therapeutic outcomes than those in adults.[1–3]

The most common *Candida* species isolated in invasive candidiasis (IC) are *Candida albicans*, *Nakaseomyces glabrata* (*C. glabrata*), *C. tropicalis*, *C. parapsilosis*, and *Pichia kudriavzevii* (*C. krusei*). Besides, a predominance of non-albicans *Candida* species has been described in pediatric and neonatal patients.[2–7] Until recently, the term multidrug-resistant (MDR) was rarely used in the literature on *Candida* spp. However, since the early 2000s, invasive infections caused by non-albicans *Candida* have been increasing in various geographical regions. These infections present diverse antifungal susceptibility profiles and biofilm-forming capacities, which is of concern. *Candida tropicalis* is associated with high mortality in invasive infections and is increasingly associated

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with azole drug resistance.[8,9] In addition, the coronavirus disease (COVID-19) pandemic has led to a significant increase in fluconazole resistance, particularly in *C. parapsilosis sensu stricto*.[10] This underscores the importance of the effective management of *Candida* spp. infections, including infection control strategies, rapid diagnosis, and characterization of susceptibility profiles to optimize antifungal therapy.[1,8,9,10].

The lack of pediatric studies to monitor the epidemiological scenario, including resistance data and molecular research in this age group, especially in Latin America, is an obstacle to the development of prevention policies. Such policies are essential to help the health system control infection at the local, regional and national levels and to facilitate data comparisons with other countries.[11–13] To evaluate the epidemiology of IC in the same institution, we conducted a 5-year retrospective analysis of IC cases in a Brazilian tertiary pediatric hospital. In a previous molecular study of *C. parapsilosis sensu stricto*, we demonstrated the genotypic diversity among isolates of this species.[14] However, information on other species and patients with IC remains lacking.

Thus, in this study, we aimed to describe the clinical characteristics and mortality rates associated with IC, as well as to examine species distribution, antifungal susceptibility patterns, biofilm formation capacity, and molecular typing of *C. albicans* and *C. tropicalis*.

Materials and methods

Study design and patients

This retrospective study included hospitalized patients from a 372-bed pediatric tertiary care teaching hospital in southern Brazil. All patients included in the study were diagnosed with IC between August 2016 and August 2021 and were aged 0–18 years.

Definitions

IC included candidemia and deep-seated candidiasis, which were defined as the recovery of *Candida* spp. from blood or other sterile sites, respectively, in symptomatic patients.[15] For patients who experienced more than one IC episode during the study period, only the first episode was evaluated. Crude mortality was defined as death occurring within 30 days of the onset of invasive *Candida* spp. infection, and IC-related mortality was defined as death occurring within 7 days of the onset of IC in the presence of persistent clinical sepsis or candidemia, or death due to candidemia-related complications.[16]

Data collection and ethical approval

Electronic medical records were retrospectively reviewed for demographic and clinical data, including age, sex, hospital setting, underlying disease, comorbidities, site of infection, and outcome. The study was approved by the Institutional Review Board (IRB) of the participating center (IRB #2.096.359) and was conducted with each patient's anonymity protected.

Statistical analysis

Data are expressed as mean ± standard deviation (SD) for continuous variables and as counts and percentages for categorical variables. In addition, we evaluated the clinical profile of patients in stratified age groups: <13 months (neonates and infants) and ≥ 13 months,[17] and aimed to determine whether any differences existed between the groups. For continuous variables, Student's *t* -test or the Wilcoxon test was used for two independent groups of normally distributed data and to compare two groups of nonparametric data, respectively. Categorical variables were compared using the χ^2 test or Fisher's exact test. A *P*-value < .05 was considered significant. All statistical analyses were performed using GraphPad Prism v 8.0.2.

Species identification and biofilm formation

All 123 non-redundant clinical isolates were stored in skim milk and frozen (–80°C) until phenotypic and molecular characterization. All isolates were cultured to assess their viability and purity, and the species were confirmed by matrix-assisted laser desorption ionization mass spectrometry using a MicroflexTM LT instrument (Bruker Daltonics, Billerica, MA, USA), according to the manufacturer's instructions. The isolation, identification, and determination of the biofilm-forming capacity of all 123 nonduplicate *Candida* isolates included in this study were performed as previously described.[14] Four isolates did not survive freezing (two *Candida tropicalis* and two *C. parapsilosis sensu stricto*) and were, therefore, not available for biofilm and antifungal susceptibility testing and molecular typing.

Antifungal susceptibility testing

Antifungal susceptibility testing for fluconazole (0.125–64 μg/ml), voriconazole (0.016–1 μg/ml), amphotericin B (0.063–8 μg/ml), and micafungin (0.0078–8 μg/ml) was performed in-house using broth microdilution method according to the European Committee for Antimicrobial Susceptibility Testing (EUCAST).[18] Two reference strains, *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258, were included as quality control isolates in each antifungal susceptibility test. The EUCAST clinical breakpoints for *Candida* species were used to interpret the results (EUCAST Antifungal Clinical Breakpoint Table v. 10.0 valid from 2020-02-04).[19]

Multilocus sequence typing (MLST)

MLST was used to type the clinical isolates of *C. albicans* and *C. tropicalis*, as previously described.[20,21] The MLST schemes comprised six to eight housekeeping genes and were determined using the PubMLST database (https://pubmlst.org/organisms/).[22] Briefly, genomic DNA extraction involved a critical step of cell lysis using zymolase to digest the fungal cell wall. This step was followed by the use of guanidium thiocyanate to extract the DNA.[23] DNA extracts were resuspended in ultrapure water, measured, and stored at –20°C until use. A total of 36 *C. albicans* isolates were typed based on seven housekeeping genes: *AAT1a*, *ACC1*, *ADP1*, *MPIb, SYA1*, *VPS13*, and *ZWF1b*. Additionally, 26 *C. tropicalis* isolates were typed based on 6 housekeeping genes: *ICL1*, *MDR1*, *SAPT2*, *SA PT4*, *XYR1,* and *ZWF1a*. Polymerase chain reaction (PCR) assays were performed as previously described.[20,21] The PCR products were first analyzed by 1.5% w/v agarose gel electrophoresis to verify the presence and size of the amplicon. Subsequently, they were purified using the ExoSAP-IT PCR Product Cleanup Reagent (Thermo Fisher Scientific, Milan, Italy). Bidirectional DNA sequencing was performed on an ABI 3500 automatic sequencer (Applied Biosystems, Foster City, CA, USA) using the same MLST locus-specific primers used for PCR. Alignments of the sequence

Table 1. Demographic and clinical characteristics of all patients with IC ($n = 123$) and risk factors by age stratification.

Variables	Total	Age groups		*P*-value
		< 13 months	≥ 13 months	
	$n = 123$ (%)	$n = 52$ (%)	$n = 71$ (%)	
Gender				.3629
Female	61 (49.6)	23 (44.2)	38 (53.5)	
Male	62 (50.4)	29 (55.8)	33 (46.5)	
Samples				.4678
Blood	110 (90)	47 (90.4)	63 (88.7)	
Fluids sterile	11 (9.0)	5 (9.6)	6 (8.5)	
Biopsy (bone fragment)	2 (1.0)	0 (0)	2 (2.8)	
Hospital Setting				**.0001**
No ICU	59 (47.9)	14 (27.0)	45 (63.4)	
ICU	64 (52.1)	38 (73.0)	26 (36.6)	
Cardiology	13 (10.7)	8 (15.4)	5 (7.0)	.1511
Surgical	20 (16.2)	8 (15.4)	12 (16.9)	> .9999
General	16 (13.0)	7 (13.4)	9 (12.7)	> .9999
Neonatal	15 (12.2)	15 (28.8)	0 (0)	**< .0001**
Prior Pathologic Conditions				
Malignancy	24 (19.5)	6 (11.5)	18 (25.4)	.0674
Hematological neoplasia	12 (9.7)	1 (1.9)	11 (15.5)	**.0132**
Solid tumor	12 (9.7)	5 (9.6)	7 (9.9)	> .9999
Heart diseases	21 (17.1)	12 (23.1)	9 (12.7)	.1505
Renal diseases	26 (21.1)	9 (17.3)	17 (23.9)	.5031
Liver diseases	8 (6.5)	5 (9.6)	3 (4.2)	.2808
Neurological disease	43 (34.9)	18 (34.6)	25 (35.2)	> .9999
Primary immunodeficiency	6 (4.9)	3 (5.7)	3 (4.2)	.6968
Surgery	87 (70.7)	41 (78.8)	46 (64.9)	.1102
CVC	109 (88.6)	46 (88.5)	63 (88.7)	> .9999
Mechanical ventilation	59 (48.0)	32 (61.5)	27 (38.0)	**.0113**
Parenteral nutrition	32 (26.0)	21 (40.4)	11 (15.5)	**.0032**
Dialysis	19 (15.4)	7 (13.4)	12 (16.9)	.8012
***Candida* species**				
Candida parapsilosis complex	44 (35.8)	22 (42.3)	22 (17.9)	.2534
C. albicans	36 (29.2)	17 (32.7)	19 (26.8)	.5489
C. tropicalis	27 (21.9)	5 (9.6)	22 (31.0)	**.0074**
Other	16 (13.1)	8 (15.4)	8 (11.3)	.5909
Mortality				.6507
IC-related death	25 (20.3)	12 (23.1)	13 (18.3)	

ICU, intensive care unit; CVC, central venous catheter. *Note*: All *P-values* were obtained using Fisher's exact test, except for samples, where the χ^2 test was used (∗).

data were manually adjusted for each gene using Bioedit v. 7.2 software.[24] We analyzed the allelic status (homozygote or heterozygote) of each nucleotide based on the chromatograms. Heterozygosity was identified by the presence of two peaks at the same polymorphic loci on both strands, and the consensus sequences of seven or six loci of all isolates were determined. The number of alleles and diploid sequence types (DSTs) were determined by comparing the sequences with those available in the *C. albicans* and *C. tropicalis* MLST databases (https://pubmlst.org/bigsdb?db=pubmlst_calbicans_seqdef and https://pubmlst.org/bigsdb?db=pubmlst_ctropicalis_seqdef).

Results

A total of 123 patients with IC were included in this study. Of them, 52 (42.3%) involved patients aged < 13 months, 5 of whom were neonates. A balanced distribution of patients according to sex was observed, and multiple underlying diseases and other risk factors associated with IC were identified. The demographic and clinical characteristics of the patients are summarized in Table 1.

Of the 123 strains, 89.4% were isolated from blood, 5.7% from ascitic fluid, 2.4% from cerebrospinal fluid, 1.6% from bone fragments, and 0.8% and pleural fluids. Changes in the incidence and crude and IC-related mortality rates during the 5-year study period are shown in Fig. 1A. The distribution of IC per hospital setting and the variation in the number of IC cases per year are shown in Fig. 1B and C. There were no significant changes in the annual incidence of IC that varied from 0.88 to 1.55 cases/1,000 hospital admissions during the period 2016–2021 ($P = .4076$). Changes in the incidence and crude and IC-related mortality rates during the 5-year study period are shown in Fig. 1A.

The IC-related mortality rate was 20.3%. No significant association was observed between patient age groups and IC-related mortality (Table 1). We also evaluated the association between IC-related mortality and the following variables: patient sex, *Candida* species, and hospital setting. Of the 25 patients who died due to IC-related causes, 13 were male ($P > .9999$), 12 were infected with *Candida parapsilosis* complex, 5 with *C. tropicalis*, 4 with *C. albicans*, and 3 with another species ($P = .1674$, .1400, and > .9999, respectively). Of these variables, only ICU stay was identified as a risk factor for IC-related mortality ($P = .0077$); 19 of the 25 deaths occurred in the ICU.

Candida albicans was isolated from 36 (29.2%) patients, whereas non-albicans *Candida* species were isolated from 87 (70.8%) patients. Table 1 shows the frequencies of the

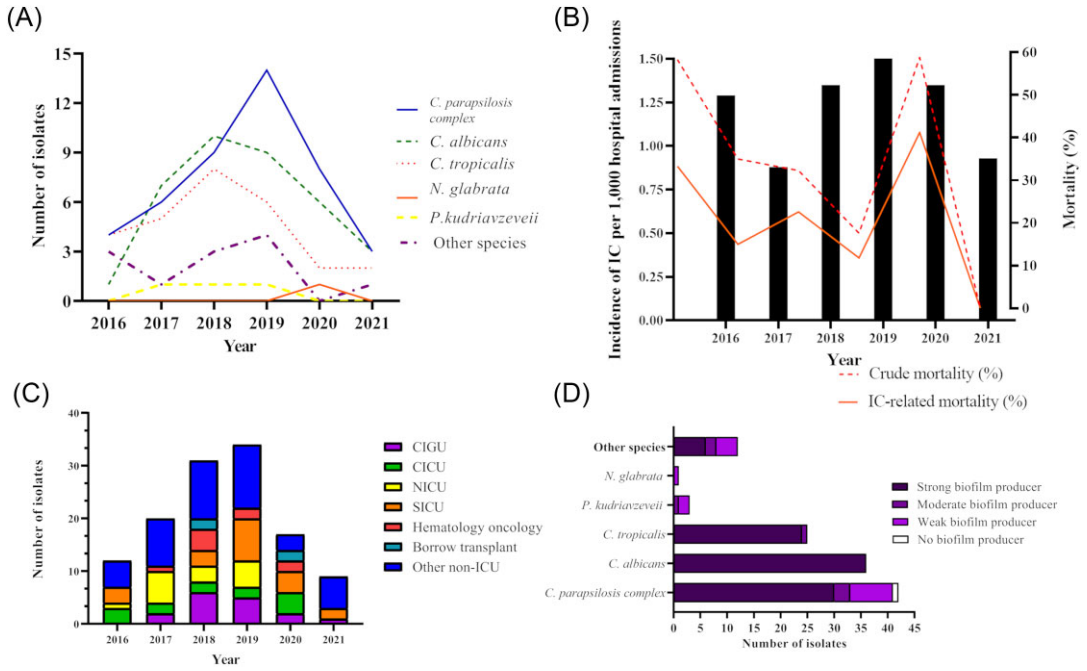

Figure 1. Summary of IC cases and *Candida* species studied. (A) Distribution of *Candida* species over the 5-year study period. (B) IC incidence and mortality data over the years. (C) Number of IC cases by hospital setting and year. (D) Biofilm formation results by *Candida* species.

predominant *Candida* species. Other species identified in this study included *C. lusitaniae* ($n = 5$), *Pichia kudriavzevii* ($n = 3$), *C. guilliermondii* (n = 2), *Nakaseomyces glabrata* ($n = 1$), *C. haemulonii* ($n = 1$), *Cyberlindnera fabianii* ($n = 1$), and *Wickerhamomyces anomalus* ($n = 3$). The latter two were previously known as *C. fabianii* and *C. pelliculosa*.

The distribution of the top five *Candida* species over the 5-year study period and their biofilm-forming capacities are shown in Fig. 1D. In total, 118 (99.2%) of the 119 isolates tested were biofilm-forming, with 96 (81.4%) of them being strong biofilm producers.

A total of 107 isolates were tested for antifungal susceptibility using the EUCAST species-specific clinical breakpoints (*C. parapsilosis sensu stricto, C. albicans, C. tropicalis, P. kudriavzevii, and N. glabrata*). All isolates were susceptible to fluconazole, voriconazole, micafungin, and amphotericin B. The minimum inhibitory concentrations (MIC50 and MIC90) against *C. parapsilosis sensu stricto*, *C. albicans*, and *C. tropicalis* are shown in Table 2.

According to the puMLST database of *C. albicans*, all DSTs of isolates included in our study were identified as unique and previously unassigned, as shown in Supplementary Tables 1 and 2. However, for *C. tropicalis*, 20 isolates were classified as new and unique DSTs, and another 6 isolates were characterized as belonging to previously described DSTs: 7, 124, 232, and 238.

Discussion

The incidence of IC varies by geographic region, type of institution, patient population, and other factors, including the lack of a universal methodology for calculating these data.[6] In Latin America, including Brazil, there is a lack of rate-based data, especially for pediatric cases. Our results show that although the rate of IC at our institution has changed over the course of the study, no significant difference was observed from 2016 to 2021, including during the COVID-19 pandemic. This is different from Europe and the United States, where there was evidence of a decrease in the incidence of candidemia (the main form of IC) prior to the COVID-19 pandemic. This decrease in the pediatric context may be partly related to the implementation of central venous catheter bundles in hospitals.[2,3,25]

One of the largest Brazilian studies performed prospective laboratory surveillance of candidemia from March 2003 to December 2004 in 11 medical centers in different regions of the country. The study included a total of 712 cases of candidemia, among which, 225 (32%) were pediatric cases, with 147 (21%) occurring in children aged < 1 year. The overall incidence was 2.49 cases/1000 admissions, and *Candida* spp. was the fourth most common pathogen isolated from blood cultures.[12] Between 2007 and 2010, the Brazilian SCOPE surveillance project collected and analyzed clinical and microbiological data on non-redundant episodes of nosocomial bloodstream infections (BSIs), including candidemia. *Candida* species were the fifth and seventh most common organisms isolated from BSIs when considering patients aged ≤ 16 years and the total sample, respectively.[11,26] A prospective laboratory surveillance study in 21 tertiary care hospitals in 7 Latin American countries, including Brazil, identified 672 episodes of candidemia between November 2008 and October 2010. Of these episodes, 44.2% occurred in children (23.7% were aged < 1 year). The overall incidence of candidemia recorded in this study was 1.18 cases/1000 admissions.[27]

A recent multicenter study involving eight hospitals in the state of Paraná, Brazil, evaluated 30 pediatric patients out of a sample of 100 patients between 2016 and 2017. The study reported an incidence of candidemia ranging from 0.22 to 1.98 cases/1000 hospital admissions. Despite the differences between the studies, the overall candidemia incidence density

Table 2. Minimum inhibitory concentrations (MIC 50 and MIC 90) of the three most important species identified in the study.

Species		Amphotericin B					Fluconazole					Voriconazole					Micafungin				
	n	Range (μg/ml)	MIC_{50}	MIC_{90}	S ≤	R >	Range (μg/ml)	MIC_{50}	MIC_{90}	S ≤	R >	Range (μg/ml)	MIC_{50}	MIC_{90}	S ≤	R >	Range (μg/ml)	MIC_{50}	MIC_{90}	S ≤	R >
Candida parapsilosis stricto sensu	40	0.06–8.0	≤0.06	≤0.06	1	1	0.125–64	0.5	1	2	4	0.016 - 1.0	≤0.016	0.31	0.13	0.25	0.07–8.0	0.5	1	2	2
C. albicans	36	0.06–8.0	0.125	0.125	1	1	0.125–64	0.25	0.5	2	4	0.016 - 1.0	≤0.016	≤0.016	0.06	0.25	0.07–8.0	≤0.007	≤0.007	0.02	0.02
C. tropicalis	25	0.06–8.0	≤0.06	0.125	1	1	0.125–64	0.5	1	2	4	0.016 - 1.0	≤0.016	0.03	0.13	0.25	0.07–8.0	0.015	0.015	IE	IE

IE, No clinical breakpoint, insufficient evidence.

of 1.2 per 1,000 hospitals admissions reported in the multicenter study aligns with the 5-year average incidence observed in the present study.[13,14] Invasive *Candida* spp. infections remain an important cause of healthcare-associated infections, contributing to a significant burden associated with high costs and a crude mortality of 20-50% despite active antifungal treatment. To address this, countries should focus on improving diagnostic capacity, enhancing management strategies and strengthening surveillance systems. These steps are critical for timely detection and effective treatment, which can help lower mortality rates.[1]

Our results show an IC-related mortality rate of 20.3%, which is in agreement with the results of other pediatric studies that also found a higher mortality rate in ICU patients.[2,5,25,28,29] Overall, 19 of 64 ICU patients died, while 6 of 59 non-ICU patients had this outcome ($P = .00777$). Consistent with our findings, findings of previous studies conducted in our hospital revealed mortality rates ranging from 14% to 32% in patients with IC.[5,30]

As expected, the main form of IC identified in this study was candidemia (90%). No differences were observed between the two sexes (61 females and 62 males) or between the distribution of ICU and non-ICU patients (64 and 59, respectively), unlike other reports wherein male and ICU patients were predominant (11 and 29). Regarding previous pathological conditions, 34.9% of the patients had a neurological disease, and 70.7% had undergone surgery. Regarding invasive medical devices, 88.6% of the patients had a central venous catheter, and 48% were on mechanical ventilation, both of which were previously described as risk factors for IC.[7,25,31]

To better understand the clinical characteristics and prognostic factors of pediatric IC, we reviewed the demographic, clinical, and laboratory characteristics of our 123 IC patients. We compared the data between patients aged < 13 months and ≥ 13 months, considering the knowledge that the highest rates of IC are recorded in neonates and infants aged < 1 year.[3]

Significant differences were observed in ICU stay at the time of IC, the use of mechanical ventilation, and parenteral nutrition between the age groups, all of which were associated with patients aged < 13 months (Table 1). It is important to note that this group (< 13 months) had only five neonates, which might explain the lack of differences in outcomes between the age groups, as previously described.[16] A difference in the occurrence of hematological neoplasia was also observed between the groups, with 11 out of 12 cases occurring in patients aged ≥ 13 months ($P = .0132$).

*C. tropicalis w*as not the most isolated species, ranking third in both age groups. However, it was a significant pathogen in the ≥13 months group ($P = .0074$), occurring in 22/71 cases versus 5/52 cases in the <13 months group, consistent with findings from other studies.[12,32] These findings are important considering that *C. tropicalis* is one of the most common non-albicans species associated with candidemia, with generally high mortality rates, even in pediatric patients (26–40%).[1]

The frequencies of isolated *Candida* spp. in this study were as follows: *C. parapsilosis complex* (35.8%), *C. albicans* (29.2%), *C. tropicalis* (21. 9%), *C. lusitaniae* (4.1%), *Pichia kudriavzevii* (2.5%), *Wickerhamomyces anomalus* (2.5%), *C. guilliermondii* (1.6%), and *Nakaseomyces glabrata*, *C. haemulonii,* and *Cyberlindnera fabianii* (0.8% each). Although some centers have reported the prevalence of *C.*

albicans, inversion to non-albicans species is common in pediatric candidiasis. This is especially notable with *C. parapsilosis*, which occupies first place in the ranking.[3,,28] This complex remains a concern due to its typical association with colonization of central venous catheters, horizontal transmission via healthcare workers' hands, and recent reports of clonal transmission of azole-resistant isolates.[33] Limited clonality has been observed in our hospital, as demonstrated in a previous article that indicated high genotypic diversity among the isolates. This diversity did not appear to have a clear association with the hospital setting and patients involved.[14]

Formal MLST schemes have been published for other pathogenic *Candida* species, including *C. albicans*, *C. tropicalis*, *N. glabrata*, and *P. kudriavzevii* (https://pubmlst.org/organisms?title=Candida). MLST is an important tool for studying the genetic diversity of multiple isolates, allowing us to compare our data with those from other regions of the world.[34] Considering our institution's epidemiological data, we investigated the circulation of clonal isolates solely for *C. albicans* and *C. tropicalis*. For *C. albicans*, all DSTs were unique and unpublished. *C. albicans* is known to have a high degree of genetic diversity, especially with a high frequency of heterozygosity, which can be observed in this study along the analyzed housekeeping genes with the description of several new alleles.[34] In *C. tropicalis*, a lower frequency of new alleles was observed among the housekeeping genes compared with *C. albicans*. A total of 20 new DSTs were identified among the clinical isolates of the species, and only three DSTs (of the 24 identified in this study) occurred in more than 1 isolate: 124, 232, and a new one (Supplementary Tables 1 and 2). Except for isolates Ctr25 and Ctr27, which were identified in the same period from blood samples of two different patients who were hospitalized in the same ward with nosocomial infections, there was no clear evidence in our study of other cases of intra-hospital transmission of *Candida* spp. This may indicate the occurrence of endogenous infections or infections from different exogenous (environmental) sources without clonal circulation. Cloning seems to be associated with the emergence of azole-resistant isolates.

Evaluation of the susceptibility profiles of *Candida* isolates confirmed another important point: the non-emergence of resistance among our isolates, even after the COVID-19 pandemic, a scenario similar to that observed in other pediatric institutions.[28,35] These data include a previously reported isolate that was not susceptible to fluconazole using gradient diffusion strips14. This isolate was now tested by broth microdilution and was susceptible. This type of major categorical error has been described previously, and the result by the gold standard method is consistent with the fact that only a silent mutation in the ERG11 gene was identified and described in this isolate.[14,36] Notably, the *C. parapsilosis* complex had a high MIC for echinocandins, probably because of a naturally occurring *FKS1* polymorphism, but all strains were susceptible (Table 2).[33] Almost all our isolates (99.2%) were able to form biofilms. This finding is important for understanding the pathophysiology of IC. *Candida* spp. are prone to forming biofilms on catheters, making them more resistant to host immune responses and antifungal therapies.[37]

In summary, this study presents a 5-year epidemiological analysis of IC in pediatric patients treated at a large Brazilian tertiary hospital. The findings provide evidence of the prevalence of non-albicans species, the absence of clonal circulation, and the presence of resistant isolates. Understanding the resistance profiles of the different *Candida* species causing IC is important for developing empirical treatment protocols. While echinocandins are currently the first-line therapy for patients, fluconazole can be considered for progressive oral therapy if the microorganism is susceptible. We emphasize the importance of continuously monitoring susceptibility profiles and maintaining infection control measures. It is noteworthy that clonal outbreaks of resistant *Candida* spp. are not limited to *C. auris* but extend to the *C. parapsilosis* complex and *C. tropicalis*. They are two of the most common species reported in this study, with *C. tropicalis* being particularly prevalent in patients aged $\geq$ 13 months. This study found that mechanical ventilation, parenteral nutrition, and ICU stay were prevalent in patients aged $<$ 13 months. Additionally, ICU stay was identified as a risk factor for IC-related mortality.

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Author contributions

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Supplementary material

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Declaration of interest

None.

Data availability

All supporting data are provided in the article or in supplementary data files. Two supplementary tables are available with the online version of this article. All new alleles and assigned diploid sequence types (DSTs) are available on pubMLST (https://pubmlst.org/).

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