ORIGINAL ARTICLE

Emerging Non-albicans *Candida* as a Cause of Urinary Tract Infection in Pediatric Patients

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ABSTRACT

Background: *Urinary tract infections (UTIs) by* Candida *species are becoming a common finding in hospitalized patients. Such association is higher in hospitalized pediatric patients. Candida albicans is the predominant fungal pathogen implicated in UTIs.* ***Objective:*** *This study aimed to demonstrate the prevalence of candiduria in pediatric patients with UTIs, characterize the Candida species involved, and evaluate their susceptibility to antifungal agents.* ***Methodology:*** *Candida species were isolated and identified in urine samples collected from 100 hospitalized children, comprising 76% from Inpatients' Units and 24% from Outpatients' Units, who were ranged in age from 25 days to 15 years. The automated VITEK 2 system was employed for both the identification of Candida species and susceptibility testing against various antifungal agents. Biofilm production from both albicans and non-albicans Candida was determined using the microtiter plate method.* ***Results:*** *Non-albicans Candida constituted more than half (52%) of the Candida isolates. A higher incidence of Candida species was observed in male patients from Inpatients' Units in the 1-5 years age group. Additionally, this study revealed a greater prevalence of Candida species among pediatric patients receiving antibiotic treatment. The seven identified Candida species exhibited varying sensitivity to antifungal agents. Biofilm formation was more prevalent in non-albicans Candida.* ***Conclusion:*** *Candida tropicalis was the most prevalent non-albicans Candida (40%), being the most prolific biofilm producer. Amphotericin B and Micafungin were the drug of choice according to their complete sensitivity pattern.*

INTRODUCTION

Funguria is a urinary tract infection (UTI) related to fungi, with almost all fungal UTIs are caused by *Candida* species[1,2]. Urinary tract instrumentation, previous antibiotic courses, extended hospitalization, age, diabetes mellitus, female sex, and use of immunosuppressive medication are among the predisposing variables usually linked with Candiduria[3]. *Candida*'s pathogenicity is largely influenced by a number of significant elements, including the development of "biofilms", that are adhering to surfaces[4]. This is especially important due to currently thought that a sizable number of all human microbial infections include the development of biofilms. Microbial biofilms inherently play a role in the resistance to anti-fungal agents, rendering them ineffective during treatment of Candiduria[5]. To ensure proper handling or to take into consideration the differences in the capacity to produce biofilms among the various species of *Candida*, the impacted devices need to be far away. Specifically, it's critical to figure out whether the medical outcome for individuals with Candiduria is impacted by the biofilms that *Candida* species generate, which are inherently linked to their infectiousness[6].

Azoles, Echinocandins, Polyenes, and Flucytosine are the commonly used antifungal medications in treatment of fungi-related illnesses, however, Azoles are the most extensively medication used[7]. The VITEK 2 System is a reliable, fully automated, rapid alternative technique which allows both fungal identification and Minimum inhibitory concentration (MIC) determination simultaneously, including Amphotericin B and azole-resistant organisms. The VITEK 2 System uses an integrated software program that verifies and clarifies the results and allows species identification through the comparison of the biochemical profile with an extensive database, where results are compared to those from the European Committee on Antimicrobial Susceptibility Testing's reference protocols (EUCAST)[8].

This study aimed to demonstrate the prevalence of candiduria in pediatric patients, characterize the

Candida species involved, and evaluate their susceptibility to antifungal agents.

METHODOLOGY

The present study has been approved by the Research Ethics Committee, Ain Shams University (ASU-SCI/MICR/2024/6/2). All procedures were conducted following the ethical consideration standards of the 1964 Declaration of Helsinki.

Study design, patients, and data collection:

Samples were collected over a one-year study between March 2017 and March 2018 from Abu El-Reesh (El-monira) Children's Hospital, Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University and included: Neonatal Intensive Care Unit (NICU), Inpatients, Outpatients, and Kidney Transplantation Unit.

Clinical specimens:

The routine microbiological examination was conducted in the Microbiology Laboratory at Abu Al-Rish Children's Hospital (Al-Munira), Kasr Al-Aini Hospital, Faculty of Medicine, Cairo University. 100 urine samples were used for culturing by laboratory workers following collection from pediatric patients who are subjected to data for UTI case selection that included: age (few days to 15 years), gender (male or female), department, and receiving antibiotic treatment or not.

Isolation and purification of *Candida* species from clinical specimens:

Urine samples were cultured on Sabouraud Dextrose Agar (SDA), (Bio-Rad, France) (LOT 4E2213), supplemented with Chloramphenicol[9] followed by incubation aerobically at 37℃ for 48 hrs.

Identification and differentiation of *Candida* species:

Identification of the suspected *Candida* cultures was conducted in the Mycology research laboratory, Department of Microbiology, Faculty of Science, Ain-Shams University. Isolates were phenotypically identified based on their morphological and physiological characteristics by: Germ tube test[10], detection of colony morphology and sub-culturing on a chromogenic agar medium. Colonies were checked for size, shape and texture. Chromogenic agar, (TM Media, India) (LOT/B.NO.M1BJ71R01), was also used to identify colonies according to their color after sub-culturing on the CHROME agar and incubation at 30℃ for 48 hrs. The chromogenic mixture produces different colored colonies that facilitate the identification and differentiation of *Candida* species[11]. All the identified *Candida* isolates were stored in 20% glycerol broth at -20℃ for future analysis[12].

Automated identification of *Candida* species using VITEK 2 System:

Confirmation of yeast species identification and the evaluation of their susceptibility profiles were performed in an automated manner by VITEK 2 yeast identification System (bioMérieux, Marcy l'Etoile, Paris) according to the manufacturing manual[13].

Antifungal susceptibility test of the yeast isolates:

The obtained *Candida* isolates were tested for susceptibility to six main antifungals: Polyenes (amphotericin B), Azoles (Fluconazole and Voriconazole), Echinocandins (Caspofungin and Micafungin), and Flucytosine using the VITEK 2 yeast identification System. The VITEK 2 technique's basic idea is based on the minimal inhibitory concentration (MIC) of broth micro dilution to be identified by comparing the growth of the tested isolates to the growth of reference isolates with known MICs. It is almost identical to having a standard curve built up in the VITEK 2 that links the reference MICs to microbial activity in antibiotic wells[13].

Biofilm production by *Candida* species:

Biofilm formation assays for *Candida* species was determined by the microtiter plate method. *Candida* isolates were grown on Sabouraud Dextrose Broth (SDB) at 37℃ for 24 hrs. The turbidity of the suspension was adjusted to approximately 3 X 10^7 CFU ml^{-1} using the DensiCheck Plus Turbidometer. Each well of polystyrene microtiter plates was inoculated with 20µL of yeast cell suspension and 180µL of SDB. The microtiter plate is read spectrophotometrically by a microtiter plate reader at a wavelength of 405 nm. The spectrophotometric readings were used to calculate the %T values. The %T value for each test sample was subtracted from the %T value of the blank. The result was interpreted as follows: Negative results when (%T value < 5) and positive results when (%T value > 5). Positive isolates scored +1 when their %T value range was 5-20, 2+ when %T value ranged from 20–35, 3+ when %T value ranged from 35–50, and 4+ when their %T value was ≥ 50.[14].

Statistical analysis:

All data were subjected to analysis with the Graphpad Prism version 5 software (Graphpad, San Diego, CA). Comparisons between the study groups were made with the Chi square (X^2) test. P-values < 0.05 were considered statistically significant[15].

RESULTS

Identification of *Candida* from clinical specimens:

Out of 100 yeast isolates, 48 isolates showed positive germ tube formation (germ tube test was positive only with *Candida albicans*). The isolated *Candida* species were distinguished on chromogenic agar medium according to their colony color. (Figure 1).

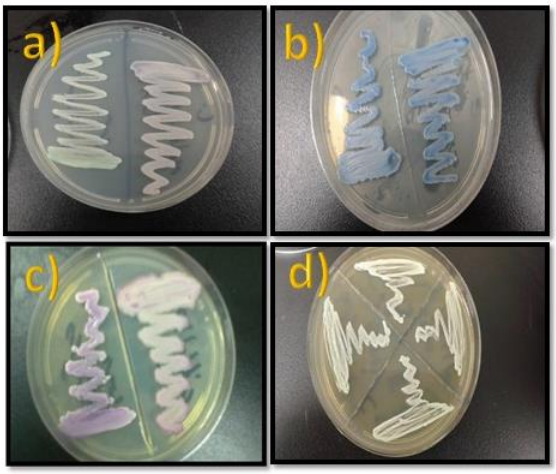

Fig. 1: Culture characteristics of *Candida* species on CHROM agar medium. (a) Light green colonies for *C. albicans* and pink colonies for *C. krusei.* (b) Blue colonies for C. tropicalis. (c) Violet colonies for C. glabrata. (d) Creamy to white colonies for other non-albicans *Candida.*

Automated identification of *Candida* species using VITEK 2 System:

Distribution of Candida species among urinary samples

The VITEK 2 System was applied to identify the isolates obtained from the collected samples. Forty-eight isolates (48%) were identified of as *Candida albicans*, while with Non-*albicans Candida* accounted for 52%. (Figure 2).

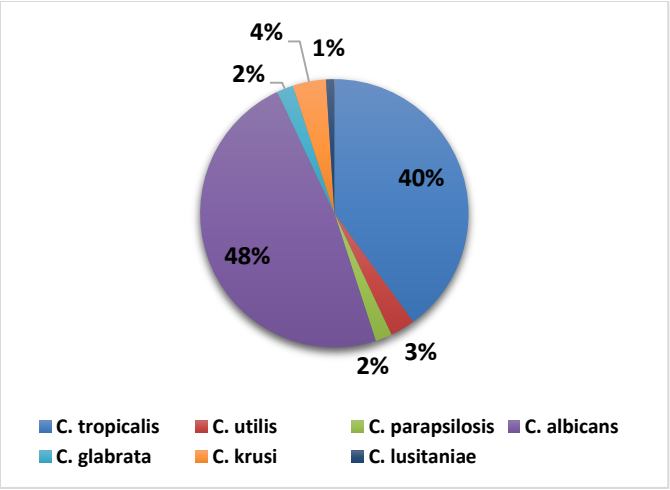

Fig. 2: Incidence of isolated *Candida* species among the 100 urinary samples.

Candida species distribution with respect to gender

Incidence of *Candida* species according to gender showed a high distribution of *Candida* infection among male pediatric patients (73 patients) compared with *Candida* infection in female pediatric patients (27 patients). The high distribution of male infection was along all different age groups. (Figure 3).

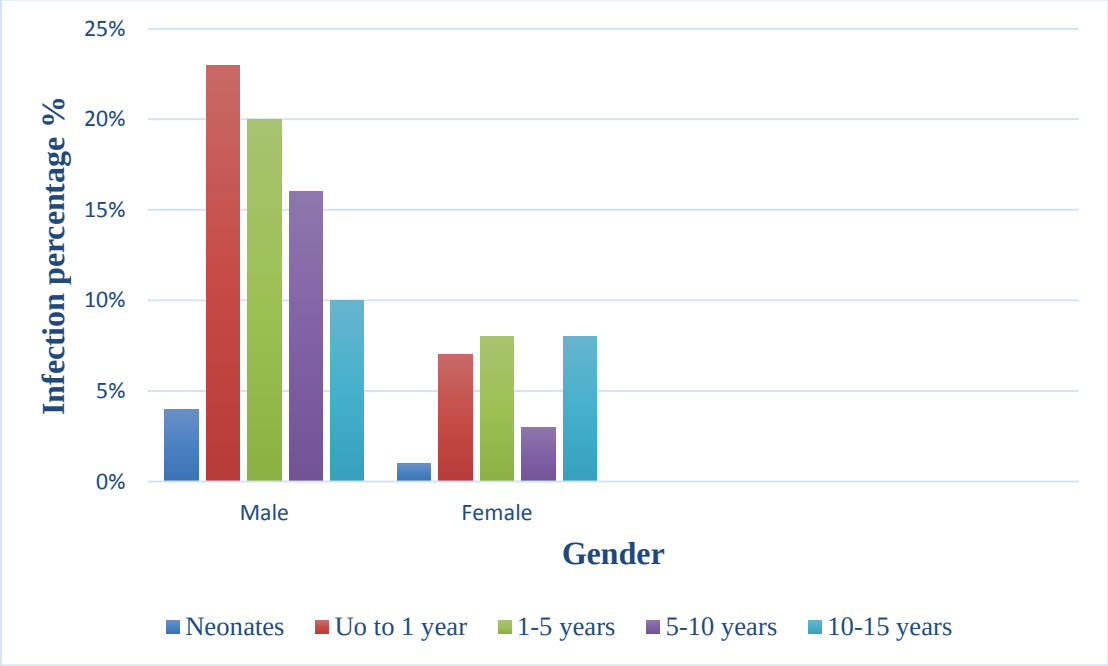

Fig. 3: Distribution of *Candida* species among male and female pediatric patients.

Six *Candida* species were isolated from samples collected from male patients, whereas four *Candida* species were isolated from female patient. Such results were statistically significant especially for the most prevalent species *Candida albicans*. (Table 1).

Table 1: Distribution of *Candida* species between children male and female patients.

Species / Gender N (%)	Children males 73 (%)	Children females 27 (%)	Total 100 (%)	P value
Candida albicans	34(46.58%)	14(51.85%)	48 (%)	**0.0163**
Candida tropicalis	30(41.09%)	10(37.04%)	40 (%)	**0.0203**
Candida parapsilosis	2(2.74%)	0(0.0%)	2 (%)	**0.0204**
Candida utilis	3(4.11%)	0(0.0%)	3 (%)	0.0638
Candida krusei	3(4.11%)	1(3.70%)	4 (%)	0.3504
Candida glabrata	0(0.0%)	2(7.41%)	2 (%)	0.2381
Candida lustaniae	1(1.37%)	0(0.0%)	1 (%)	0.9808

Candida species distribution with respect to patient's age group

The distribution of *Candida* species isolated in this study was correlated with different age groups of pediatric patients. Results were significantly varied among different species of *Candida*, *with a* P-value < 0.0001. (Table 2).

Table 2: Distribution of *Candida* species among different age groups.

Age Groups / N (%)	Neonates 5 (%)	Up to 1 year 29 (%)	(1-5) years 26 (%)	(6-10) years 19 (%)	(11-15) years 18 (%)	P value
Candida albicans	5 (100%)	20(68.97%)	13(44.83%)	7(36.84%)	3(16.67%)	< 0.0001
Candida tropicalis	0(0.0%)	8 (27.59%)	11(37.93%)	9(47.37%)	12(66.67%)	< 0.0001
Candida parapsilosis	0(0.0%)	0(0.0%)	1(3.44%)	1(5.26%)	0(0.0%)	< 0.0001
Candida utilis	0(0.0%)	0(0.0%)	1(3.44%)	2(10.53%)	0(0.0%)	< 0.0001
Candida krusei	0(0.0%)	1(3.44%)	2(6.91%)	0(0.0%)	1(5.55%)	< 0.0001
Candida glabrata	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	2(11.11%)	< 0.0001
Candida lustaniae	0(0.0%)	0(0.0%)	1(3.44%)	0(0.0%)	0(0.0%)	< 0.0001

Candida species distribution with respect to Antibiotics treatments

Number of patients who received antibiotic treatment was found to be (68%), compared with patients not received antibiotic treatment (32%). The seven tested *Candida* species were recognized in samples from pediatric patients received antibiotics treatment. Whereas, only five species of *Candida* were identified in samples from non-treated pediatric patients. Results revealed non-statistically significant differences (*P*-values > 0.05) between the different species of *Candida* respecting Antibiotics treatments. (Table 3).

Table 3: Distribution of *Candida* species among children patients treated & not treated with antibiotics

Species / Antibiotics N (%)	Treated 68 (%)	Not-treated 32 (%)	P value
Candida albicans	35 (51.47%)	13 (40.62%)	0.086
Candida tropicalis	26 (38.24%)	14 (43.75%)	0.187
Candida parapsilosis	2 (2.94%)	0 (0.0%)	0.196
Candida utilis	1 (1.47%)	2 (6.25%)	0.767
Candida krusei	2 (2.94%)	2 (6.25%)	0.917
Candida glabrata	1 (1.47%)	1 (3.13%)	0.930
Candida *lustaniae*	1 (1.47%)	0 (0.0%)	0.938

Incidence of Candida species with respect to hospital units

Number of patients from Inpatient's Units was found to be (78%), compared with Outpatient's Units (22%). Seven *Candida* species were identified in samples from hospitalized pediatric Inpatient's Units. While, Samples from hospitalized pediatric Outpatient's Units showed the presence of only four species. Results were statistically significant for *Candida albicans among samples collected from In- and* Outpatient's Units. (Table 4).

Table 4: Incidence of different *Candida* species among the Inpatient's versus Outpatient's Units

Species / Hospital unit N (%)	Inpatients 78 (%)	Outpatients 22 (%)	P value
Candida albicans	39 (50%)	9 (40.91%)	**0.038**
Candida tropicalis	29 (37.18%)	11 (50%)	0.072
Candida parapsilosis	2 (2.56%)	0 (0.0%)	0.114
Candida utilis	2 (2.56)	1 (4.54%)	0.207
Candida krusei	4 (5.13%)	0 (0.0%)	0.273
Candida glabrata	1 (1.28%)	1 (4.54%)	0.879
Candida lustaniae	1 (1.28%)	0 (0.0%)	0.976

Antifungal susceptibility testing

The susceptibility test of six tested antifungal agents on different *Candida* species showed that Micafungin and Amphotericin B were the most effective against all tested species. Results were statistically significant. (Table 5).

Table 5: The susceptibility test of different antifungal agents on different *Candida* species.

Antifungal / Species	*Candida albicans* (no.=48)	*Candida tropicalis* (no.=40)	*Candida parapsilosis* (no.=2)	*Candida utilis* (no.=3)	*Candida krusei* (no.=4)	*Candida glabrata* (no.=2)	*Candida lustaniae* (no.=1)	*P value*
Fluconazole								
Sensitive	48(53.93%)	34(38.20%)	2(2.25%)	2(2.25%)		2(2.25%)	1(1.12%)	*< 0.0001*
Intermediate								
Resistant		6(54.55%)		1(9.09%)				
Voriconazole								
Sensitive	48(48.48%)	39(39.39%)	2(2.02%)	3(3.03%)		2(2.02%)	1(1.01%)	*< 0.0001*
Intermediate								
Resistant		1(100%)						
Flucytocine								
Sensitive	48(51.06%)	38(40.43%)	2(2.13%)	3(3.19%)	0(0.0%)	2(2.13%)	1(1.06%)	*< 0.0001*
Intermediate								
Resistant		2(33.33%)			4(66.67%)			
Caspofungin								
Sensitive	48(48.98%)	38(38.77%)	2(2.04%)	3(3.06%)	4(4.08%)	2(2.04%)	1(1.02%)	*< 0.0001*
Intermediate		1(100%)						
Resistant		1(100%)						
Micafungin								
Sensitive	48(48%)	40(40%)	2(2%)	3(3%)	4(4%)	2(2%)	1(1%)	
Intermediate								
Resistant								
Amphotericin B								
Sensitive	48(48%)	40(40%)	2(2%)	3(3%)	4(4%)	2(2%)	1(1%)	
Intermediate								
Resistant								

Biofilm production test by isolated *Candida* species:

Biofilm production test showed that 25% of non-*albicans Candida* were positive biofilm producers compared with only 3% in case of *Candida albicans*. Results were significantly varied among different species of *Candida* with a P-value < 0.0001. (Table 6).

Table 6: Biofilm production test for *Candida* species.

Species / Biofilm production	Number of isolates (%)		P value
	Positive 28 (28%)	Negative 72 (72%)	
Candida albicans	3(10.71%)	45(62.5%)	< 0.0001
Candida tropicalis	24(85.71%)	16(22.22%)	< 0.0001
Candida parapsilosis	0(0.00%)	2(2.78%)	< 0.0001
Candida utilis	1(3.57%)	2(2.78%)	< 0.0001
Candida krusei	0(0.00%)	4(5.55%)	< 0.0001
Candida glabrata	0(0.00%)	2(2.78%)	< 0.0001
Candida lustaniae	0(0.00%)	1(1.39%)	< 0.0001

* All positive isolates scored +1 as their %T value range was "5-20".

** Negative results had %T value < 5

DISCUSSION

Recently, there is strong evidence showing a rise in the rate of UTIs produced by fungi, mainly the *Candida* species, especially in critically ill patients. Infections either by *Candida albicans* or by non-*albicans Candida* species are among the most common causes of serious conditions, which have been increased significantly over the past ten years and have substantial negative effects on public health[16]. Urinary tract infection, widespread Candidiasis, was related to the existence of *Candida* species in the urine[17].

Candida glabrata, *Candida parapsilosis*, *Candida tropicalis*, and *Candida lusitanae* have been isolated from urine cultures, however *Candida albicans* remains the species most frequently reported[18,19]. *Candida krusei*, the multidrug-resistant pathogen (MDR), is intrinsic resistant to the Azoles (Fluconazole and Voriconazole) because of its complicated susceptibility profile[20,21].

Many risk factors have been proposed for Candiduria: such as broad spectrum antibiotics therapy, prolonged antibiotics, which all increase the colonization risk by *Candida* species[22].

Our findings, in this study, concluded that (5%) of the reported Candiduria were persisting in neonates, statistical analysis of obtained data showed that (29%) of them was both in patients up to one year (one month - one year), and in patients (one - five years), (19%) in patients (6 - 10 years), whereas (18%) in patients (11 - 15 years) with high statistically significance for *Candida albicans* to neonates. These findings are in good agreement with Malhotra et al.[23] where neonates and pediatric ICUs (up to one year) had the highest rates of Candiduria. Out of the total *Candida* isolates used in this study, 22% were from outpatients' Clinics while 78% were from inpatients' Clinics, among all isolates, *Candida albicans* was highly significant in collected samples from inpatients' units**.** These agree with the obtained results by Gajdács et al.[18] who recorded high percentage of infections for inpatients' compared with outpatients' Clinics**.** Patients in this study who had received antibiotics during their hospitalization period, developed higher infection with Candiduria (68%) than these who did not receive any treatment (32%). This finding was also encountered by different researchers who recognized that the use of antibiotics is considered the major risk factor in progress of *Candida* urinary tract infection (UTI), with more evidence that Candiduria occurs most frequently in patients who had received two or three antibiotics during their hospital stay[23].

Out of the one hundred urine samples collected from the pediatric patients at Abu El-Reesh (El-monira) Children's Hospital, Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University, predominant species were: *Candida albicans* (48%); *Candida tropicalis* the most common of non-*albicans* species (40% out of 52%); *Candida krusei* (4%); *Candida utilis* (3%); *Candida glabrata* (2%); *Candida parapsilosis* (2%), and *Candida lusitaniae* (1%). This agrees with the findings of predominant species (*Candida albicans*) as the mostly isolated from urine of the patients in previous studies, followed by *Candida tropicalis*, *Candida glabrata* and *Candida parapsilosis*[23-26]. However, *Candida tropicalis* was reported in results by other studies as most common isolated species followed by *Candida albicans*[27,28].

Bochicchio et al.[29] and Kauffman[30] reported that non-*albicans Candida* species accounted for more than (50%) of urinary *Candida* isolates in agreement with our study findings.

Antifungal resistance among *Candida* species is beneficial because apart from tracking and detection of such resistance, it also gives clues to the emerging threat by new resistance strains which may aid to examine experimental treatment recommendation. In our study, *Candida albicans* were sensitive 100% to six tested antifungal agents, whereas 85% of tested *Candida tropicalis* were sensitive to Fluconazole, 100% were sensitive to Amphotericin B and 95% were sensitive to Flucytosin. Such results are in accordance with those obtained by Jain et al.[24] who proved that (80%) of isolated *Candida tropicalis* were sensitive to Fluconazole and (100%) were sensitive to Amphotericin B and Flucytosin. For other non-*albicans Candida* species, this study proved that *Candida krusei* was the only species resistant to treatment with Flucytosin (but intrinsically resistant to Azoles) and sensitive to other

three antifungals. Results are in agreement with those recorded by Seifi et al.[31] who found that 100% of the tested *Candida krusei* isolated were 100% Fluconazole resistance. *Candida utilis* in our results was recorded to have resistance to Fluconazole (33.33%), but has sensitivity to Voriconazole, Caspofungin, Micafungin, Amphotericin B and Flucytosin.

Jain et al.[24] reported also Fluconazole resistance by isolates of *Candida glabrata*, confirming previous data by Seifi et al.[31] who reported Fluconazole resistant in (66.6%) of *Candida glabrata* isolates. Whereas, *Candida glabrata*, *Candida parapsilosis* and *Candida lusitaniae* isolates were all sensitive to all the six used antifungals. Observation was directed to biofilm production among all the clinical *Candida* isolates, our results varied significantly and ranged from high to low with the highest percentage of biofilm-production among *Candida* isolates was recorded for the non-*albicans* group especially among the isolates of *Candida tropicalis* (25%) compared with (3%) only among *Candida albicans* isolates. These results are in accordance with those reported by Shin et al.[32] who proved the biofilm positivity occurring most frequently in isolates of *Candida tropicalis* and with the findings of Girish Kumar et al.[33] who reported that biofilm production was found to be common in non-*albicans Candida.*

CONCLUSION

This study documents the prevalence of Candiduria in pediatric patients and record a possible shift towards non-*albicans Candida* species as predominant. It also concludes *Candida albican* as the most common among Candiduria cases (by 48%) that requires early diagnosis and treatment. *Candida tropicalis* was the most prevalent non-*albicans Candida* (40%). Biofilm formation among the *Candida* isolates was highly significant in non-*albicans Candida* species compared with *Candida albicans*, especially in *Candida tropicalis*. Amphotericin B and Micafungin were the drug of choice according to their complete sensitivity pattern detected on all tested *Candida* isolates. Health care professionals' action may help to lessen some of these infections emerge. Also, to stop *Candida* from spreading throughout hospitals, infection control procedures are crucial. Avoiding needless invasive procedures, antibiotics, and parenteral feeding are also crucial in lowering *Candida* possible infection.

Declarations:

Consent for publication: Not applicable

Availability of data and material: Data are available upon request.

Competing interests: The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article. This manuscript has not been previously published and is not under consideration in another journal.

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REFERENCES

1. Pal M, Hofmeister M, Gutama KP, Paula CR, Leite Jr DP. Growing role of Candida albicans as an important cause of nosocomial infection. Journal of Advances in Microbiology Research. 2022;3(1):47-52.
2. Zheng YJ, Xie T, Wu L, Liu XY, Zhu L, Chen Y, Mao EQ, Han LZ, Chen EZ, Yang ZT. Epidemiology, species distribution, and outcome of nosocomial Candida spp. bloodstream infection in Shanghai: an 11-year retrospective analysis in a tertiary care hospital. Annals of Clinical Microbiology and Antimicrobials. 2021 May 13;20(1):34.
3. Sapna S, Unar AA, Maitlo M, Ahmed Z, Unar K, Malik ZA, Kumar P, Parkash O, Lal S. Determination of predisposing factors in developing Candida albicans associated urinary tract infection and antifungal sensitivity profile. Journal of Pharmaceutical Research International. 2021 Mar 2;33(6):40-9.
4. Ponde NO, Lortal L, Ramage G, Naglik JR, Richardson JP. Candida albicans biofilms and polymicrobial interactions. Critical reviews in microbiology. 2021 Jan 2;47(1):91-111.
5. Shah S. Nanostructure-Biofilm Interactions: A Study of Candida albicans Biofilm Behaviors on Different Polymer Surfaces With Nanoscale Surface Modifications. The University of North Carolina at Greensboro; 2023.
6. del Carmen Morales-Ramírez K, Avila-Sosa R, Cid-Pérez TS, Avelino-Flores F, Duarte-Escalante E, Munguía-Pérez R. Environmental and Social Determinants Related to Candidiasis. 2024.
7. Jorgji E. *Yeast Killer Fungus (YKF): characterisation of a promising antifungal compound against Candida species* (Master's thesis, University of Kent (United Kingdom)). 2020.
8. Rodriguez-Tudela JL, Arendrup MC, Barchiesi F, Bille J, Chryssanthou E, Cuenca-Estrella M, Dannaoui E, Denning DW, Donnelly JP, Dromer F, Fegeler W. EUCAST Definitive Document EDef 7.1: method for the determination of broth dilution MICs of antifungal agents for fermentative yeasts: Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)∗.

Clinical Microbiology and Infection. 2008 Apr 1;14(4):398-405.

9. Abdulla H, Mustafa EA. Rapid Detection of Candida species Isolated from Denture Stomatitis Patients using Phenotypic methods and Chromogenic agar media. Al-Rafidain Dental Journal. 2020 Apr 1;20(1):125-33.
10. Sheppard DC, Locas MC, Restieri C, Laverdiere M. Utility of the germ tube test for direct identification of Candida albicans from positive blood culture bottles. Journal of clinical microbiology. 2008 Oct;46(10):3508-9.
11. Bayona JV, García CS, Palop NT, Cardona CG. Evaluation of a novel chromogenic medium for Candida spp. identification and comparison with CHROMagar™ Candida for the detection of Candida auris in surveillance samples. Diagnostic Microbiology and Infectious Disease. 2020 Dec 1;98(4):115168.
12. Carroll KC, Pfaller MA. Manual of clinical microbiology. Washington, DC: ASM Press, 2019.
13. Lee H, Choi SH, Oh J, Koo J, Lee HJ, Cho SI, Shin JH, Lee HK, Kim SY, Lee CH, Kim YR. Comparison of six antifungal susceptibilities of 11 Candida species using the VITEK2 AST–YS08 card and broth microdilution method. Microbiology spectrum. 2022 Apr 27;10(2):e01253-21.
14. Girish Kumar CP, Menon T. Biofilm production by clinical isolates of Candida species. Sabouraudia. 2006 Feb 1;44(1):99-101.
15. Mitteer DR, Greer BD, Randall KR, Briggs AM. Further evaluation of teaching behavior technicians to input data and graph using GraphPad Prism. Behavior Analysis: Research and Practice. 2020 May;20(2):81.
16. Mancuso G, Midiri A, Gerace E, Marra M, Zummo S, Biondo C. Urinary tract infections: the current scenario and future prospects. Pathogens. 2023 Apr 20;12(4):623.
17. Gharanfoli A, Mahmoudi E, Torabizadeh R, Katiraee F, Faraji S. Isolation, characterization, and molecular identification of Candida species from urinary tract infections. Current Medical Mycology. 2019 Jun;5(2):33.
18. Gajdács M, Dóczi I, Ábrók M, Lázár A, Burián K. Epidemiology of candiduria and Candida urinary tract infections in inpatients and outpatients: results from a 10-year retrospective survey. Central European journal of urology. 2019;72(2):209.
19. Fazeli A, Kordbacheh P, Nazari A, Ghazvini RD, Mirhendi H, Safara M, Bakhshi H, Yaghoubi R. Candiduria in hospitalized patients and identification of isolated Candida species by morphological and molecular methods in Ilam, Iran. Iranian journal of public health. 2019 Jan;48(1):156.
20. Ricardo ET. *Genetic an Molecular Insights of Candida Kruesei Antifugal Resistence* (Doctoral dissertation, Universidade do Porto (Portugal)). 2015.
21. Munoz P, Sánchez-Somolinos M, Alcalá L, Rodríguez-Créixems M, Peláez T, Bouza E. Candida krusei fungaemia: antifungal susceptibility and clinical presentation of an uncommon entity during 15 years in a single general hospital. Journal of Antimicrobial Chemotherapy. 2005 Feb 1;55(2):188-93.
22. Malik AW, Awad AK, Qaddoori HT. Candida species associated with urinary tract infections. World Journal of Advanced Research and Reviews. 2022;16(1):111-21.
23. Malhotra S. Occurrence of candiduria in paediatric patients and its antifungal susceptibility in a tertiary care centre. J Infect Dis Med. 2017;2(1):2-5.
24. Jain S, Ahmad N, Tomar S. Epidemiology, characterization and antifungal susceptibility profile of candida species isolated from suspected cases of urinary tract infections at tertiary care centre of North Delhi. group. 2020;16:32.
25. Jain M, Dogra V, Mishra B, Thakur A, Loomba PS, Bhargava A. Candiduria in catheterized intensive care unit patients: emerging microbiological trends. Indian journal of pathology and microbiology. 2011 Jul 1;54(3):552-5.
26. Paul N, Mathai E, Abraham OC, Mathai D. Emerging microbiological trends in candiduria. Clinical infectious diseases. 2004 Dec 1;39(11):1743-4.
27. Sharma F, Mamoria VP, Sabharwal ER, Sharma R. Prevalence of Candidiasis Infection & Antifungal Susceptibility Pattern at Tertiary Care Hospital, Jaipur. 2020.
28. Gajdács M, Dóczi I, Ábrók M, Lázár A, Burián K. Epidemiology of candiduria and Candida urinary tract infections in inpatients and outpatients: results from a 10-year retrospective survey. Central European journal of urology. 2019;72(2):209.
29. Bochicchio GV, Joshi M, Shih D, Bochicchio K, Tracy K, Scalea TM. Reclassification of urinary tract infections in critically ill trauma patients: a time-dependent analysis. Surgical infections. 2003 Dec 1;4(4):379-85.
30. Kauffman CA. Candiduria. Clinical Infectious Diseases. 2005 Sep 15;41(Supplement_6):S371-6.
31. Seifi Z, Azish M, Salehi Z, Mahmoudabadi AZ, Shamsizadeh A. Candiduria in children and susceptibility patterns of recovered Candida species

to antifungal drugs in Ahvaz. Journal of nephropathology. 2013 Apr;2(2):122.

32. Shin JH, Kee SJ, Shin MG, Kim SH, Shin DH, Lee SK, Suh SP, Ryang DW. Biofilm production by isolates of Candida species recovered from nonneutropenic patients: comparison of bloodstream isolates with isolates from other sources. Journal of clinical microbiology. 2002 Apr;40(4):1244-8.
33. Girish Kumar CP, Menon T. Biofilm production by clinical isolates of Candida species. Sabouraudia. 2006 Feb 1;44(1):99-101.