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Evaluation of Epidemiological Pattern of *Candida* Species Associated with Candidemia from A Tertiary Care Facility in South India

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Abstract

Candidemia ranks the 4th most prevalence cause of bloodstream infections and stands out as the primary cause of invasive fungal infections among hospitalized patients. Its incidence varies globally from 0.33 to 6.51 episodes per 1000 admissions, representing a major public health burden due to its increasing incidence and high mortality rates. The present research work has been conducted to identify the distribution of *Candida* species among septicemic patients and to determine the patterns of antifungal susceptibility of *Candida* species isolates from them in a tertiary care center in South India. Among the 88 *Candida* isolates, 13 (14.8%) were speciated and identified as *C. albicans* and 75 (85.2%) were *Candida non-albicans*. Of them, *C. tropicalis* (42%) ranks more prevalent. The distribution of virulence factors among 88 *Candida* isolates revealed that 49 isolates (55.7%) exhibited phospholipase activity, hemolysin production was detected in 68.2% of isolates, biofilm production was demonstrated in 73.9% isolates and coagulase activity was observed in 46.7% isolates. In the present study, Candida species were most sensitive to Amphotericin B (94.3%), which is followed by Caspofungin (93.2%), Voriconazole (92%), Micafungin (90.9%), and the least was observed with Flucytosine (78.4%) and Fluconazole (71.5%). Thus, in order to improve treatment responses, the insights acquired from this research will aid in clinical management and the development of antifungal stewardship recommendations.

Keywords: Candidemia, *Candida* Species, Virulence Factors, Antifungal Agents, Antifungal Stewardship Guidelines

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INTRODUCTION

Candidemia remains the most prevalent invasive nosocomial fungal infection worldwide. Its incidence varies globally from 0.33 to 6.51 episodes per 1000 admissions, representing a major public health burden due to its increasing incidence and high mortality rates.[1] Frequently administering antibiotics, employing central venous catheters, as well as other invasive medical devices, along with conditions including stays in the intensive care units (ICUs) and could make patients at risk of obtaining a *Candida* infection.[2] Global reports have indicated rising incidence of candidemia brought on by *Candida krusei, Candida tropicalis, Candida glabrata*, *Candida parapsilosis,* despite the fact that *Candida albicans* remains the most prevalent species being responsible for more than 50% of cases in some series.[3]

Candida spp. are commensal organisms present in the gut and skin of 50-70% of healthy individuals in low numbers due to competition within the microbiome.[4] Moreover, *Candida* translocation from the gut into the bloodstream can be facilitated by increased permeability of the gut epithelia (for example, due to mucositis in onco-haematological patients or patients with inflammatory bowel disease) or breaches in the intestinal barrier following abdominal surgery, all of which significantly increase the risk of candidaemia.[4-6]

The evolution of *Candida* from a commensal organism to a formidable pathogen is facilitated by a number of host variables as well as the virulence of the infecting species. Patients who are critically sick yet are immunocompetent can also frequently have candidiasis as *Candida* formerly thought to play a passive part in the overall process of infection initiation and development.[7] *Candida* has a variety of virulence factors that determine its capacity for penetration of host tissues. The virulence factors of *Candida* are multifaceted and include the formation of biofilms as well as the release of extracellular hydrolytic enzymes that damage tissue, such as phospholipases, hemolysin, and proteinases. The capacity for it to adhere to medical equipment and host tissues, as well as the development of pseudohyphae makes it pathogenic.[8] Comprehension and evaluation of these virulence characteristics in newly developing drug-resistant yeast infections will aid in the creation of innovative target-specific medications in the future.[9]

A growing number of strains of *Candida* species are emerging that are resistant to azoles, mostly in the form of prophylaxis and to a lesser extent with echinocandins have been associated with the occurrence of breakthrough infections with resistant *Candida* species.[10] This is an extremely disturbing trend, possibly associated with increased use of azoles as prophylaxis, especially in surgical units and intensive care units.[11] Therefore, there is a need for continuous surveillance to monitor trends in incidence, species distribution and antifungal drug susceptibility profiles of *Candida* BSI.[12] Hence, the present research work has been conducted to identify the distribution of *Candida* species among septicemic patients and to determine the patterns of antifungal susceptibility of *Candida* species isolates from them in a tertiary care center in South India.

MATERIALS AND METHODS

The present cross-sectional study has been undertaken at a tertiary care centre, and from the Institute Ethical Committee for Human Studies, ethical permission (2896/IEC/2021) was acquired. A sum of 2114 blood samples from suspected septicaemia cases was collected in blood culture bottles throughout ICUs and various wards between August 2021 and December 2022. In order to detect gram-positive budding yeasts, bottles displaying positive signals were subjected to direct gram staining technique and cultured onto Sabouraud dextrose agar (HiMedia, India) incubated for a duration of 24 to 48 hours at 25°C and 37°C. *Candida* colonies were detected and speciated in VITEK 2 Compact (Biomerieux) using VITEK® 2 PC LIS-compatible software with Yeast Identification 21343 after being confirmed by Gram staining and the germ tube test and Yeast AST YS08 420739 cards, was used for determination of antifungal susceptibility test (AFST) patterns were carried out. The AFST panel comprised the following drugs: Flucytosine, Micafungin, Amphotericin B, Voriconazole, Fluconazole, and Caspofungin with the recommendations established by the

Clinical and Laboratory Standards Institute (CLSI) guidelines.

Analysis of MIC results

To compute the percentage of essential agreement (A) between the MIC values and the species identification, the repeatability and accuracy of the data produced with the VITEK 2 system were compared to the reference methodologies. The critical agreement was determined by comparing differences in MIC endpoints of more than ±2 log2 dilutions, following Pfaller *et al*.[13]

Comparisons were made between the reference broth microdilution (BMD) panels read at 24 and 48 hours and the MIC values from the VITEK 2 yeast susceptibility test. Similar to other research, low off-scale MIC results were not altered while high off-scale MIC values were translated to the next highest concentration.[14-16] The essential agreement (EA) was determined by comparing the MIC endpoints of more than two dilutions (two wells) in disagreement. The CLSI guidelines (M27-A2 4th Edition) were utilised to interpret the MIC breakpoints for Flucytosine, Micafungin, Amphotericin B, Voriconazole, Fluconazole, and Caspofungin. The MICs produced by VITEK 2 and the reference BMD were then compared to calculate the percentage of categorical agreement (CA).[17] When the VITEK 2 MIC showed S and the reference MIC indicated R, very substantial errors (VME) were found. When the isolate was categorised as R by VITEK 2 and S by the reference technique, major errors (ME) were found. When the findings of one test technique were S or R and the other was SDD, minor flaws were identified. The C. krusei MIC data were utilised as-is (in micrograms per millilitre) to evaluate EA; however, while calculating CA, the CLSI forced the results into the R category.[17]

Assessments of virulence factors

Phospholipase Production.

The standard test strain was then inoculated onto agar enriched with egg yolk using a 5 µL aseptically produced inoculum. Following a 48-hour incubation period at 37°C, the Petri plates were given time to dry at room temperature. The colony was encircled with precipitation zone existence was then studied and this showed that the phospholipase enzyme was expressed. *C. albicans* ATCC 10231 served as the positive control. The phospholipase index (Pz) is obtained by dividing the colony diameter by the precipitation zone ratio. Positive activity is shown by Pz < 1, whereas no phospholipase synthesis is shown by Pz > 1. For every isolate, the test was conducted three times in duplicate to reduce experimental error.[18]

Haemolysin production

It was demonstrated on SDA supplemented with sheep blood and gentamicin and inoculated with 10 µL of prepared inoculum obtained from the isolates. Following this, *C. albicans* ATCC 90028 was used as a control and 48 hours of 37°C incubation was required for the aforementioned medium-containing petri plates. Hemolytic activity (Hz) is determined as the ratio of the colony diameter to the visible hemolysis zone (in millimetres).[19]

Biofilm production - crystal violet assay

The Crystal Violet test technique described by Kuhn *et al*. was used to measure the production of biofilms.[20] The microtiter plate was added with 0.1% aqueous solution of crystal violet (120 µL) for 15 minutes. Sterilised distilled water was used to wash the wells four times. A 15-minute incubation period at room temperature was then followed by the addition of 125 µL of 95% methanol to each well to de-stain the experiment. Then, using an Enzyme-Linked Immunosorbent Assay reader, the de-stained wells were examined using spectroscopy at 570 nm. Reference strains of *C. albicans* (ATCC 90028) served as a positive control strain, while *C. glabrata* (ATCC 90030) was used as a negative control strain.[21,22]

The cut-off optical density (ODc) was defined as three standard deviations above the mean OD of the negative control, and the strains were classified as follows:

OD Values	Biofilm Formation
ODc < OD	strong biofilm producer
2 x ODc < OD ≤ 4 x ODc	moderate biofilm producer
ODc < OD ≤ 2 x ODc	weak biofilm producer
OD ≤ ODc	no biofilm producer

Table 1. Species-wise distribution (n=88)

Candida species	Total number of isolates	Percentage (%)
C. albicans	13	14.8%
C. parapsilosis	21	23.9%
C. tropicalis	37	42%
C. glabrata	6	6.8%
C. krusei	5	5.6%
C. auris	3	3.4%
C. lipolytica	3	3.4%
Total	88	100%

Coagulase activity

Coagulase production was measured in accordance with the procedure devised by Yigit *et al*.[23] After adding 500 µL of rabbit plasma as a supplement, 0.1 mL of an overnight inoculum was aseptically added to a tube. The tubes were examined after being incubated at 35°C for 2, 4, 6, and 24 hours. When a coagulase test is positive, clot formation will appear.

Data analysis

SPSS software (version 22, IBM Inc. Chicago) was used for analysis following data collection. P-values <0.05 were significant.

RESULTS

Distribution and prevalence of *Candida* species

In the present study, out of 88 *Candida* isolates following identification and speciation, 13 (14.8%) were *C. albicans* and 75 (85.2%) were identified as *Candida non-albicans* (CNA). Among CNA isolates, *C. tropicalis* was the most prevalent species, constituting 37 isolates (42%) followed by *C. parapsilosis* with 21 isolates (23.9%), 13 (14.8%) *C. albicans*, 6 (6.8%) *C. glabrata*, 5 (5.6%) *C. krusei*, and both *C. lipolytica* and *C. auris*, each with 3 isolates (3.4%), respectively (Table 1).

Virulence activity among *Candida* isolates

The distribution of phospholipase activity among 88 *Candida* isolates revealed that 49 isolates (55.7%) exhibited phospholipase activity. Phospholipase activity was better in *C. albicans* in comparison with CNA isolates ($p < 0.05$*) as it showed statistically significant results. Notably, *C. tropicalis* had the highest prevalence of phospholipase activity, with 19 isolates (38.8%), followed by *C. albicans* with 11 isolates (22.4%), *C. parapsilosis* with 9 isolates (18.4%), *C. glabrata* with 5 isolates (10.2%), *C. krusei* with 2 isolates (4.1%), *C. auris* with 1 isolate (2%), and *C. lipolytica* with 2 isolates (4.1%) (Table 2 and Table 3).

Moreover, hemolysin production was detected in 60 isolates (68.2%), predominantly in *C. tropicalis* with 25 cases (41.7%), followed by *C. parapsilosis* with 20 cases (33.3%), *C. albicans* with 6 cases (10%), *C. glabrata* with 4 cases (6.6%), *C. krusei* with 3 cases (5%), *C. auris* with 1 case (1.7%), and *C. lipolytica* with 1 case (1.7%). Whereas there was no statistically relevant difference was observed between hemolysin production of *C. albicans* and CNA isolates ($p > 0.05$) (Table 2 and Table 3).

Regarding coagulase activity, it was observed in 42 isolates (46.7%), with *C. albicans* exhibiting the highest incidence among 13 isolates (31%), followed by *C. tropicalis* with 12 isolates (28.6%), *C. parapsilosis* with 10 isolates (23.8%), *C. glabrata* with 4 isolates (9.4%), *C. krusei* with 2 isolates (4.8%), and *C. lipolytica* with 1 isolate (2.4%). There was statistically significant difference was found between coagulase production of *C. albicans* and CNA isolates ($p < 0.05$*) (Table 2 and Table 3).

Furthermore, biofilm production was demonstrated by 70 isolates (73.9%) through crystal violet assay, with *C. tropicalis* predominantly displaying biofilm production in 31 isolates (44.3%), followed by *C. parapsilosis* with 18 isolates (25.7%), *C. albicans* with 9 isolates (12.9%), *C. glabrata* with 4 isolates (5.6%), and *C. krusei* with 3 isolates (4.3%). There was statistically significant difference was found between biofilm production of *C. albicans* and CNA isolates ($p > 0.05$) (Table 2 and Table 3).

Antifungal susceptibility pattern of *Candida* isolates by VITEK 2

The 88 *Candida* isolates underwent Antifungal Drug Susceptibility tests using VITEK 2 against Flucytosine, Micafungin, Amphotericin B (100 U), Voriconazole, Fluconazole, and Caspofungin. Based on their MIC values, the isolates were categorized as Sensitive (S) and

Table 2. Comparison of various virulence factors expressed by *Candida albicans* and *Candida non-albicans* isolated from candidemia patients

Virulence activity	Interpretation	*C. albicans* (n-13)	*Candida non-albicans* (n-75)	p value
Phospholipase Activity (n-49)	Positive	11	38	0.0328*
	Negative	2	37	
Hemolysin production (n-60)	Positive	6	54	0.1037
	Negative	7	21	
Biofilm production (n-65)	Positive	9	56	0.7359
	Negative	4	19	
Coagulase Activity (n-42)	Positive	13	29	0.0000*
	Negative	0	46	

The result is significant at $p < .05$

Table 3. Distribution of Virulence activity among *Candida* isolates (n=88)

Candida species	Phospholipase activity (%)	Hemolysin production (%)	Biofilm production (%)	Coagulase activity (%)
C. albicans (n=13)	11 (22.4%)	6 (10%)	9 (12.9%)	13 (31%)
C. tropicalis (n=37)	19 (38.8%)	25 (41.7%)	31 (44.3%)	12 (28.6%)
C. parapsilosis (n=21)	9 (18.4%)	20 (33.3%)	18 (25.7%)	10 (23.8%)
C. glabrata (n=6)	5 (10.2%)	4 (6.6%)	4 (5.6%)	4 (9.4%)
C. krusei (n=5)	2 (4.1%)	3(5%)	3 (4.3%)	2 (4.8%)
C. auris (n=3)	1 (2%)	1 (1.7%)	0 (0%)	0 (0%)
C. lipolytica (n=3)	2 (4.1%)	1 (1.7%)	0 (0%)	1 (2.4%)
Total (n=88)	49 (55.7%)	60 (68.2%)	65 (73.9%)	42 (46.6%)

Resistant (R) to each antifungal drug. In the present study, the most sensitive antifungal agent was Amphotericin B (94.3%), which is followed by Caspofungin (93.2%), Voriconazole (92%), Micafungin (90.9%), and the least was observed with Flucytosine (78.4%) and Fluconazole (71.5%) as shown in Table 4.

Out of 88 *Candida* isolates, 13 *C. albicans* were 100% sensitive to Voriconazole, Amphotericin B, and Caspofungin. Whereas, among them, 3 (23%) isolates showed resistance to fluconazole and 1 (7.7%) isolate was resistant to each of Micafungin and flucytosine. Among CNA, *C. auris* and *C. lipolytica* demonstrated 100% sensitivity to all the antifungals used. The highest resistance was observed against Fluconazole (29.5%). Nonetheless, due to their intrinsic resistence, *C. krusei* (100%) displayed total resistance to fluconazole. In turn, it has been noted in this investigation that CNA isolates exhibited greater resistance to antifungal drugs in comparison to *C. albicans* (Table 4).

DISCUSSION

In the current study, *C. tropicalis* (n=37; 42%) emerged to be the species with the greatest prevalence detected out of the total. The results of the current investigation were consistent with those of studies by Tak *et al*., Rajni *et al*., and Selvan *et al*., which indicated that *C. tropicalis* isolated species frequently in India, accounting for 39%, 38%, and 47.16% of the total.[24-26] Additionally, *C. tropicalis* (27.7%) was reported to be the major species causing candidemia in Chile by Ajenjo *et al*.[27] Conversely, the research findings by Tan *et al*. demonstrated that the most common isolate from individuals with candidemia was *C. albicans* (41.3%).[28] However, over the past several decades, there was a steady rise in the isolation of CNA isolates from candidemia patients. CNAs are known to be associated with greater death rates because of their enhanced virulence and decreased sensitivity to antifungal medications.[28]

Table 4. Distribution of Antifungal susceptibility and minimum inhibitory concentration (MIC) range of isolated *Candida* species from VITEK 2 (n=88)

Candida species	Fluconazole (0.5 to 64 µg/ml)		Voriconazole (0.125 to 8 µg/ml)		Amphotericin B (0.5 to 8 µg/ml)		Caspofungin (0.125 to 8 µg/ml)		Micafungin (0.06 to 8 µg/ml)		Flucytosin (1 to 64 µg/ml)	
	S	R	S	R	S	R	S	R	S	R	S	R
C. albicans (n=13)	10 (77%)	3 (23%)	13 (100%)	0 (0%)	13 (100%)	0 (0%)	13 (100%)	0 (0%)	12 (92.3%)	1 (7.7%)	12 (92.3%)	1 (7.7%)
C. tropicalis (n=37)	28 (75.7%)	9 (24.3%)	36 (97.3%)	1 (2.7%)	34 (91.9%)	3 (8.1%)	34 (91.8%)	3 (8.1%)	35 (86.5%)	2 (13.5%)	33 (89.2%)	4 (10.8%)
C. parapsilosis (n=21)	15 (71.4%)	6 (28.6%)	18 (85.7%)	3 (14.3%)	19 (90.5%)	2 (9.5%)	20 (85.7%)	1 (14.3%)	16 (76.2%)	5 (23.8%)	15 (71.5%)	6 (28.5%)
C. glabrata (n=6)	1 (16.7%)	5 (83.9%)	4 (66.7%)	2 (33.3%)	6 (100%)	0 (0%)	5 (83.3%)	1 (16.7%)	6 (100%)	0 (0%)	2 (33.3%)	4 (66.7%)
C. krusei (n=5)	0 (0%)	5 (100%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)	1 (20%)	4 (80%)
C. auris (n=3)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)
C. lipolytica (n=3)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)	3 (100%)	0 (0%)
Total (n=88)	63 (71.5%)	26 (29.5%)	81 (92%)	7 (8%)	83 (94.3%)	5 (5.7%)	82 (93.2%)	6 (6.8%)	80 (90.9%)	8 (9.1%)	69 (78.4%)	19 (21.6%)

A notable finding in the current research is the identification of *C. auris* in 3 isolates (3.4%) among all cases of candidemia. The findings did not agree with the results of another recent study in India by Rajni *et al.* and Shastri *et al*. In the previous research, the prevalence of *C. auris* accounted for about 11% and 39.9% of candidemia cases, respectively.[25,29] The development of this *C. auris* is extremely worrying since it causes serious infections in critically sick patients and spreads quickly across the hospital due to its resistance to numerous antifungals. The inability of the widely used phenotypic commercial method to correctly detect this fungus is another significant problem. When creating a treatment strategy, a precise identification of this yeast is crucial. We speculate that the low number of studies from India reporting *C. auris* may be due to misidentification by traditional methods. However, healthcare professionals must be aware of this multidrug-resistant fungus and ready for any possible breakout.[30]

A wide range of virulence factors, the transition from yeast to hyphae, involving biofilm formation, the release of tissue-damaging hydrolytic enzymes like phospholipases, proteases and hemolysins), adherence and invasion to target cell surfaces, and immune cell evasion, all contribute to *Candida's* pathogenicity.[31,32] *Candida* species secrete phospholipases that are involved in tissue invasion, and they hydrolyze phospholipids as substrates, rupturing host cell membranes in the process.[31,33] Out of the 88 *Candida* isolates found in this study, 49 (55.7%) showed evidence of phospholipase activity. These results were compared with the findings of a study by Sachin C *et al.* (60.9%), with *C. tropicalis* having the highest prevalence of phospholipase activity (38.8%).[34] These results are comparable to those of the study conducted by Sharma *et al*., which found that in 30% of patients had *C. tropicalis* displaying significant phospholipase activity.[35] On the other hand, according to a prior work by Saiprom *et al*. all 26.3% of the *C. albicans* isolates generated high phospholipase activity, but none of the NAC spp. showed phospholipase activity.[31]

The ability of *Candida* to produce hemolysin, which lyses red blood cells to extract iron from haemoglobin and promotes hyphal penetration and yeast spread in the host, is a critical component of the virulence of *Candida.*[31,36] Hemolysin production was found in 60 (68.2%) *Candida* isolates in our investigation; the current study's findings were consistent with those of Galan-Ladero *et al*. study, which revealed that around 77.2% of *Candida* isolates had hemolysin production.[37] In this investigation, hemolysin production was predominantly reported in 25 (41.7%) of *C. tropicalis*. The results of the current investigation were consistent with those of Selvan *et al*. study, which indicated that 61.1% of *C. tropicalis* was a hemolysin producer and the proportion of hemolysin producers was significantly lower than that of our study.[26] However, the findings of the study by Nouraei *et al*. demonstrated that 100% of *Candida albicans* generated hemolysin activity.[38] Additionally, the findings of the study by Badran *et al*. revealed that isolates of *C. albicans* (84.9%) exhibited hemolysin activity the most frequently.[39]

One of the most studied virulence variables linked to bloodstream infections caused by *Candida* is biofilm development, which has also been linked to pathogenicity in candidemia connected to catheter use.[40] Furthermore, the production of biofilm makes it easier for *Candida* to adhere to prosthetic joints, vascular catheters, cardiac devices.[41] Due to its well-known strong resistance to antifungal medications, *Candida* biofilm is a major factor in the infection's fatality.[40] By using the crystal violet assay, 70 isolates (73.9%) in the current investigation were able to produce biofilms, and these results were correlated with Tulasidas *et al*. study, which found biofilm activity in 74% of *Candida* isolates.[42] According to our findings, *C. tropicalis* (44.3%) formed the majority of biofilm, which is consistent with earlier research by Sasani *et al*. that found *C. tropicalis* (47%) produced the most biofilm relative to other *Candida* species.[43] Alternatively, *C. parapsilosis* (78%) demonstrated strong biofilm generation, according to findings published by Sriphannam *et al*.[40]

Of 42 (46.6%) *Candida* isolates that showed coagulase activity among 88 *Candida* isolates, 13 (31%) were *C. albicans*, which demonstrated the greatest coagulase activity. These results were quite similar to those reported

by Yigit *et al*., whose work found that coagulase activity was found in *Candida albicans* isolates, accounting for 50.6% of the isolates.[23]

Candida species has a dynamic resistance pattern that differs across different regions.[44] The antibiogram pattern of 88 *Candida* isolates in this study indicated that the most sensitive antifungal agent was Amphotericin B (94.3%), which was consistent with the findings of studies by Siopi *et al*. and Giri *et al*. that showed 100% of the *Candida* isolates were Amphotericin B sensitive.[45,46] The current study demonstrates that the greatest resistance was seen against fluconazole (29.5%), and these results were consistent with research studies by Giri *et al*. that indicated the greatest percentage of *Candia* isolates (30.8%) were resistant to fluconazole.[46] Because fluconazole is the most commonly used antifungal medication that is empirically administered to all high-risk patients, resistance to it is increasing. This has led to the emergence of resistant strains, including *C. glabrata* and intrinsically fluconazole-resistant forms of *C. krusei*.[47,48] In contrast, CNA species exhibited higher resistance to flucytosine (16.04%) and fluconazole (14.81%) in research by Gautam *et al*. than *C. albicans.*[38] In line with other research findings by Bhattacharjee *et al.* and Gautam *et al.*, a lower prevalence of resistance has been determined for Micafungin (8.57%), Voriconazole (8%), Caspofungin (6.8%), and Amphotericin B (1.43%). A few more isolates also showed resistance to Flucytosine (20%).[44,48]

In this investigation, all 13 of the *C. albicans* isolates showed complete sensitivity to caspofungin, amphotericin B, and voriconazole. These results coincide with the findings presented by Solomon *et al*., which demonstrated that all isolates were susceptible to echinocandins (caspofungin), voriconazole, and amphotericin B.[49] Conversely, the results of the study by Bhattacharjee *et al*. revealed that all of the *C. albicans* isolates were 100% susceptible to fluconazole, and that resistance to flucytosine (64.3%), amphotericin B (53.6%), itraconazole (21.4%), and voriconazole (10.7%) was identified.[44] Out of all the CNA isolates, *C. lipolytica* and *C. auris* showed complete sensitivity to every antifungal that was used. In contrast, *C. auris* was shown to have a high resistance pattern for fluconazole in research by Solomon *et al*., suggesting that 9 *Candid*a isolates tested against the drug were sensitive.[49]

There has been a significant shift in the prevalence of *Candida* bloodstream infections from *C. albicans* to CNA species. Consequently, the sensitivity of each species to the antifungal medications now in use varies greatly, early and precise detection of *Candida* infection is imperative. Aside from assisting clinicians to administer the right antifungal medication in a timely manner, laboratory testing for antifungal susceptibility may also limit the empirical use of existing antifungal drugs.[49]

CONCLUSION

The present research concludes by emphasizing the rising prevalence of *C. tropicalis* as the leading cause of candidaemia while highlighting the increasing incidence of rarer *Candida* species such as *C. auris* and *C. lipolytica*. The emergence of various CNA species as significant pathogens underscores the critical need for routine and precise differentiation in clinical laboratories. Additionally, the alarming rise in Fluconazole resistance further accentuates the necessity for accurate species identification and antibiogram assessments in routine laboratory procedures to ensure effective patient management and treatment strategies.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

The study was approved by the Institutional Ethical Committee of SRM Medical College Hospital and Research Centre (2896/IEC/2021).

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