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SPECIES DISTRIBUTION AND ANTIFUNGAL SUSCEPTIBILITY OF INVASIVE CANDIDIASIS IN TERTIARY CARE RURAL HOSPITAL IN CENTRAL INDIA: AN OBSERVATIONAL STUDY

Dr. Shweta Kumari[1], Dr. Dipak Thamke[2]*, Dr.Ajay Kumar[3]

[1]Assistant professor, Department of Microbiology, Integral Institute of Medical Science and Research, Lucknow, Uttar Pradesh, India.
[2*]Professor, Department of Microbiology, MGIMS Sevagram, Wardha, Maharastra, India.
[3]Assistant professor, Department of Plastic surgery ,Command hospital Lucknow, , Uttar Pradesh, India.

***Corresponding Author:** Dr. Shweta Kumari
*Email ID: shwetambbs07@gmail.com

ABSTRACT

Background: Invasive candidiasis (IC), a potentially lethal illness that affects hospitalised patients, is still mostly ignored by the public health sector. People with impaired immune systems are at serious risk due to the paucity of worldwide epidemiological data on IC and the limits of diagnosis. Effective therapy requires exposure to antifungal medications and knowledge of the presence of Candida species.

Materials & Methods: Over the course of 18 months, 35 different species of Candida were identified in IC patients' blood and other sterile bodily fluids. "An automated technique was used to determine fungal susceptibility and species identification. (BacT/ALERT 3D and Vitek 2).

Results: In the present study it was observed that*Non-albicans Candida* species predominated (83%), with*C. parapsilosis* (26%), *C.tropicalis*(17%), *C. ciferrii* (14%), *C. famata* (8%), *C. auris* (6%), *C. glabrata* (3%), *and C. krusei* (3%). *C. albicans* comprised16%of the isolates. Overall, 69% of the samples tested were resistant to fluconazole, while 60% of the samples tested were somewhat resistant to micafungin and caspofungin. With 88% of isolates being responsive, amphotericin B showed the greatest level of sensitivity.

Conclusion: The research sheds light on the evolving epidemiology of candida species that cause IC, which is vital knowledge. In addition, it discusses how to choose empirical antifungal drugs for treating infections caused by candida species other than C. albicans.

Keywords: Invasive candidiasis, Candida, antifungal resistance, species distribution, (BacT/ALERT 3D)

INTRODUCTION

There is growing consensus that invasive candidiasis is a leading cause of death and disability in healthcare facilities, and that this new disease has a clear correlation to technological developments in medicine. (1,2) Candida infections, such as candidiasis or candidemia, may have deep roots.

The infectious diseases society of America (IDSA) and the centre for disease control and prevention (CDC) define candidemia as the presence of Candida species in at least one blood culture together with systemic fungal infection symptoms. (3)

Conversely, deep-seated candidiasis is more difficult to identify and may show up in many organs such as the kidneys, bones, meninges, peritoneum, eyes, spleen, liver, kidneys, and heart, with or without concurrent candidemia. (4)
The yearly incidence of IC ranges from 250,000 to 700,000 cases, with a death rate of 40 to 55 percent and a frequency of 2 to 14 cases per person. (5)
About 150 species of Candida are known to exist at this time. However, after being isolated from patients, only fifteen of these species were ultimately recognised as infectious diseases. (6,7) While additional Candida species may cause infections in humans, five pathogens—Candida krusei, Candida tropicalis, Candida albicans, Candida glabrata, and Candida parapsilosis—are responsible for most severe infections. (6,7) A new opportunistic Candida species, C. auris, has emerged and is spreading fast over the world. (8)
The prevalence of this species in clinical quarantines is worrisome since it seems to be resistant to several antifungal drugs. This limits the treatment options available and has been associated with high mortality rates. range of 30-60%. (9).
In recent years, there has been significant concern over the management of invasive fungal infections due to antifungal drug resistance. The three forms of drug resistance are innate, acquired, and primary. (10). Mechanisms of resistance to antifungal medications differ across drug classes. Reduced absorption and accumulation reduced the drug's affinity for its target; alterations to metabolic pathways that disturb cellular drug concentrations may also lead to antifungal medication resistance. (11)

Study Design
This research used a prospective observational design and lasted for 18 months, from January 2021 to July 2022, at a rural tertiary care hospital's Department of Microbiology.

Inclusion Criteria: Participants were hospitalised patients across all age groups who were thought to be showing signs of invasive candidiasis and were admitted to various wards and ICUs (Intensive Care Units).

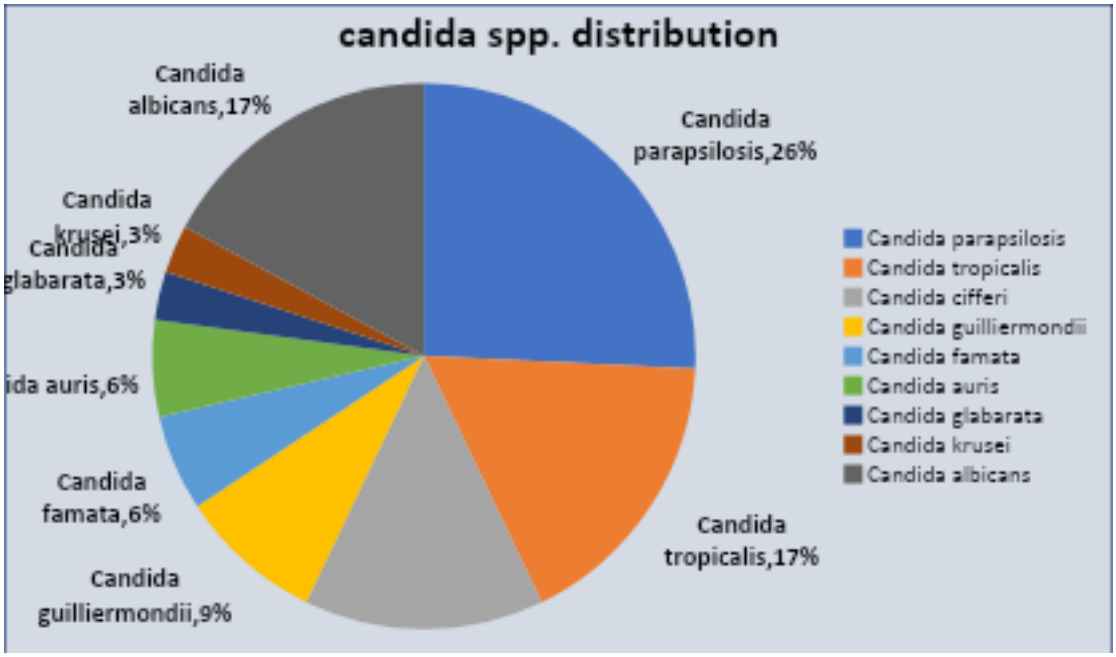
Exclusion Criteria: Participants were not included in the trial if they had invasive candidiasis in the past.

Ethical Considerations: Under the reference number MUHS/Medical/MUHS-029661/2019, the study was approved by the Institutional Review Board (IRB). All participants or their legal guardians gave their informed permission before they were enrolled.

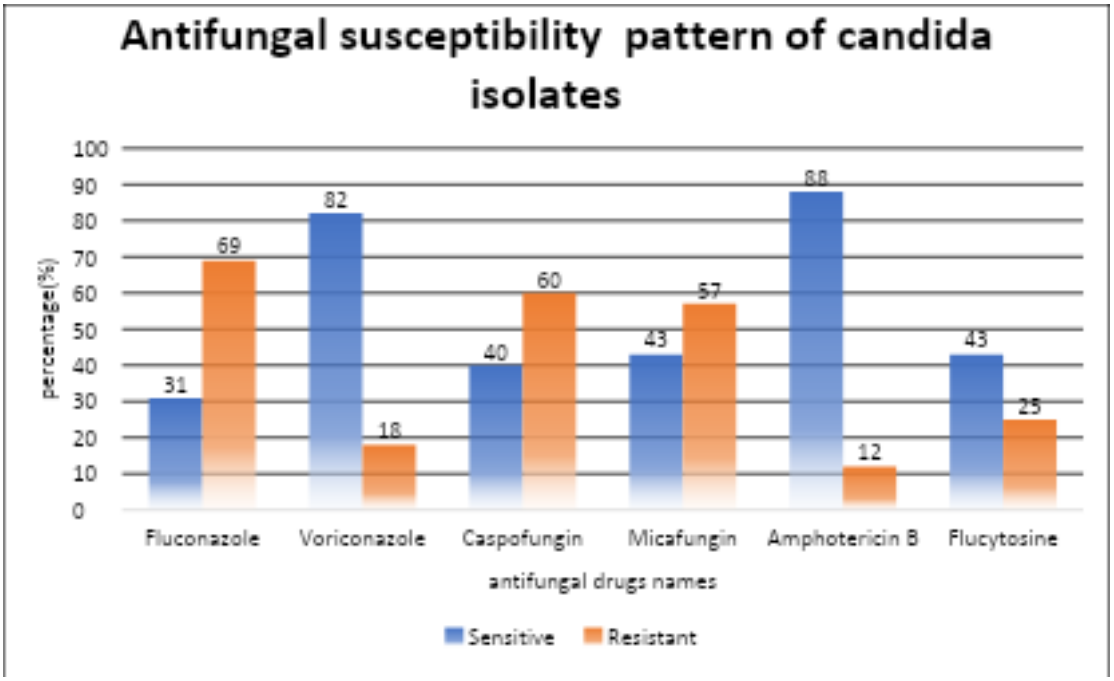
MATERIAL AND METHODS
Blood samples were grown in BacTalert vials and then subcultivated on several agars, including blood agar, SDA (Sabouraud dextrose agar), chocolate agar, and MacConkey agar.
Cultures of non-blood samples (such as cerebrospinal fluid, pleural fluid, synovial fluid, and ascitic fluid) were carried out using conventional methods on SDA, Chocolate agar, Blood agar, and MacConkey agar.
Utilising the Vitek 2 automated system, Candida speciation and antifungal susceptibility testing have been conducted. Testing for Resistance to Antifungals Amphotericin B (AMB), itraconazole (ITC), voriconazole (VRC), 5-flucytosine (5-FC), fluconazole (FLC), and micafungin (MCA) were all subjected to in vitro exposure tests using the CLSI broth microdilution method (M27-A3). In accordance with the Detection of Antifungal Resistance & Standard Operating Procedures for Fungal Identification (2nd Edition 2019), the minimum inhibitory concentration (MIC) of each reagent has been assessed for each isolate.
Each analysis has included the quality control strains of Bacillus parapsilosis ATCC 22019 and Bacillus krusei ATCC 6258.

Data Analysis:
The statistical analysis was conducted using SPSS using descriptive statistics to describe demographic factors, clinical presentations, and outcomes related to invasive candidiasis. A significance threshold of $p<0.05$ was used for all analyses.

RESULTS
Throughout 18 months, a range of 35 *Candida* strains have been isolated. These, 6 (17%) were *Candida albicans*, and 29 (83%) were non-albicans *Candida*.



C. parapsilosis was the most common Candida isolate, making up around 26% of all isolates. Candida glabrata (3% of the total) and Candida krusei (3% of the total) were the two most uncommon isolates.



The sensitivity rates of amphotericin B and voriconazole were 88% and 82%, respectively, whereas micafungin and caspofungin were 43% and 40%, respectively.

Table 13 - Antifungal sensitivity of Candida spp. isolated

Antifungal agents	**Fluconazole**	**Voriconazole**	**Caspofungin**	**Micafungin**	**Amphotericin B**	**Flucytosine**
C.parapsilosis (n=9)	(3/9)33 %	(7/9)78 %	(4/9)44 %	(5/9)55 %	(8/9)89%	(4/9)44%
C. tropicalis (n=6)	(1/6)16 %	(6/6)100 %	(2/6)33 %	(2/6)33 %	(6/6)100%	(3/6)50%
C. cifferi (n=5)	(3/5)60%	(4/5)80 %	(3/5)60 %	(2/5)40 %	(5/5)100%	(1/5)20%
C.albicans (n=6)	(4/6)66 %	(6/6)100 %	(5/6)83 %	(5/6)83 %	(6/6)100%	(4/6)66%
C.guilliermondii (n=3)	(1/3)33 %	(3/3)100 %	(1/3)33 %	(1/3)33 %	(3/3)100%	(1/3)33%
C.famata (n=2)	0 %	(2/2)100 %	0 %	(2/2)100 %	(2/2)100%	(2/2)100%
C. glabarata (n=1)	0 %	0 %	0 %	0 %	(1/1)100%	0%
Candida auris (n=2)	0 %	0 %	0 %	0 %	0%	0%
Candida krusei(n-1)	0%	(1/1)100%	(1/1)100%	(1/1)100%	(1/1)100%	0%

All antifungal medicines were ineffective against Candida auris, however fluconazole was the only one to which Candida albicans exhibited a good sensitivity (66% sensitivity). Although fluconazole was less effective against C. parapsilosis, voriconazole and amphotericin B were more effective against Candida tropicalis. Fluconazole, voriconazole, and amphotericin B were too strong for C. ciferri. While amphotericin B and voriconazole were effective against C. guilliermondii, caspofungin, fluconazole, flucytosine, and micafungin were ineffective against them. Voriconazole, amphotericin B, and micafungin were very effective against Candida glabrata, while only amphotericin B was effective against Candida famata and C. krusei.

DISCUSSION

In our investigation, the percentage of Candida albicans decreased to less than 50% of all Candida species, indicating a shift towards Candida species other than albicans (12).

Studies conducted in northern Europe, the United States, and Australia followed a similar pattern to the present inquiry. According to research by Ericsson J. et al. (13) and Lamoth F. et al. (12), Candida glabrata is the second most common type in these regions, and it routinely replaces Candida albicans.

Mareković I et al. (14) discovered that among the patients, C. albicans was the most frequently isolated species (43.53%) over a 3-year period. Additionally, C. parapsilosis, the second most common species, was significantly more common, accounting for 31.76% of all isolates, followed by C. glabrata, which accounted for 11.35%.

Candida parapsilosis was the most prevalent Candida isolate in our investigation, comprising around 26% of all isolates. However, Bhattacharjee P (15)observed that *C. tropicalis &C. albicans* have the prevalent species, which are within line with other Indian studies by Xess I et al.(16) Kothari A et al. (17) , Chakrabarti A et al (18) and Singh RI et al (19).

This finding is in line with previous research from India by Kumar CP et al.(20) and Kothari A et al.(17) and it is similar to what Bhattacharjee P15 found: a range of resistance to fluconazole of 34.8%. Endurance to Fluconazole Important for azole form prevention of candidiasis and candidemia, it is utilised extensively. Fluconazole has an excellent bioavailability, is available in both oral and intravenous formulations, and is less expensive than other antifungal drugs". Although Amphotericin B is effective against most species of Candida, it is not recommended as a first line of therapy for candidemia because of the kidney damage it causes.

Adhikary R et al.(21) showed that Candida isolates are highly resistant to Fluconazole, contrary to what Western data has shown, which indicates that Candida species is dependably too vulnerable to azoles, echinocandins, and polyenes.

Invasive candidiasis (IC) represents a severe and potentially lethal fungal infection predominantly affecting hospitalized and immunocompromised individuals. Historically, Candida albicans was considered the primary pathogen; however, recent evidence points to a rising prominence of non-albicans Candida (NAC) species, which often exhibit higher intrinsic and acquired resistance to commonly used antifungals.(22,23) Accurate regional data on species distribution and antifungal susceptibility profiles are critical for guiding empirical therapy and improving patient outcomes. This observational study investigates the prevalence of Candida species isolated from sterile body fluids in a rural tertiary-care hospital in central India, alongside their susceptibility patterns—providing valuable insight into local epidemiological trends and informing optimal antifungal management strategies.

CONCLUSION

In order to optimise treatment results and inform empiric therapy recommendations adapted to the epidemiological environment in India, continuous monitoring of Candida species supply and antifungal susceptibility forms is used. Healthcare professionals may improve patient outcomes and decrease healthcare-associated infections by filling these knowledge gaps and using treatments supported by evidence to control and alleviate the impact of invasive candidiasis.

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