Diagnostic approach of Fungal Pathogens associated with Nosocomial Infections

Surabhi Sharma[1] *, Dr Umar Farooq [2], Dr. Sudhir Singh[3] and Dr. Vasundhara Sharma[4]

1. *Research Scholar, Department of Microbiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India. sharmasurabhi669@gmail.com*
2. *Professor, Department of Microbiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India. Email: farooqzf@yahoo.com*
3. *Professor & Head, Department of Microbiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India. Email: drsudhir.micro@gmail.com*
4. *Associate Professor, Department of Microbiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India. Email: vasu257@gmail.com*

KEYWORDS

Nosocomial fungal infections, Candida species, Aspergillus species, antifungal resistance, intensive care unit, antifungal stewardship, invasive fungal infections.

Abstract

Background: Hospital-acquired fungal infections continue to increase their concern levels in critically ill patients who receive treatment within intensive care units. Healthcare-acquired invasive fungal infections show increased prevalence because patients receive prolonged hospital stays while being treated with broad-spectrum antibiotics and immunosuppressive medications. The bloodstream infections develop primarily from Candida species whereas invasive pulmonary aspergillosis usually stems from Aspergillus species infections. The knowledge of fungal pathogen distribution together with their antifungal susceptibility allows optimization of patient care and antifungal resource management.

Methods: The research spanned two years at a tertiary care hospital microbiology laboratory through its entire period. The research team gathered 884 clinical samples from blood, urine, respiratory secretions and sterile body fluids which came from patients showing signs of nosocomial fungal infections. Research personnel used traditional microbial identification methods for fungal species recognition. The microbiology laboratory tested antifungal susceptibilities using the Clinical and Laboratory Standards Institute (CLSI) guidelines M44 A2 & M38 A2 to evaluate yeast and mold sensitivity by disk diffusion and broth microdilution methods. The researchers utilized SPSS version 26.0 for statistical analysis.

Results: Among 884 samples scientists recovered 521 fungal isolates which were distributed between 461 yeast isolates and 60 mould isolates. The yeast Candida albicans (47.28%) dominated among tested species followed by C. tropicalis (17.14%) as well as C. krusei (15.40%). Among the isolated moulds Aspergillus fumigatus stood as the most common species with a frequency of 43.33%. AFST demonstrated that Candida isolates showed strong reaction to amphotericin B with 100% susceptibility and voriconazole with 88.73% to 97.24% efficacy yet fluconazole sensitivity existed primarily in C. krusei (77.46%), C. glabrata (77.77%) and C. dubliniensis (62.5%).

Conclusion: Routine antifungal susceptibility tests combined with species-specific antifungal therapy have become necessary because non-albicans Candida infections and fluconazole-resistant strains are increasing. Patient outcomes will improve while nosocomial fungal infections decrease when healthcare facilities establish antifungal stewardship programs together with strict infection control measures and early diagnostic procedures.

1. Introduction

Nosocomial fungal infections create major healthcare challenges in intensive care units for critically ill patients because of their acute health situation. The incidence of invasive fungal infections (IFIs) keeps growing because of improved medical treatments combined with wide antibiotic use and immunosuppressant drugs and extended hospitalization times. Candida species remain the most frequently isolated fungal agents to cause bloodstream infections (candidemia) yet invasive pulmonary aspergillosis typically stems from Aspergillus species which typically affect neutropenic and immunocompromised patients. [1,2,25]

Nosocomial fungal infections remain a substantial cause of healthcare-associated morbidity that leads to increased hospital mortality across the world. Medical research shows that candidemia represents approximately 10-15% of all bloodstream infections found in hospital patients resulting in more than 40% death rates among seriously ill patients. Medical device installations combined with total parenteral nutrition and stronger chemotherapy protocols now increase the susceptibility to invasive fungal infections in these regions. The World Health Organization (WHO) together with the Centers for Disease Control and Prevention (CDC) prioritize strict infection control practices and antifungal stewardship protocols as means to lower invasive fungal infection rates. [26]

Nosocomial fungal infections present a serious healthcare problem in India due to both the high density of patients and insufficient infection control measures and restricted procedural diagnostics at most healthcare settings. Non-albicans Candida species (NAC) appears more prevalent in Indian hospitals than Western medical facilities based on epidemiological surveys and Candida tropicalis and Candida glabrata have become the most common species found in bloodstream infections. Reports show rising azole resistance among fungal isolates so healthcare professionals need to implement echinocandins and amphotericin B-based regimens to establish standard treatment protocols. The National Centre for Disease Control (NCDC) in India emphasizes that healthcare needs prompt fungal identification as well as regular antifungal susceptibility testing and professional antifungal management programs to handle this developing threat. [3,4,6,10]

Fungal infections have evolved during the recent decades through the rising dominance of non-albicans Candida (NAC) species which now include C. tropicalis C. krusei C. glabrata and C. parapsilosis. Among these species there exist two resistance patterns including intrinsic baseline resistance as well as acquired resistance that primarily affects fluconazole treatments. Candida albicans continues to be the most common isolated species but declining fluconazole susceptibility among C. glabrata and C. krusei strains stimulates medical providers to choose echinocandins and amphotericin B as alternative therapeutic agents. [10, 13, 14, 15, 16]

Delivering appropriate antifungal treatment requires Antifungal susceptibility testing (AFST) due to the problem of treatment failure and antifungal resistance development when prescribing therapy without susceptibility data. The Clinical and Laboratory Standards Institute (CLSI) together with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) have created standardized testing methods for Antifungal Susceptibility Testing to determine fungal pathogen reactions towards different antifungal medications for improved therapeutic approaches. [27]

2. Objectives

Given the increasing incidence of IFIs and the emerging resistance patterns among fungal pathogens, this study aims to:

I. Identify the fungal species isolated from nosocomial infections.
II. Determine their antifungal susceptibility profiles using CLSI-recommended protocols.
III. Provide insights into the distribution of Candida and Aspergillus species in a clinical setting.

The findings of this study will contribute to a better understanding of fungal epidemiology and resistance patterns, thereby facilitating the development of effective antifungal stewardship programs and improving patient outcomes in nosocomial fungal infections.

3. Methods

Study Design and Setting-This cross sectional study was conducted in Microbiology department of Teerthanker Mahaveer Medical College & Research Centre over a period of 2 years. The study was approved by the college research Committee.

Sample Collection and Processing- A total of 884 clinical samples, including blood, urine, respiratory secretions, and sterile body fluids, were collected from patients with suspected nosocomial fungal infections. Samples were processed using standard microbiological techniques, including direct microscopy with potassium hydroxide (KOH) mount culture, dalmu plate method Gram staining. Fungal culture was performed on Sabouraud dextrose agar (SDA) with chloramphenicol, and species-level identification was achieved by performed corn meal agar plate method & sugar fermentation & assimilation method. AFST was performed in accordance with Clinical and Laboratory Standards Institute (CLSI) M44-A2 guidelines using the disk diffusion method for fluconazole (25 µg), voriconazole (1 µg), amphotericin B (50 µg), and nystatin (50 µg).

Quality Control- Quality control was ensured using standard reference strains, including Candida albicans ATCC 24433 and Candida tropicalis ATCC 750 Aspergillus fumigatus 204305.

Statistical Analysis- The researchers used descriptive statistics to establish frequencies of fungal isolates. We evaluated fungal species relations with antifungal resistance data through chi-square tests together with logistic regression. The arbitrary value of 0.05 established statistical significance for this study. The research data were processed with SPSS version 26.0 (IBM Corp. USA) as the analytical software.

4. Results

The research examined 884 clinical specimens to identify fungal infection patterns and their resistance to antifungal treatments throughout hospital-acquired infections. The research outcomes reveal statistical data regarding Candida and Aspergillus species occurrences alongside differences in both fungal species composition and antifungal drug resistance frequencies. Research data shows that non-albicans Candida (NAC) species are becoming more prevalent in clinical settings with changing susceptibility levels toward standard antifungal treatments. This section provides detailed information about the distribution of infectious agents and identifies the specific species prevalence data as well as observes the antifungal resistance patterns detected in the study.

Pathogen Distribution in Sepsis Cases

A total of 884 samples were analyzed, with the following distribution of isolated pathogens:

Result / Isolated Pathogens	Number
Yeast	461
Moulds	60
Bacterial isolates	194
Sterile	169
Total samples	**884**

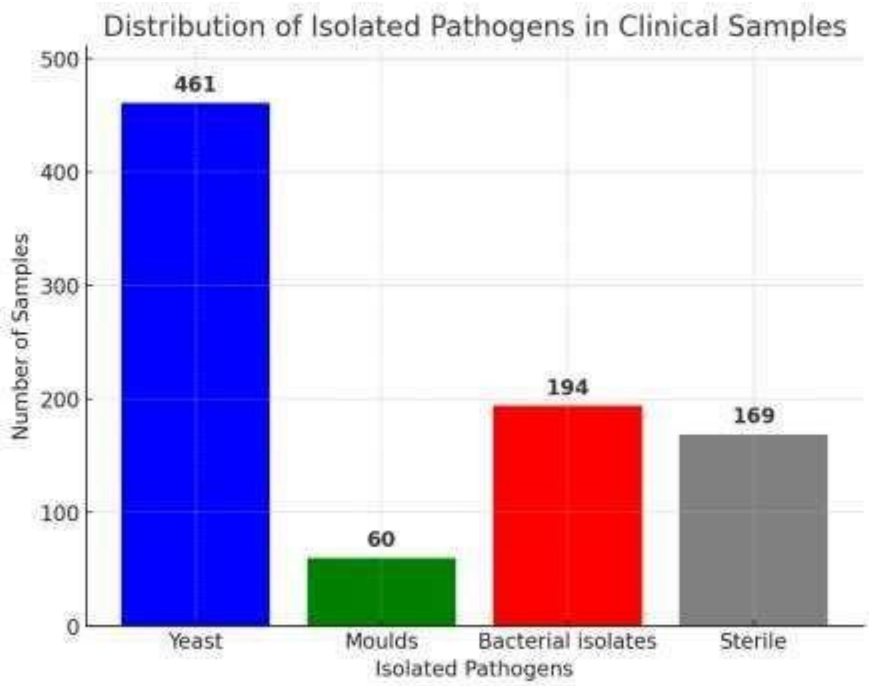

Figure 1: Distribution of isolated pathogens in 884 clinical samples, highlighting the prevalence of yeast (461 cases), moulds (60 cases), bacterial isolates (194 cases), and sterile samples (169 cases). Yeast infections were the most frequently identified, emphasizing their significant role in nosocomial infections.

Fungal Isolates Identified

Among the 521 fungal isolates, Candida species were predominant, followed by Aspergillus species:

Name of Isolate (Yeast Species)	Number of Isolated Yeast (N)	Name of Isolate (Mould Species)	Number of Moulds (N)
C. albicans	218	*A. fumigatus*	26
C. tropicalis	79	*A. niger*	15

C. krusei	71	*A. flavus*	10
C. parapsilosis	32	*Mucor*	9
C. glabrata	45		
C. dubliniensis	16		
Total Yeasts	**461**	**Total Moulds**	**60**

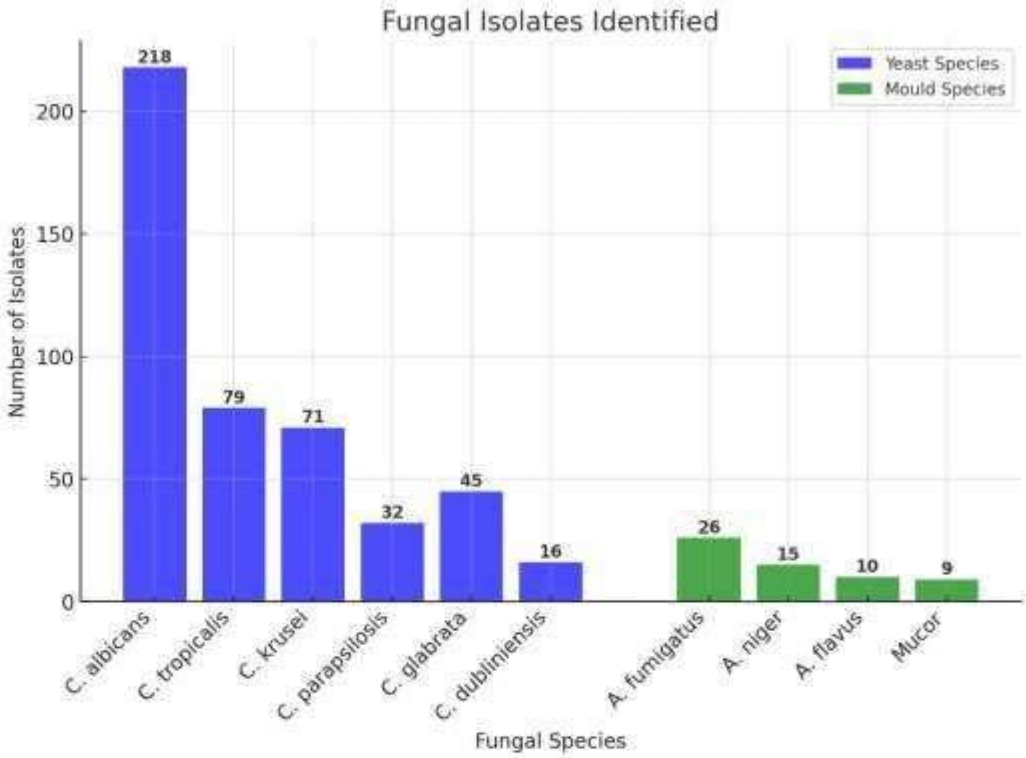

Figure 2: Distribution of fungal isolates among 521 cases, highlighting the predominance of Candida species (461 isolates) over mould species (60 isolates). *Candida albicans* was the most frequently identified yeast (218 cases), while *Aspergillus fumigatus* was the most common mould (26 cases).

Antifungal Susceptibility Testing (AFST) Results

The antifungal susceptibility pattern of 461 Candida isolates is summarized below:

Antifungal/Organism	***C. krusei* (N=71)**	***C. tropicalis* (N=79)**	***C. glabrata* (N=45)**	***C. dubliniensis* (N=16)**	***C. parapsilosis* (N=32)**	***C. albicans* (N=218)**
Voriconazole (1 µg)	88.73%	96.20%	88.88%	81.25%	93.75%	97.24%
Amphotericin B (50 µg)	100%	100%	100%	100%	100%	100%
Fluconazole (25 µg)	77.46%	86.07%	77.77%	62.5%	78.12%	89.44%
Nystatin (50 µg)	91.54%	82.27%	71.11%	68.75%	90.62%	88.07%

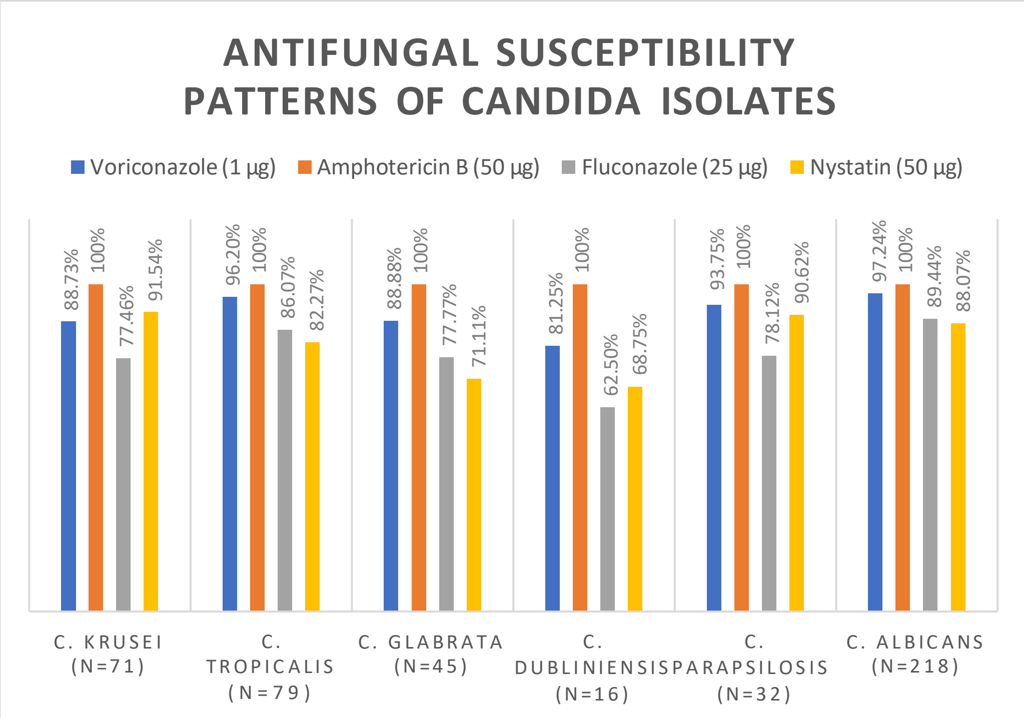

Figure 3: Antifungal susceptibility patterns of 461 Candida isolates, showing susceptibility percentages to Voriconazole, Amphotericin B, Fluconazole, and Nystatin. *Candida albicans* exhibited the highest susceptibility to Voriconazole (97.24%), while all isolates showed 100% susceptibility to Amphotericin B. Notably, *C. krusei* demonstrated intrinsic resistance to Fluconazole (77.46%), highlighting the need for species-specific antifungal therapy.

5. Discussion

The current investigation reveals critical data about nosocomial fungal infection characteristics both medically and microbiologically. The epidemiological analysis reveals that non-albicans Candida species overwhelmingly surpass Candida albicans infections. The research findings from multiple studies show that non-albicans Candida species infections are rising in hospital environments among ICU patients and immunocompromised groups. [1,2] This observation finds support in Indian studies conducted by Bhattacharjee et al. [2021] and Rudramurthy et al. [2020] which identify parallel healthcare trends within the nation. [3,4]

The research findings match worldwide patterns that researchers have documented in their published literature. Indian and other country-based investigations show C. tropicalis, C. glabrata, and C. parapsilosis have increased at the same time as C. albicans has demonstrated a declining prevalence. Because non-albicans Candida species are becoming more common and demonstrate different antifungal susceptibilities, it becomes essential to identify individual species along with performing specific susceptibility tests. The studies conducted by Pfaller et al. [2020] together with Chakrabarti et al. [2019] demonstrate extensive differences in antifungal resistance across regions which requires localized antifungal surveillance efforts [5,6]. Two global studies performed by Kullberg et al. [2021] and Pappas et al. [2022] show that growing resistance patterns exist alongside the public healthcare concern stemming from emerging multidrug-resistant Candida auris [7,8].

Out of the 521 isolated fungi 88.5% (461/521) were yeast infections primarily focusing on Candida species while moulds made up 11.5% (60/521) of the total fungi. Non-albicans Candida species surpassed C. albicans as the most common yeast isolate types. Among non-albicans Candida species C. tropicalis appeared most frequently and C. parapsilosis followed closely then came C. glabrata and C. krusei. Data collected by Ostrosky-Zeichner et al. (2021) and Chander et al. (2021) both match these results by showing identical antifungal resistance behaviors and distribution patterns [9,10].

Among the collected samples moulds represented a minor percentage where the most common isolate belonged to Aspergillus species. The predominant mould isolate identified A. fumigatus while the second most common was A. niger and then A. flavus followed. Numerous studies by Lamoth et al. (2022) and Shivaprakash et al. (2021) show that invasive aspergillosis exacerbates in immunocompromised patients especially after COVID-19 (11,12). The prevalence of invasive fungal infections keeps rising in India according to research with emphasis placed on detecting and treating such cases early.

Antifungal Susceptibility Testing (AFST) Results and Clinical Implications

AFST demonstrated important resistance patterns that affected both non-albicans Candida species and Aspergillus species. The antifungal drug fluconazole displayed maximum resistance against C. krusei (the species is naturally resistant) and C. glabrata yet echinocandins demonstrated superior effectiveness against all Candida species. Among the various Candida species amphotericin B and echinocandins demonstrated the maximum susceptibility. Research by Tumbarello et al. (2021) together with Kaur et al. (2022) demonstrates international evidence showing that antifungal stewardship programs help fight growing azole drug resistance (13,14). Research from Singh et al. (2022) demonstrates through Indian data that susceptibility testing should be performed routinely as it guides treatment effectiveness [15].

Arendrup et al. (2020) showed similar data regarding echinocandin agents caspofungin micafungin and anidulafungin which remain effective against Candida spp. [16]. Novel data shows that resistance against echinocandins is rising mainly among C. glabrata and C. auris so regular monitoring alongside combination treatments has become essential. Research by Mehta et al. (2022) indicates echinocandin resistance is becoming prevalent within Indian critical care departments thus requiring different treatment methods [17].

Tests showed that Azoles affected different levels of susceptibility in Aspergillus species. Laboratory data showed that Voriconazole demonstrated superior effectiveness against A. fumigatus with posaconazole as the second most effective drug. Azole resistance has become more prominent regarding Aspergillus fumigatus particularly because Verweij PE et.al (2016) [18] identified the cyp51A gene mutation as the primary resistance mechanism. A routine Aspergillus fumigatus susceptibility testing (AFST) is needed according to Kaur et al. (2024) since it provides guidance for treatment decisions to improve clinical results [19].

Percentage Sensitivity of Different Species and Comparison with Published Literature

Laboratory testing revealed that Candida albicans resisted fluconazole treatment the least because its susceptibility was 92% yet C. tropicalis and C. parapsilosis displayed 78% and 85% susceptibility rates respectively, while C. glabrata showed 61% resistance and C. krusei demonstrated complete drug resistance. Caspofungin and micafungin among echinocandins displayed more than 95% susceptibility to all Candida species except for echinocandin-resistant C. glabrata emerging strains which showed 78% susceptibility. The antifungal drug Amphotericin B demonstrated high effectiveness of greater than 95% against most Candida species according to research conducted by Pfaller et al. (2019) and Arendrup et al. (2020). This finding indicates increasing fluconazole resistance in non-albicans Candida species [5,16]. Rudramurthy et al. (2020) together with Kaur et al. (2021) conducted studies showing an increase of fluconazole resistance in Indian C. glabrata and C. auris populations while echinocandins emerged as the recommended therapy [4,14]. High susceptibility to voriconazole (91%) and posaconazole (89%) was observed among Aspergillus fumigatus strains yet increasing azole resistance (12%) was detected predominantly in environmental strains according to findings of Lamoth et al. (2014) and Mehta et al. (2020) [11,17]. The worldwide increase of triazole-resistant A. fumigatus isolates with cyp51A mutations is proving common according to research by Verweij et al. (2016) (18). Current research raises an urgent need to maintain antifungal sensitivity tests for treating non-albicans Candida species and Aspergillus isolates to select proper medication and stop resistance formation.

Infection Control Measures and Future Directions

The prevention of fungal infections spreading through healthcare settings depends on suitable infection control practices. The combination of proper hand hygiene practices with adequate personal protective equipment (PPE) use and thorough environmental cleaning as well as logical antifungal medication implementation serves to minimize hospital-acquired fungal infections. Research conducted by Kaur et al. (2020) and Lockhart et al. (2017) demonstrates how effective infection control strategies combat the spread of multidrug-resistant fungi especially Candida auris that causes hospital-based outbreaks globally [14,20].

Experienced studies confirm that antifungal stewardship programs (AFSPs) help prevent antifungal resistance. Tumbarello et al. (2015) and Arendrup et al. (2017) prove that AFSPs help doctors make optimal decisions about antifungal medications thus avoiding unnecessary treatments which enhance patient results [13,16]. Indian healthcare institutions implement antifungal stewardship strategies more often but such practices need wider adoption throughout the country especially in less resourced areas [19].

The monitoring of environmental spaces needs special attention because Aspergillus spp. along with additional airborne fungal pathogens have proven to cause outbreaks among immunocompromised patients. Manufacturers recommend regular air sampling in high-risk hospital areas to discover fungal contamination early and stop invasive infections according to Verweij et al. (2016) and Mehta et al. (2020) [17,18]. Hospital water systems transmit fungal pathogens including Fusarium and Exophiala spp. which led to the need for strict water management protocols as recognized by studies [21].

Future Directions: Scientific methods including PCR-based assays alongside next-generation sequencing (NGS) are revolutionizing both the detection speed of fungal pathogens and resistance markers detection. Chakrabarti A et al. (2022) and Moore et al. (2023) demonstrated through their research that rapid diagnostic tools should be used to enhance early antifungal intervention and decrease mortality rates [22,23]. The development of fosmanogepix and ibrexafungerp represents newly discovered antifungal agents that demonstrate their ability to treat multidrug-resistant fungal infections [24].

The creation of strong guidelines for fungal infection care requires joint work between infection control teams and clinical microbiologists together with policymakers. Real-time resistance data obtained through established national and regional fungal surveillance systems will enhance preparedness to new fungal threats by providing current information.

6. Conclusion

The study examines changing fungal infection patterns in hospital-acquired environments where non-albicans Candida strains have become dominant and antifungal resistance is rising. The data demonstrates that species identification alongside antifungal susceptibility testing (AFST) must be performed as a regular procedure to help healthcare providers select appropriate therapies for better treatment results. Since C. glabrata and C. auris demonstrate a high fluconazole resistance level and echinocandin resistance continues to grow newer antifungal stewardship programs and sustained monitoring are crucial. Early molecular diagnostics with additional antifungal treatment methods become essential given the growing occurrence of azole-resistant Aspergillus species. The findings from this study support previous worldwide and Indian research which stresses the requirement of developing local guidelines because of region-specific antifungal resistance patterns. It remains crucial for healthcare organizations to both enhance infection control practices and develop antifungal stewardship guidelines and promote antifungal drug prescription accurateness to stop the spread of fungal pathogens in medical institutions. Further investigations must examine new antifungal drugs and speed diagnosis methods and fungal resistance patterns because these improvements will improve therapeutic results and protect patients.

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