

# Epidemiology and Antifungal Susceptibility Trends of Candidemia: A 5-Year Retrospective Study at King Abdulaziz University Hospital

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**Background:** Candidemia, a bloodstream infection caused by *Candida* species, poses a significant clinical challenge, especially in immunocompromised individuals and intensive care unit (ICU) patients. Prompt diagnosis and treatment are crucial, as delayed antifungal therapy is associated with higher mortality rates. This study, conducted at King Abdulaziz University Hospital (KAUH) in Saudi Arabia, aimed to investigate the clinical and microbiological aspects of candidemia.

**Methods:** This study is a retrospective analysis, KAUH in Saudi Arabia, using data from January 2017 to March 2021. Advanced fungal diagnostic technologies, including MALDI-TOF MS, BioFire, and Vitek 2 systems, were utilized. Patient demographics, clinical characteristics, *Candida* species distribution, and antifungal susceptibility were assessed. Univariate, bivariate, and multivariate statistical analyses were conducted.

**Results:** Among 418 patients, *Candida albicans* was the most prevalent species (32.1%), followed by *C. tropicalis* (23.4%) and *C. parapsilosis* (18.4%). Various *Candida* species exhibited different antifungal susceptibility patterns, with high sensitivity to Amphotericin B (95%) and Fluconazole (94%). Sensitivity to Caspofungin varied significantly among species ( $p = 0.023$ ), with *C. parapsilosis* showing the highest sensitivity (95%). The overall mortality rate was 67%. None of *Candida* Species exhibited a statistically significant association with death, however other factors including age, autoimmune diseases, and dialysis were associated with increased mortality risk.

**Conclusion:** This study provides valuable insights into the epidemiology and clinical characteristics of candidemia at KAUH, highlighting the importance of species identification and tailored antifungal therapy. These findings can inform strategies to improve patient care and infection control in Saudi Arabian healthcare settings, contributing to global efforts to mitigate the impact of invasive fungal infections.

**Keywords:** candidemia, *Candida* species, antifungal susceptibility, epidemiology, Saudi Arabia

## Introduction

Candidemia, a bloodstream infection caused by *Candida* species, presents a significant clinical challenge, particularly in immunocompromised individuals and intensive care unit (ICU) patients.<sup>1</sup> *Candida* spp. rank among the top four pathogens contributing to hospital-acquired infections, notably catheter-associated urinary tract and bloodstream infections.<sup>2</sup> Most of these invasive infections are attributed to four principal *Candida* species: *Candida albicans*, *Nakaseomyces glabrata*, *Candida parapsilosis* and *Candida tropicalis*, with other species playing a less pronounced role.<sup>1–3</sup> However, region-specific outbreaks involving different species have been documented, highlighting a dynamic epidemiological landscape.<sup>4,5</sup> Although extensive global surveillance has mapped the epidemiology and antifungal resistance patterns of candidemia, there is a paucity of published epidemiological and antifungal susceptibility data

from Saudi Arabia, particularly in tertiary care centers such as KAUH. Addressing this local knowledge gap is crucial for developing effective, region-specific treatment and infection control strategies.

The prevalence and distribution of *Candida* species in bloodstream infections vary widely by geography and clinical setting. *C. albicans* and *Nakaseomyces glabrata* are more common in North America and Europe, while *C. parapsilosis* dominates in Latin America and Asia-Pacific regions.<sup>6</sup> US data show species variation across states and demographics,<sup>7</sup> while Italian hospitals report *C. albicans* as dominant overall, but *C. parapsilosis* is more frequent in oncohematology units.<sup>8</sup> A meta-analysis further showed that *C. tropicalis* has higher biofilm formation and resistance in Spain than in Italy.<sup>9</sup>

Antifungal susceptibility among *Candida* species shows considerable variation, often influenced by geographical and clinical contexts. A study evaluating global trends from 1992 to 2001 indicated that while *C. albicans*, *C. tropicalis*, and *C. parapsilosis* remained highly susceptible to fluconazole, resistance was more variable among *Nakaseomyces glabrata* isolates, especially in the United States.<sup>6</sup> Another study spanning multiple US states found that approximately 7% of *Candida* isolates were resistant to fluconazole, with higher resistance noted among non-*albicans* species.<sup>7</sup> In Italy, an upward trend in azole resistance was observed among *Candida* species, particularly in hospital settings.<sup>8</sup> Furthermore, a meta-analysis of studies from Europe and Asia reported significant antifungal resistance in biofilm-forming *Candida* species, with *C. tropicalis* showing notable resistance to fluconazole and other antifungals.<sup>9</sup> A study conducted in Iran on immunocompromised patients revealed that while voriconazole was highly effective against all *Candida* isolates, resistance to itraconazole was observed across all *Candida* species.<sup>10</sup>

While global studies have established general trends in *Candida* species distribution and antifungal resistance, these findings may not reflect regional patterns. In Saudi Arabia, and particularly in tertiary care centers like KAUH, there remains a paucity of epidemiological and susceptibility data on candidemia. Local data are essential for guiding targeted therapy, enhancing antifungal stewardship, and improving patient outcomes in this high-risk population.

Therefore, the aim of this study is to provide a comprehensive analysis of candidemia cases at King Abdulaziz University Hospital. Specifically, we sought to examine the distribution of *Candida* species responsible for bloodstream infections, assess their antifungal susceptibility profiles, and explore the demographic and clinical characteristics associated with different species. In addition, we evaluated the impact of candidemia on patient mortality to better understand outcomes and inform clinical management.

## Methods

### Study Site

The study was conducted at King Abdulaziz University Hospital (KAUH) in Jeddah, Kingdom of Saudi Arabia. KAUH is a tertiary care hospital with over 1000 beds, offering a range of healthcare services across various departments, including the Intensive Care Unit (ICU) and the Microbiology Laboratory. The hospital serves a diverse patient population, including local residents and patients referred from other regions. Advanced diagnostic technologies such as MALDI-TOF MS, BioFire, and the Vitek 2 system are utilized at KAUH for the diagnosis and management of infections, including candidemia.

### Study Design and Time Period

This study implemented a retrospective design, investigating into cases of candidemia that occurred at King Abdulaziz University Hospital (KAUH) from January 2017 to March 2021.

### Sample

All candidemia infections diagnosed at the study site during the study period were included in the sample. This included patients with at least one positive blood culture for *Candida* species, identified using diagnostic technologies such as MALDI-TOF MS, BioFire, and the Vitek 2 system.

### Data Collection

Data collection involved identifying all episodes of candidemia from the Microbiology Laboratory's data system during the study period. The collected data included patient demographics, underlying health conditions, immunosuppression

details, laboratory results, and antifungal therapy specifics. Information was gathered from electronic medical records to ensure comprehensive coverage of each patient's clinical history and treatment details. This dataset was used for statistical analyses to evaluate clinical characteristics, species distribution, and antifungal susceptibility patterns.

## Laboratory Procedures

### Blood Culture Processing

Blood cultures Bottle (Aerobic, Anaerobic, Paediatric) were incubated for up to 5 days using, BACT/ALERT VIRTUO microbial detection system (BioMérieux, Durham, NC, USA) automated blood culture systems. All positive Blood cultures bottle demonstrating yeast or *Candida* pseudo or true hyphae presence on Gram staining underwent subsequent subculturing on Sabouraud Dextrose Agar (SDA) (Saudi Prepared Media Laboratories) which incubated aerobically at 35–37°C for 24–48 hrs and the ordinary media included 5% sheep blood agar, or chocolate agar, and MacConkey agar (Saudi Prepared Media Laboratories) which incubated at 35–37°C, on 5% Co 2 for 24–48 hrs.

### Fungal Identification and Susceptibility Testing

Yeast identification were conducted BioFire Blood Culture Identification 2 (BCID2) Panel and VITEK MS (BioMérieux, Durham, NC, USA) which is The system used MALDI-TOF (Matrix-assisted laser desorption ionization time-of-flight) technology to identify the Yeast species, genus, or group level in minutes using pure bacterial colonies from cultural media.

For Yeast Susceptibility Testing, Vitek 2 System (BioMérieux, Marcy-L'Étoile, France) (employing AST-YS01 card) used to antifungal susceptibility profiling and discerning their susceptibility patterns against commonly utilised antifungals like amphotericin B, fluconazole, flucytosine and voriconazole and micafungin, Caspofungin all susceptibility result reported depend on CLSI M27 Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts.

## Definitions and Criteria

### Episode of Candidemia

An episode of candidemia was defined by the growth of *Candida* spp. from at least one blood culture. If another episode occurred 2 weeks after the resolution of the previous with clear resolution of clinical sepsis features in between, it was regarded as a separate episode.

### Intravascular Device (IVD) Association

An IVD was considered a candidemia focus if a *Candida* species was isolated from the IVD tip amidst an ongoing episode of candidemia.

### Antifungal Therapy Appropriateness

Antifungal therapy was deemed appropriate if the *Candida* spp. isolate demonstrated sensitivity to the antifungal agent provided for the patient.

## Statistical Analysis

The statistical analyses involved univariate, bivariate and multivariate analyses. All the analysis was done in R programming language.

### Univariate Analysis

Descriptive statistics were used for the univariate analysis. Categorical variables were presented as frequencies and percentages for overall data and disaggregated by species. Continuous variables were expressed as mean  $\pm$  standard deviation (SD) or median and interquartile range (IQR) based on the data distribution.

### Bivariate Analysis

In the bivariate analysis, the association between each independent variable and the occurrence of candidemia was assessed using various statistical tests. Pearson's chi-square test and Fisher's exact test were utilized for categorical variables, while the Kruskal–Wallis test was applied for continuous variables. A *p*-value cut-off point of 0.05 was considered to identify variables significantly associated with the outcome for further analysis.

## Multivariate Analysis

Subsequently, a multivariate logistic regression model was constructed with mortality as the dependent outcome variable and *Candida* species as the exposure variable. The variables, including age in years, autoimmune disease, diabetes mellitus, kidney disease, dialysis and cancer and chemotherapy, were controlled as confounding factors in the model due to their significant association ( $p < 0.05$ ) in the bivariate analysis. In addition, the sensitive antifungal treatment administered was included in the model because of its relevance in other literature. Odds ratios (OR) were derived from the logistic regression model and presented with 95% confidence intervals (CI). The fit of the model was evaluated using the global  $p$ -value, with a predetermined significance level of 0.2. Factors with a  $p$ -value less than 0.05 in the multivariate analysis were considered statistically significant. Statistical analyses were conducted using the R programming language.

## Ethical Considerations

Approval for this study was obtained from the Research Committee of the Unit of Biomedical Ethics at King Abdulaziz University's Faculty of Medicine. Patient data were anonymised to ensure confidentiality and compliance with ethical research practices.

## Results

The study included 418 patients diagnosed with candidemia at King Abdulaziz University Hospital (KAUH) between January 2017 and March 2021. The median age of the patients was 46 years, with an interquartile range (IQR) of 6 to 68 years. The group consisted of slightly more males (58%) than females (42%). Notably, a small percentage of patients (2.9%) were smokers (See [Table 1](#)).

**Table 1** Demographic and Clinical Characteristics of Candidemia Patients in King Abdulaziz University Hospital, January 2017 to March 2021, KSA

| Characteristics                             | N = 418<br>n (%) |
|---------------------------------------------|------------------|
| Median age in Years (IQR)                   | 46 (6, 68)       |
| Sex                                         |                  |
| Female                                      | 177 (42%)        |
| Male                                        | 241 (58%)        |
| Smoking                                     | 12 (2.9%)        |
| History of Previous Surgery                 | 158 (38%)        |
| Autoimmune Disease                          | 26 (6.2%)        |
| HIV                                         | 8 (1.9%)         |
| Diabetes Mellitus                           | 178 (43%)        |
| COVID-19                                    | 26 (6.2%)        |
| Kidney Diseases                             | 153 (37%)        |
| Organ Transplant                            | 3 (0.7%)         |
| Cancer and Chemotherapy                     | 81 (19%)         |
| Dialysis                                    | 96 (23%)         |
| Central peripheral line                     |                  |
| Central line                                | 101 (24%)        |
| Peripheral line                             | 158 (38%)        |
| Peripheral line & Central line              | 159 (38%)        |
| Previous history of Candidemia              | 140 (33%)        |
| Medical Device Present                      | 330 (79%)        |
| Sensitive Antifungal Treatment Administered | 104 (25%)        |
| Deceased                                    | 280 (67%)        |

**Abbreviation:** IQR, Inter Quartile Range.

Several comorbidities were prevalent among the patients, with diabetes mellitus being the most common, affecting 43% of the group. Kidney diseases were present in 37% of the patients, and 23% were undergoing dialysis. Autoimmune diseases and HIV were less common, observed in 6.2% and 1.9% of patients, respectively. The presence of COVID-19 was noted in 6.2% of the cases during the study period (See Table 1).

A significant proportion of patients had a history of previous surgery (38%) and candidemia (33%). The use of medical devices was widespread, with 79% of the patients having at least one device in place. Central lines were used in 24% of cases, peripheral lines in 38%, and both types of lines in another 38%. Sensitive antifungal treatment was administered to 25% of the patients, and the overall mortality rate in this group was notably high at 67% (See Table 1).

## Distribution of Candida Species

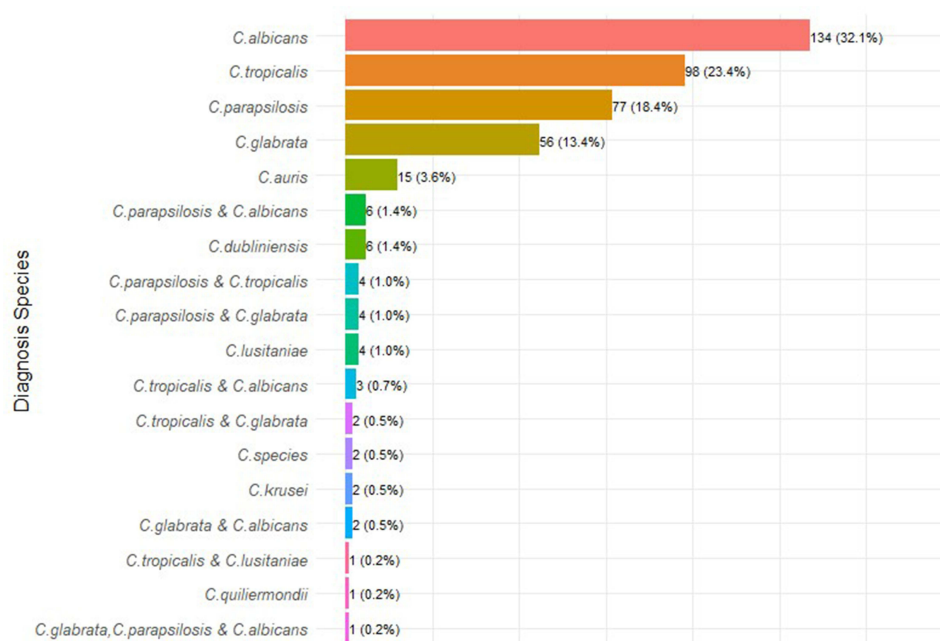
Our investigation of the distribution of *Candida* species revealed a notable prevalence of *C. albicans*, identified in 134 instances, constituting 32.1% of the cases. This was followed by *C. tropicalis* and *C. parapsilosis*, which were detected in 98 (23.4%) and 77 (18.4%) cases, respectively (See Figure 1).

Interestingly, several instances of co-occurring species were identified, albeit less frequently. For example, the combination of *C. parapsilosis* and *C. albicans* was observed in 6 cases (1.4%), while *C. parapsilosis* and *C. tropicalis* co-occurred in 4 instances (1%). A particularly intriguing observation was the simultaneous identification of *Nakaseomyces glabrata*, *C. parapsilosis* and *C. albicans* in a single case (0.2%) (See Figure 1).

Less common species were also identified, such as *C. auris* and *Clavispora lusitaniae*, which were found in 15 (3.6%) and 4 (1%) instances, respectively. Moreover, certain species were identified only sporadically; for example, *C. quiliiermondii* and *Pichia kudriavzevii* were each identified in 1 (0.2%) and 2 (0.5%) cases, respectively (See Figure 1).

## Antifungal Susceptibility of Candida Species

Table 2 delineates the sensitivity of various *Candida* species to diverse antifungal agents as ascertained by Vitek testing across a cohort of 418 individuals. A predominant sensitivity was observed for amphotericin B (95%) and fluconazole (94%) across all species, with minimal variations among the different *Candida* species groups. The highest sensitivity to fluconazole was observed in the *C. parapsilosis* group (99%), although the difference was not statistically significant ( $p$ -value: 0.14).



**Figure 1** Distribution of candida species among patients in King Abdulaziz University Hospital, January 2017 to March 2021, KSA.

**Table 2** Sensitivity of *Candida* Species to Antifungal Drugs, King Abdulaziz University Hospital, KSA

| Antifungal drugs                                | Overall<br>N = 418<br>n (%) | <i>C. albicans</i><br>N = 134<br>n (%) | <i>N. glabrata</i><br>N = 56<br>n (%) | <i>C. parapsilosis</i><br>N = 77<br>n (%) | <i>C. tropicalis</i><br>N = 98<br>n (%) | Other<br>Multiple<br>Species<br>N = 23<br>n (%) | Other<br>Single<br>Species<br>N = 30<br>n (%) | p-value <sup>2</sup> |
|-------------------------------------------------|-----------------------------|----------------------------------------|---------------------------------------|-------------------------------------------|-----------------------------------------|-------------------------------------------------|-----------------------------------------------|----------------------|
| Vitek sensitivity to amphotericin B             | 398 (95%)                   | 129 (96%)                              | 51 (91%)                              | 75 (97%)                                  | 93 (95%)                                | 22 (96%)                                        | 28 (93%)                                      | 0.6                  |
| Vitek sensitivity to fluconazole                | 395 (94%)                   | 127 (95%)                              | 49 (88%)                              | 76 (99%)                                  | 93 (95%)                                | 22 (96%)                                        | 28 (93%)                                      | 0.14                 |
| Vitek sensitivity to voriconazole               | 12 (2.9%)                   | 5 (3.7%)                               | 2 (3.6%)                              | 1 (1.3%)                                  | 4 (4.1%)                                | 0 (0%)                                          | 0 (0%)                                        | 0.8                  |
| Vitek sensitivity to caspofungin                | 352 (84%)                   | 108 (81%)                              | 46 (82%)                              | 73 (95%)                                  | 79 (81%)                                | 18 (78%)                                        | 28 (93%)                                      | <b>0.023</b>         |
| Vitek sensitivity to micafungin                 | 6 (1.4%)                    | 3 (2.2%)                               | 0 (0%)                                | 1 (1.3%)                                  | 2 (2.0%)                                | 0 (0%)                                          | 0 (0%)                                        | > 0.9                |
| Vitek sensitivity to micafungin/<br>caspofungin | 1 (0.2%)                    | 0 (0%)                                 | 0 (0%)                                | 1 (1.3%)                                  | 0 (0%)                                  | 0 (0%)                                          | 0 (0%)                                        | 0.4                  |

Note: <sup>1</sup>n (%) <sup>2</sup> bold face =  $p < 0.05$ .

There was a notable variation in sensitivity to caspofungin, with a significantly higher sensitivity recorded in the *C. parapsilosis* group (95%) compared to the overall sensitivity of 84% across all species groups ( $p$ -value: 0.023).

Sensitivity to voriconazole, micafungin and the combined sensitivity to micafungin or caspofungin was relatively low across all species groups at 2.9%, 1.4% and 0.2%, respectively. The discrepancies in sensitivities among the species groups for these antifungal agents were not statistically significant, with  $p$ -values of 0.8, > 0.9 and 0.4, respectively (See Table 2).

## Distribution and Correlation of *Candida* Species with Demographic and Clinical Characteristics of Patients

Table 3 shows that a total of 418 individuals were examined to investigate the distribution and effects of various *Candida* species on different patient characteristics and outcomes. The analysis segregated the population into seven groups based on the diagnosed *Candida* species: *C. albicans* ( $N = 134$ ), *Nakaseomyces glabrata* ( $N = 56$ ), *C. parapsilosis* ( $N = 77$ ), *C. tropicalis* ( $N = 98$ ), other multiple species ( $N = 23$ ) and other single species ( $N = 30$ ).

The median age across the entire sample was 46 years, with an interquartile range (IQR) of 6 to 68 years. However, notable differences were observed among the *Candida* species groups. For instance, individuals diagnosed with *Nakaseomyces glabrata* had a median age of 60 years (IQR: 30–77), which was significantly higher compared to those with *C. parapsilosis* (median age: 36, IQR: 5–67) ( $p$ -value: 0.018).

Sex distribution showed a statistically significant variation among the groups ( $p$ -value: 0.038), with a higher proportion of females (55%) in the *C. parapsilosis* group compared to the other groups.

A small proportion of individuals were identified as smokers (2.9%), with the highest smoking rate observed in the other multiple species group (13%). Although the difference was marginal, it was nearly statistically significant ( $p$ -value: 0.057).

Autoimmune diseases were present in 6.2% of the entire sample, with a higher prevalence of 23% observed in the other single-species group. This shows a statistically significant variation across the groups ( $p$ -value: 0.007).

Kidney diseases were prevalent in 37% of the individuals, with a higher rate of 53% in the other single-species group, showcasing significant variation ( $p$ -value: 0.008).

**Table 3** Summary Statistics of Demographic and Clinical Characteristics Among Candidemia Patients Stratified by *Candida* Species, King Abdulaziz University Hospital, KSA

| Characteristics                             | Overall<br>N = 418<br>n (%) | <i>C. albicans</i><br>N = 134<br>n (%) | <i>N. glabrata</i><br>N = 56<br>n (%) | <i>C. parapsilosis</i><br>N = 77<br>n (%) | <i>C. tropicalis</i><br>N = 98<br>n (%) | Other<br>Multiple<br>Species N =<br>23<br>n (%) | Other<br>Single<br>Species<br>N = 30<br>n (%) | p-value <sup>1</sup> |
|---------------------------------------------|-----------------------------|----------------------------------------|---------------------------------------|-------------------------------------------|-----------------------------------------|-------------------------------------------------|-----------------------------------------------|----------------------|
| Median age in Years (IQR)                   | 46 (6, 68)                  | 43 (5, 66)                             | 60 (30, 77)                           | 36 (5, 67)                                | 50 (7, 67)                              | 40 (9, 62)                                      | 58 (34, 68)                                   | <b>0.018</b>         |
| Sex                                         |                             |                                        |                                       |                                           |                                         |                                                 |                                               | <b>0.038</b>         |
| Female                                      | 177 (42%)                   | 55 (41%)                               | 25 (45%)                              | 42 (55%)                                  | 41 (42%)                                | 4 (17%)                                         | 10 (33%)                                      |                      |
| Male                                        | 241 (58%)                   | 79 (59%)                               | 31 (55%)                              | 35 (45%)                                  | 57 (58%)                                | 19 (83%)                                        | 20 (67%)                                      |                      |
| Smoking                                     | 12 (2.9%)                   | 5 (3.7%)                               | 1 (1.8%)                              | 0 (0%)                                    | 2 (2.0%)                                | 3 (13%)                                         | 1 (3.3%)                                      | 0.057                |
| History of previous surgery                 | 158 (38%)                   | 45 (34%)                               | 19 (34%)                              | 34 (44%)                                  | 36 (37%)                                | 11 (48%)                                        | 13 (43%)                                      | 0.5                  |
| Autoimmune disease                          | 26 (6.2%)                   | 8 (6.0%)                               | 4 (7.1%)                              | 3 (3.9%)                                  | 2 (2.0%)                                | 2 (8.7%)                                        | 7 (23%)                                       | <b>0.007</b>         |
| HIV                                         | 8 (1.9%)                    | 5 (3.7%)                               | 1 (1.8%)                              | 1 (1.3%)                                  | 0 (0%)                                  | 0 (0%)                                          | 1 (3.3%)                                      | 0.3                  |
| Diabetes mellitus                           | 178 (43%)                   | 48 (36%)                               | 29 (52%)                              | 29 (38%)                                  | 47 (48%)                                | 9 (39%)                                         | 16 (53%)                                      | 0.2                  |
| COVID-19                                    | 26 (6.2%)                   | 7 (5.2%)                               | 4 (7.1%)                              | 2 (2.6%)                                  | 7 (7.1%)                                | 1 (4.3%)                                        | 5 (17%)                                       | 0.2                  |
| Kidney diseases                             | 153 (37%)                   | 36 (27%)                               | 24 (43%)                              | 32 (42%)                                  | 41 (42%)                                | 4 (17%)                                         | 16 (53%)                                      | <b>0.008</b>         |
| Organ transplant                            | 3 (0.7%)                    | 1 (0.7%)                               | 0 (0%)                                | 1 (1.3%)                                  | 1 (1.0%)                                | 0 (0%)                                          | 0 (0%)                                        | > 0.9                |
| Cancer and chemotherapy                     | 81 (19%)                    | 22 (16%)                               | 11 (20%)                              | 12 (16%)                                  | 25 (26%)                                | 3 (13%)                                         | 8 (27%)                                       | 0.4                  |
| Dialysis                                    | 96 (23%)                    | 28 (21%)                               | 10 (18%)                              | 17 (22%)                                  | 30 (31%)                                | 3 (13%)                                         | 8 (27%)                                       | 0.3                  |
| Central peripheral line                     |                             |                                        |                                       |                                           |                                         |                                                 |                                               | <b>0.015</b>         |
| Central line                                | 101 (24%)                   | 33 (25%)                               | 9 (16%)                               | 21 (27%)                                  | 26 (27%)                                | 4 (17%)                                         | 8 (27%)                                       |                      |
| Peripheral line                             | 158 (38%)                   | 55 (41%)                               | 26 (46%)                              | 30 (39%)                                  | 34 (35%)                                | 1 (4.3%)                                        | 12 (40%)                                      |                      |
| Peripheral line and Central line            | 159 (38%)                   | 46 (34%)                               | 21 (38%)                              | 26 (34%)                                  | 38 (39%)                                | 18 (78%)                                        | 10 (33%)                                      |                      |
| Previous history of candidemia              | 140 (33%)                   | 40 (30%)                               | 18 (32%)                              | 27 (35%)                                  | 30 (31%)                                | 19 (83%)                                        | 6 (20%)                                       | <b>&lt; 0.001</b>    |
| Medical device present                      | 330 (79%)                   | 108 (81%)                              | 43 (77%)                              | 56 (73%)                                  | 75 (77%)                                | 22 (96%)                                        | 26 (87%)                                      | 0.2                  |
| Sensitive antifungal treatment administered | 104 (25%)                   | 21 (16%)                               | 13 (23%)                              | 31 (40%)                                  | 24 (24%)                                | 9 (39%)                                         | 6 (20%)                                       | <b>0.002</b>         |
| Deceased                                    | 280 (67%)                   | 90 (67%)                               | 43 (77%)                              | 44 (57%)                                  | 71 (72%)                                | 12 (52%)                                        | 20 (67%)                                      | 0.094                |

Note: <sup>1</sup> bold face =  $p < 0.05$ .

Abbreviation: IQR, Inter Quartile Range.

A notable variation was also observed in the usage of central and peripheral lines among the groups ( $p$ -value: 0.015), particularly a higher usage of both lines (78%) in the other multiple species group.

A history of candidemia was observed in 33% of cases, with a significant difference among the groups ( $p < 0.001$ ), with a substantial 83% of individuals in the other multiple species group having a previous history.

The administration of sensitive antifungal treatment varied significantly among the groups ( $p$ -value: 0.002), with the highest administration rate of 40% observed in the *C. parapsilosis* group.

The overall mortality rate was 67%, with a slightly higher rate of 77% observed in the *Nakaseomyces glabrata* group, although this variation was not statistically significant ( $p$ -value: 0.094).

## Effect of Candidemia on Mortality

Table 4 presents the results of a logistic regression analysis exploring the association between the diagnosis of different *Candida* species, selected patient characteristics, and the outcome of death while controlling for potential confounders.

The *Candida* species did not exhibit a statistically significant association with death, and administration of sensitive antifungal treatment also did not show statistical significance. However, other characteristics have shown a statistically significant association with being deceased.

**Table 4** Association of Candida Species with Mortality of Patients, King Abdulaziz University Hospital, KSA

| Characteristics                             | OR <sup>1</sup> | 95% CI <sup>2</sup> | p-value <sup>3</sup> |
|---------------------------------------------|-----------------|---------------------|----------------------|
| Candida species                             |                 |                     |                      |
| <i>C. albicans</i>                          | —               | —                   |                      |
| <i>N. glabrata</i>                          | 1.13            | (0.52 2.54)         | 0.8                  |
| <i>C. parapsilosis</i>                      | 0.54            | (0.27 1.04)         | 0.065                |
| <i>C. tropicalis</i>                        | 0.96            | (0.51 1.81)         | 0.9                  |
| Other multiple species                      | 0.49            | (0.18 1.32)         | 0.2                  |
| Other single species                        | 0.44            | (0.17 1.18)         | 0.10                 |
| Sensitive antifungal treatment administered | 1.31            | (0.76 2.27)         | 0.3                  |
| Age in years                                | 1.02            | (1.01 1.03)         | <b>0.002</b>         |
| Autoimmune disease                          | 4.43            | 1.35 20.3           | <b>0.027</b>         |
| Diabetes mellitus                           | 1.13            | (0.58 2.16)         | 0.7                  |
| Kidney diseases                             | 1.75            | (0.90 3.51)         | 0.11                 |
| Dialysis                                    | 3.11            | (1.31 7.76)         | <b>0.012</b>         |
| Cancer and chemotherapy                     | 1.74            | (0.93 3.37)         | 0.090                |

**Abbreviation:** <sup>1</sup>OR = odds ratio, <sup>2</sup>CI = confidence interval <sup>3</sup>bold face =  $p < 0.05$ .

The odds of death increased by 2% for each one-year increment in age (OR = 1.02, 95% CI: 1.01–1.03,  $p$ -value: 0.003). Individuals with autoimmune diseases were associated with significantly higher odds of death, with an OR of 4.25 (95% CI: 1.30–19.4,  $p$ -value: 0.030). Similarly, individuals undergoing dialysis have about three times higher odds of death compared to those not undergoing dialysis (OR = 2.99, 95% CI: 1.26–7.42,  $p$ -value: 0.015).

## Discussion

This study provides a comprehensive overview of candidemia's epidemiology and antifungal susceptibility at King Abdulaziz University Hospital (KAUH) from January 2017 to March 2021. The findings offer valuable insights into the distribution of Candida species, their resistance patterns, and associated patient outcomes, contributing to the global understanding of candidemia.

Our study identified *Candida albicans* as the most prevalent species, accounting for 32.1% of the cases. This finding aligns with global trends where *C. albicans* remains a dominant pathogen in candidemia.<sup>11</sup> However, the significant presence of non-*albicans* Candida species, such as *C. tropicalis* (23.4%) and *C. parapsilosis* (18.4%), underscores the importance of comprehensive species identification. These non-*albicans* species often exhibit different antifungal resistance patterns, necessitating tailored treatment approaches.<sup>12,13</sup>

The antifungal susceptibility results highlighted high sensitivity to Amphotericin B (95%) and Fluconazole (94%), which supports their continued use as primary antifungal agents. Similar findings have been reported in other studies.<sup>14,15</sup> However, notable resistance to Voriconazole and Micafungin across all species groups in your research indicates a need for careful selection of antifungal therapy based on susceptibility profiles. This resistance pattern is consistent with findings from China, where *C. tropicalis* showed significant non-susceptibility to fluconazole and voriconazole, and some *Nakaseomyces glabrata* isolates exhibited cross-resistance to these azoles.<sup>16</sup> Similarly, a study from Iran reported resistance to voriconazole among non-*albicans* Candida species, highlighting the variability in resistance patterns.<sup>17</sup> Notably, the significant sensitivity to Caspofungin in *C. parapsilosis* (95%) suggests it is a viable option for infections caused by this species. This aligns with studies from South Korea, where nearly all Candida isolates, including *C. parapsilosis*, were susceptible to caspofungin and micafungin.<sup>18</sup> A study from Malaysia found high susceptibility rates to amphotericin B and caspofungin among various Candida species, further supporting the use of these antifungals.<sup>19</sup> More recent studies also reported consistent findings.<sup>20,21</sup>

The study's mortality analysis revealed an overall mortality rate of 67%, with age, autoimmune diseases, and dialysis identified as significant risk factors. The increased mortality risk associated with older age (OR = 1.02) and autoimmune diseases (OR = 4.25) emphasizes the need for heightened clinical vigilance and potentially more aggressive treatment

strategies in these populations. The strong association between dialysis and mortality (OR = 2.99) further highlights the vulnerability of patients with renal impairment to severe outcomes from candidemia.

This study has several limitations. Its retrospective design may introduce selection bias, and the reliance on electronic medical records means the accuracy of data is contingent on the completeness and correctness of these records. Additionally, the study was conducted at a single institution, which may limit the generalizability of the findings to other settings. Future studies should include multiple centres to provide a broader perspective on candidemia epidemiology and resistance patterns. Another limitation of this study is the absence of a temporal trend analysis of antifungal resistance. While we report overall susceptibility patterns, we did not statistically evaluate changes in resistance across the study period (2017–2021). Future studies should aim to include year-by-year analyses to better detect shifts in resistance dynamics over time.

In conclusion, our study provides a comprehensive overview of the epidemiology and antifungal susceptibility of candidemia at King Abdulaziz University Hospital. The findings highlight the predominant role of *C. albicans*, underscoring the significant presence and clinical implications of non-*albicans* *Candida* species, such as *C. tropicalis* and *C. parapsilosis*. The observed resistance patterns, particularly the notable resistance to voriconazole and micafungin, emphasize the necessity for continuous surveillance and tailored antifungal stewardship. Given the high mortality rate associated with candidemia, especially among vulnerable patient populations, it is imperative to enhance diagnostic accuracy and optimize therapeutic strategies. Future research should focus on multi-center studies to validate these findings, explore the mechanisms driving antifungal resistance, and evaluate the impact of emerging diagnostic technologies on clinical outcomes. These efforts will contribute to improved patient management and infection control practices, ultimately reducing the burden of candidemia in healthcare settings.

## Conclusion

In conclusion, our study not only reaffirms the predominant role of *C. albicans* in candidemia in KAUH but also highlights the emerging threat posed by non-*albicans* *Candida* species, underscoring the necessity for enhanced diagnostic strategies and individualized treatment plans. Amphotericin B and fluconazole demonstrated the highest susceptibility rates across *Candida* species, reinforcing their continued role as first-line agents in empiric antifungal therapy. The high resistance to voriconazole and variable susceptibility to echinocandins underscore the importance of routine antifungal susceptibility testing and species-level identification. These findings should inform local antifungal stewardship efforts and guide empirical therapy protocols to improve patient outcomes and limit the emergence of resistance. Future research should focus on developing targeted therapies and rapid diagnostic tools to manage candidemia's dynamic epidemiology effectively.

## Data Sharing Statement

All the datasets are available on reasonable request to Community Medicine Department, Faculty of Medicine, King Abdulaziz University.

## Ethics Approval and Consent to Participate

This study was conducted in accordance with the ethical guidelines. Ethical approval for the research was obtained from the Institutional Review Board (IRB) of the Research Committee of the Unit of Biomedical Ethics at King Abdulaziz University's Faculty of Medicine with reference No 328 – 22. Data confidentiality and participant anonymity were strictly maintained throughout the study.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Consent for Publication

Not applicable. This manuscript does not contain any individual person's data in any form (including individual details, images, or videos) that would require consent for publication.

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## Disclosure

The authors declare that they have no competing interests.

## References

1. Dimopoulos G, Ntziora F, Rachiotis G, Armaganidis A, Falagas ME. Candida albicans versus non-albicans intensive care unit-acquired blood-stream infections: differences in risk factors and outcome. *Anesthesia Analg.* 2008;106(2):523. doi:10.1213/ane.0b013e3181607262
2. Wisplinghoff H, Ebberts J, Geurtz L, et al. Nosocomial bloodstream infections due to Candida spp. in the USA: species distribution, clinical features and antifungal susceptibilities. *Int J Antimicrob Agents.* 2014;43(1):78–81. doi:10.1016/j.ijantimicag.2013.09.005
3. Barberino MG, Silva N, Rebouças C, et al. Evaluation of blood stream infections by Candida in three tertiary hospitals in Salvador, Brazil: a case-control study. *Braz J Infect Dis.* 2006;10:36–40. doi:10.1590/S1413-86702006000100008
4. Chowdhary A, Sharma C, Meis JF. Candida auris: a rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. *PLOS Pathogens.* 2017;13(5):e1006290. doi:10.1371/journal.ppat.1006290
5. Yamin D, Husin A, Harun A. Distribution of candidemia in Malaysian tertiary care hospital revealed predominance of Candida parapsilosis. *Trop Biomed.* 2020;37(4):903–910. doi:10.47665/tb.37.4.903
6. Pfaller MA, Diekema DJ. Twelve years of fluconazole in clinical practice: global trends in species distribution and fluconazole susceptibility of bloodstream isolates of Candida. *Clin Microbiol Infect.* 2004;10:11–23. doi:10.1111/j.1470-9465.2004.t01-1-00844.x
7. Toda M. Population-based active surveillance for culture-confirmed candidemia — four Sites, United States, 2012–2016. *MMWR Surveill Summ.* 2019;68. doi:10.15585/mmwr.ss6808a1
8. Caggiano G, Coretti C, Bartolomeo N, Lovero G, De Giglio O, Montagna MT. Candida bloodstream infections in Italy: changing epidemiology during 16 years of surveillance. *Biomed Res. Int.* 2015;2015(1):256580. doi:10.1155/2015/256580
9. Atencia-Carrera MB, Cabezas-Mera FS, Tejera E, Machado A. Prevalence of biofilms in Candida spp. bloodstream infections: a meta-analysis. *PLoS One.* 2022;17(2):e0263522. doi:10.1371/journal.pone.0263522
10. Badiee P, Alborzi A, Shakiba E, Farshad S, Japoni A. Susceptibility of Candida species isolated from immunocompromised patients to antifungal agents. *East Mediterr Health J.* 2011;17(5):425–430. doi:10.26719/2011.17.5.425
11. Falagas ME, Roussos N, Vardakas KZ. Relative frequency of albicans and the various non-albicans Candida spp among candidemia isolates from inpatients in various parts of the world: a systematic review. *Inter J Infect Dis.* 2010;14(11):e954–e966. doi:10.1016/j.ijid.2010.04.006
12. Khatib R, Johnson LB, Fakih MG, Riederer K, Briski L. Current trends in candidemia and species distribution among adults: candida glabrata surpasses C. albicans in diabetic patients and abdominal sources. *Mycoses.* 2016;59(12):781–786. doi:10.1111/myc.12531
13. Pfaller M, Neofytos D, Diekema D, et al. Epidemiology and outcomes of candidemia in 3648 patients: data from the Prospective Antifungal Therapy (PATH Alliance®) registry, 2004–2008. *Diagnostic Microbiol Infectious Dis.* 2012;74(4):323–331. doi:10.1016/j.diagmicrobio.2012.10.003
14. Calgin MK, Cetinkol Y. Distribution and antifungal susceptibility patterns of Candida species at a university hospital in Northern Turkey. *J Infect Developing Countries.* 2018;12(02):97–101. doi:10.3855/jidc.9698
15. Sakagami T, Kawano T, Yamashita K, et al. Antifungal susceptibility trend and analysis of resistance mechanism for Candida species isolated from bloodstream at a Japanese university hospital. *J Infect Chemother.* 2019;25(1):34–40. doi:10.1016/j.jiac.2018.10.007
16. Xiao M, Fan X, Chen SCA, et al. Antifungal susceptibilities of Candida glabrata species complex, Candida krusei, Candida parapsilosis species complex and Candida tropicalis causing invasive candidiasis in China: 3 year national surveillance. *J Antimicrob Chemother.* 2015;70(3):802–810. doi:10.1093/jac/dku460
17. Mirhendi H, Charsizadeh A, Eshaghi H, Nikmanesh B, Arendrup MC. Species distribution and antifungal susceptibility profile of Candida isolates from blood and other normally sterile foci from pediatric ICU patients in Tehran, Iran. *Med Mycol.* 2020;58(2):201–206. doi:10.1093/mmy/myz047
18. Jung SI, Shin JH, Song JH, et al. Multicenter surveillance of species distribution and antifungal susceptibilities of Candida bloodstream isolates in South Korea. *Med Mycol.* 2010;48(4):669–674. doi:10.3109/13693780903410386
19. Amran F, Aziz MN, Ibrahim HM, et al. In vitro antifungal susceptibilities of Candida isolates from patients with invasive candidiasis in Kuala Lumpur Hospital, Malaysia. *J Med Microbiol.* 2011;60(9):1312–1316. doi:10.1099/jmm.0.027631-0

20. Memon S, Farooqi J, Zafar U, Naqvi SF, Zafar A, Jabeen K. Antifungal susceptibility profile of invasive *Candida glabrata* isolates (2009–2020) from a tertiary care hospital laboratory in Pakistan. *J Med Microbiol.* 2021;70(12):001459. doi:10.1099/jmm.0.001459
21. Sinh CT, Loi CB, Minh NTN, et al. Species distribution and antifungal susceptibility pattern of candida recovered from intensive care unit patients, vietnam national hospital of burn (2017–2019). *Mycopathologia.* 2021;186(4):543–551. doi:10.1007/s11046-021-00569-7

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