Research Article

Epidemiological Characteristics and Drug Resistance of Fungemia in General Hospitals from 2010 to 2019

Yanling Bai,1 Zhigang Zheng,2 Ting Liu,3 Zhongqiang Yan,4 Mingmei Du,1 Hongwu Yao,1 Yunxi Liu,1 and Jijiang Suo1

1Department of Disease Control and Prevention, The First Medical Center of Chinese PLA General Hospital, Beijing 100853, China
2Fuxing Road Outpatient Department, Jingnan Medical District of Chinese PLA General Hospital, Fuxing Road No. 22, Beijing 100842, China
3First Department of Health Care, The Second Medical Center & National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing 100853, China
4Department of Disease Control and Prevention, The Second Medical Center & National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing 100853, China

Correspondence should be addressed to Yunxi Liu; liuyunxi301@qq.com and Jijiang Suo; sjj301@qq.com

Received 9 June 2021; Accepted 8 October 2021; Published 2 November 2021

Objective. This study intends to analyze the data of fungemia in a large tertiary hospital from 2010 to 2019, and is aimed at understanding its epidemic characteristics and drug resistance.

Methods. The “Hospital Infection Real-Time Monitoring System” was used to retrieve the case information of patients who were hospitalized for more than 48 hours from 2010 to 2019. The questionnaire was designed to collect patients’ basic information, infection situation, drug resistance, and other related information. Statistical software was used for analysis.

Results. The fungi detection rate was in the range of 0.19% ~ 0.75% in ten years, the average rate was 0.29%, and the rate 0.2% ~ 0.3% since 2013, which was lower than that from 2010 to 2012. Non-Candida albicans was the main fungus, accounting for 62.50%. The drug resistance of non-C. albicans was higher than that of C. albicans, among which C. glabrata had the highest resistance rate. Data analysis showed that the patients with more serious basic diseases, combined with infection of other sites, surgery, long hospital stay, combination of antibiotics, and invasive catheterization, were more likely to occur fungemia.

Conclusion. We should pay more attention to the patients with high-risk factors of fungemia and focus on the drug resistance of non-C. albicans, choose the right antifungal drugs, so as to improve the level of diagnosis and treatment.

1. Introduction

In recent years, with the increasing use of immunosuppressive agents, broad-spectrum antibiotics, and biological agents, as well as the extensive development of traumatic diagnosis and treatment measures, the incidence of fungemia has been increasing [1]. Compared with bacterial infections, the primary manifestations of fungemia are not obvious, as well as the diagnosis, the mortality is higher, and the prognosis is even worse. The results of other studies showed that fungemia ranks the fourth in hospital-acquired bloodstream infection cases [2], and the infection rate increases year by year [3, 4]; the mortality can be as high as 50%-71% [5]. The types of antifungal drugs are limited, mainly including triazole, polyene, and echinomycin. Currently, fluconazole and amphotericin B are mostly used empirically in clinical practice, resulting in an increasingly serious problem of fluconazole resistance.

In 2009, the first new “Candida auris” was reported in Japan, which was resistant to all three classes of antifungal agents, known as “super fungi” [6]. So far, the drug resistance of fungal infection has been widely concerned. Up to now, “C. auris” has been found in more than 30 countries and regions around the world, including China. Fungemia,
due to its high mortality and poor prognosis, has attracted enough attention in clinical practice; if the drug resistance is widespread, the consequences are unimaginable.

This paper retrospectively analyzed the data from 2010 to 2019 of a large general hospital in Beijing, China, which had nearly 4,000 beds and received more than 200,000 patients annually, to investigate the epidemiological characteristics and drug resistance of fungemia in the past 10 years, so as to provide reference for the prevention, control, and treatment of fungemia, as follows.

2. Materials and Methods

2.1. Materials. From January 1, 2010, to December 31, 2019, all patients met the inclusion and exclusion criteria in the medical, surgical, and intensive care units of the hospital. The diagnosis of fungemia was confirmed by professional physicians engaged in nosocomial infection control and clinicians according to the diagnostic criteria and clinical symptoms of patients. A total 680 cases of the fungi were detected, resulting in 615 fungemia in 598 patients. There were 378 males and 220 females, age ranging from 1 day to 94 years old, with an average age of 60.77 ± 20.025 years old. This study was approved by the Ethics Committee of the hospital with the approval number S2019-142-02.

Inclusion criteria: (1) blood samples submitted during hospitalization; (2) patients hospitalized for more than 48 hours; (3) complete case data.

Exclusion criteria: (1) patients with less than 48 hours of hospitalization; (2) complicated with community-acquired bloodstream infection; (3) repeated strains of the same patient within 7 days; (4) blood culture results suspect contamination; (5) patients with missing data.

Diagnostic criteria for fungemia: the same fungus has been cultured from blood sample for twice or more; one blood culture was positive, and the same fungal infection was confirmed by biopsy or autopsy specimens. Diagnostic criteria for concomitant bacteremia: positive bacterial blood culture before and after positive fungal culture.

The clinical diagnosis was combined with the "Diagnostic Criteria for Hospital Infection (Trial)" issued by the Ministry of Health of the People's Republic of China in 2001 [7], including fever greater than 38°C or hypothermia less than 36°C, accompanied by shivering, and combined with one of the following conditions: invasion of portal or migration lesions; symptoms of systemic poisoning; SBP of less than 12 kPa (90 mmHg) or more than 5.3 kPa (40 mmHg) below the original SBP.

Diagnostic criteria for Catheter-Related Blood Stream Infection (CRBSI): according to the 2011 CDC guidelines for the prevention of CRBSI [8], CRBSI refers to patients with endovascular catheter or removal of endovascular catheter within 48 hours of bacteremia or mycosis, accompanied by fever (>38°C), chills, or hypotension and other manifestations of infection. There is no other specific source of infection except for the vascular catheter. Laboratory microbiological examination showed that bacteria or fungi cultured in peripher-
of the four fungi detected in recent 10 years. See Table 2 and Figure 1 for details.

3.3. Drug Sensitivity Analysis. The drug susceptibility testing (DST) was mainly carried out for Itraconazole, Fluconazole, Voriconazole, and Amphotericin B. The total resistance rate was 5.2%. The resistance rate to Itraconazole was the highest (7.9%), followed by Fluconazole (6.1%) and Voriconazole (3.1%); no resistance to amphotericin B was found. *C. albicans* had low drug resistance to all drug, and the highest resistance rate to Itraconazoleon only as 1.5%. Among non-*C. albicans*, the drug resistance rate of *C. glabrata* to Voriconazole was the highest at 28.8%, and that of *C. tropicalis* to Voriconazole was the highest at 12.7%, and that of *C. parapsilosis* to Fluconazole was 4.8%. In 10 years, a total of 8 strains were found which were resistant to three kinds of antibiotics (Voriconazole, Fluconazole, and Itraconazole) and mediated to Amphotericin B, including 5 strains of *C. tropicalis*, 1 strain of *C. albicans*, 1 strain of *C. glabrata*, and 1 strain of *C. parapsilosis*. The distribution years were 1 strain in 2014, 3 strains in 2015, 2 strains in 2017, 1 strain in 2018, and 1 strain in 2019, respectively. See Table 3 for details.

3.4. Clinical Characteristics Description of Fungemia. There were 615 cases of fungemia in 598 patients; among them, 207 cases were CRBSI. The overall mortality rate was 19.90%. Male patients accounted for 63.21%; female patients accounted for 36.79%. The age of 60-79 years old was the highest, accounting for 39.30%, and 68.73% of the patients were 60-79 days. The average hospitalization days were 66.26 ± 142.696 days. See Table 4 for details.

### Table 1: The detection of fungi in blood culture from 2010 to 2019.

| Year   | No. of samples | No. of fungi | Rate of fungi (%) | Proportion of fungi (%) |
|--------|----------------|--------------|-------------------|-------------------------|
| 2010   | 11439          | 86           | 0.75              | 12.65                   |
| 2011   | 12226          | 82           | 0.67              | 12.06                   |
| 2012   | 15734          | 66           | 0.42              | 9.71                    |
| 2013   | 21794          | 44           | 0.20              | 6.47                    |
| 2014   | 23300          | 63           | 0.27              | 9.26                    |
| 2015   | 26721          | 59           | 0.22              | 8.68                    |
| 2016   | 29996          | 72           | 0.24              | 10.59                   |
| 2017   | 30330          | 83           | 0.27              | 12.21                   |
| 2018   | 31496          | 59           | 0.19              | 8.68                    |
| 2019   | 30153          | 66           | 0.22              | 9.71                    |
| Total  | 233189         | 680          | 0.29              | 100.00                  |

### Table 2: Detection of fungi in blood culture from 2010 to 2019.

| Fungal pathogens | No. of fungi | Proportion (%) |
|------------------|--------------|----------------|
| *C. albicans*    | 255          | 37.50          |
| Non-*C. albicans*| 425          | 62.50          |
| *Candida parapsilosis* | 175      | 25.74          |
| *Candida tropicalis* | 104       | 15.29          |
| *Candida glabrata* | 86         | 12.65          |
| *Candida krusei*  | 13           | 1.91           |
| Filamentous fungi | 11          | 1.62           |
| Ji Yemeng candida | 6           | 0.88           |
| *Candida inconspicua* | 4         | 0.59           |
| *Aspergillus fumigatus* | 2     | 0.29           |
| *Trichosporon cutaneum* | 1 | 0.15           |
| *Candida lusitaniae* | 1          | 0.15           |
| *Simulon Candida*  | 1            | 0.15           |
| Nameless candida  | 1            | 0.15           |
| Others            | 20           | 2.94           |
| Total             | 680          | 100.00         |

### 4. Discussion

*Candida* sp. is a conditional pathogen of human gastrointestinal tract, oral and vaginal mucosa, and epidermis. Under normal circumstances, even if the culture is positive in the host site, it cannot be considered as a pathogen, but the blood is a sterile part of the human body; once cultivated, it is significant. In recent years, it has been reported that the incidence of hospital-acquired fungemia has been on the rise, due to the widespread use of broad-spectrum antibacterial drugs, glucocorticoids, immunosuppressants, and chemotherapy drugs, as well as the development of multiple invasive diagnosis and treatment operations such as central venous catheterization and hemodialysis [9, 10]. In this study, we investigated the detection of fungi in blood culture from 2010 to 2019 and found that the detection rate did not increase, but decreased from 2013. The analysis found that the total number of blood culture samples was 11439 in 2010, rising to 21,794 in 2013, and to 30,153 in 2019, increasing by about three times. However, the total number of positives samples did not increase significantly, leading to a decrease in the detection rate. The reasons may be as follows: (1) with the development of medical technology, clinical emphasis has been placed on strengthening the submission of blood culture for examination. The number of submission for examination has been improved significantly, but the detection rate may not increase significantly, but the detection rate is lower. There may be excessive submission, invalid submission, or clinicians’ lax grasp of symptoms and signs. (2) With the improvement of medical technology and antibiotic efficacy, the resistance of fungi has increased, but the detection rate may not increase significantly, and more large sample studies are needed to verify this conclusions.
In recent years, it has been reported that the increasing clinical application of azole-based antifungal drugs has led to a gradual increase in the incidence of non-\textit{C. albicans} bacteremia \cite{11, 12}. In our study, non-\textit{C. albicans} accounted for 62.50%, which was higher than that of 50.00% in related studies \cite{13}, and the common non-\textit{C. albicans} isolated from blood culture were \textit{C. parapsilosis}, \textit{C. tropicalis}, and \textit{C. glabrata}, which were consistent with related studies \cite{14}. \textit{C. albicans} accounted for 37.50%, which was the most common fungi causing hospital-acquired fungemia \cite{15, 16}. There was no increasing or decreasing trend in the analysis of the four main fungi detected in recent 10 years.

Drug susceptibility testing is an important means to guide clinical medication and monitor drug resistance. In this study, among non-\textit{C. albicans}, \textit{C. glabrata} had the highest drug resistance rate, and the drug resistance rates to Itraconazole, Fluconazole, and Voriconazole were 28.8%, 12.1%, and 3.8%, respectively, which were higher than the mediating rate and drug resistance rate of \textit{C. albicans} reported in related studies \cite{17}, which is similar to the report of Chinese Hospital Invasive Fungi Surveillance Network (CIF-NET) \cite{18}. The highest resistance rate of \textit{C. parapsilosis} to Fluconazole was 4.8%; the highest resistance rate of \textit{C. tropicalis} to Itraconazole was 12.7%; but \textit{C. albicans} had low drug resistance to all drug, and the highest resistance rate to Itraconazole only as 1.5%, which was consistent with the results of higher drug resistance of non-\textit{C. albicans} reported by relevant studies \cite{19}. In recent years, Amphotericin B-resistant fungi have been reported \cite{18}, but no drug-resistant strains have been found in this study.

A total of 8 strains were found to be resistant to three kinds of antifungal agents (Voriconazole, Fluconazole, and Itraconazole) and mediated to Amphotericin B, including 5 strains of \textit{C. tropicalis}, 1 strain of \textit{C. albicans}, 1 strain of \textit{C. glabrata}, and 1 strain of \textit{C. parapsilosis}. Among the 8 patients, there were 3 cases of hematopathy, 3 cases of abdominal surgery, 1 case of pediatric medicine, and 1 case of neurology care unit. Among them, 7 cases were complicated with fungal infection of other parts and were treated with antifungal drugs and indwelling vessels for a long time. 3 of them died. The remaining patient was hemopathy who was repeatedly hospitalized with multiple antibiotics. "\textit{Candida auris}" is resistant to three kinds of commonly used
antifungal drugs (including azoles, polyenes, and echinocandins) [20]. In this study, the susceptibility tests of Echinocandins has not been detected in our hospital, and the mass spectrometric method for “Candida auris” was not developed, so these 8 strains could not be identified as “Candida auris”; however, the results also reminded us to pay attention to the drug resistance of non-C. albicans and the emergence of “Candida auris.”

In this group of data, the incidence of fungemia in male patients is higher than that in females, and the age range is 60~79 years, which is consistent with the European research reports that among patients with fungemia, the infection rate in male patients is higher than that in females, and the difference is particularly significant over the age of 50 [21]. In our study, the mortality of patients with fungemia was 19.90%, which was lower than that reported at home and abroad 28.00% [22, 23], which was related to the lack of data due to the automatic discharge of some critical patients. Potential risk factors include hemodialysis, invasive therapy (such as central static catheter, urinary catheter, and mechanical ventilation), extensive gastrointestinal surgery, application of broad-spectrum antibiotics, multiple sites, or continuous colonization of Candida, which is consistent with the results reported in relevant studies [24, 25]. In this study, most of the fungemia were distributed in the surgery department (hepatobiliary surgery (including ICU) (18.23%), intensive care unit (10.87%), indicating that major surgery before admission to ICU or major surgery during admission to ICU (especially gastrointestinal surgery) and intestinal bacterial shift may be the risk factors for the occurrence of fungemia. This is consistent with the results of Chow et al. [26]. In addition, fungemia is also distributed in respiratory, gastroenterology, cardiology, and hematology departments, which suggest that the detection of fungemia should not be limited to some departments; doctors of all departments should pay attention to fungemia.

In conclusion, patients with fungemia have the characteristics of more basic diseases, severe illness, and high mortality, and the patients are distributed in a wide range of departments. Non-C. albicans have high resistance to antifungal drugs. Clinicians should pay enough attention to the patients with high-risk factors of fungemia, to detect the occurrence trend, strain distribution, and antifungal drug resistance, in order to choose reasonable antifungal drugs to improve the level of diagnosis and treatment of fungemia [27].

Data Availability

This study only used the data from 2010 to 2019 for the purpose of analyzing the changes of fungus, which did not involve personal privacy and disputes. The data used to support the findings of this study are available from the author and corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

| Variables                        | Grouping, no (%). of cases |
|----------------------------------|---------------------------|
| Gender                           | Male, 378 (63.21%); female, 220 (36.79%) |
| Age                              | ≤18, 32 (5.35%); 18~59, 222 (37.12%); 60~79, 235 (39.30%); ≥80, 109 (18.23%) |
| Prognosis of disease             | Death, 119 (19.90%); discharge, 477 (79.77%); other, 4 (0.67%) |
| Combined with other site infection | Yes, 411 (68.73%); no, 187 (31.27%) |
| Departments                      | Hepatobiliary surgery, 109 (18.23%); intensive care unit, 65 (10.87%); respiratory medicine, 52 (8.70%); gastroenterology, 48 (8.03%); cardiovascular medicine, 46 (7.69%); cardiovascular surgery, 41 (6.86%); general surgery department, 40 (6.69%); neurology department, 35 (5.85%); emergency department, 33 (5.52%); hematology department, 25 (4.18%); oncology department, 22 (3.68%); other, 82 (13.71%) |
| Operations                       | Yes, 379 (63.38%); no, 219 (36.62%) |
| Indwelling deep vein catheter    | Yes, 537 (89.80%); no, 61 (10.20%) |
| Used ventilator                  | Yes, 346 (57.86%); no, 252 (42.14%) |
| Indwelling catheter              | Yes, 474 (79.26%); no, 124 (20.74%) |
| Used antibiotics                 | Yes, 596 (99.67%); no, 2 (0.33%) |
| Combined antibiotic use          | Yes, 584 (97.66%); no, 12 (2.01%); unused, 2 (0.33%) |
| Days of indwelling deep vein catheter | 41.39 ± 57.415 |
| Days of used ventilator          | 16.17 ± 40.502 |
| Days of indwelling catheter      | 27.23 ± 52.993 |
| Days of antibiotic use           | 47.97 ± 56.098 |
| Inpatient days                   | 66.26 ± 142.696 |
Authors’ Contributions

Yanling Bai, Zhigang Zheng, and Ting Liu contributed equally to this work. Zhigang Zheng and Ting Liu are co-first authors.

Acknowledgments

The authors wish to thank all members of expert team for helping data analysis and scientific research guidance (the submission of the manuscript in the preprint “https://www.researchsquare.com/article/rs-399853/v1”[27]). Thanks for giving me suggestions on the revision of the paper we submitted earlier. Thanks for the revision advice given by the professor, which will make the article more reasonable and scientific. This study is funded by the National Key R&D Program of China (2017YFC0806308 and 18CZX038). This work was also supported by the Priority Project on Infection Disease Control and Prevention (grant no. 2018ZX10733402) from the Ministry of Science and Technology of the People’s Republic of China.

References

[1] D. Bitar, O. Lortholary, Y. le Strat et al., “Population-based analysis of invasive fungal infections, France, 2001–2010,” Emerging Infectious Diseases, vol. 20, no. 7, pp. 1163–1169, 2014.
[2] B. J. Kullberg and M. C. Arendrup, “Invasive candidiasis,” The New England Journal of Medicine, vol. 373, no. 15, pp. 1445–1456, 2015.
[3] J. Delaloye and T. Calandra, “Invasive candidiasis as a cause of sepsis in the critically ill patient,” Virulence, vol. 5, no. 1, pp. 161–169, 2014.
[4] P. Phoompoung and M. Chyakulkeeree, “Recent progress in the diagnosis of pathogenic Candida species in blood culture,” Mycopathologia, vol. 181, no. 5–6, pp. 363–369, 2016.
[5] M. C. Arendrup and T. F. Patterson, “Multidrug-resistant Candida: epidemiology, molecular mechanisms, and treatment,” The Journal of Infectious Diseases, vol. 216, suppl_3, pp. S445–S451, 2017.
[6] S. Tsay, A. Kallen, B. R. Jackson, T. M. Chiller, and S. Vallabhaneni, “Approach to the investigation and management of patients with Candida auris, an emerging multidrug-resistant yeast,” Clinical Infectious Diseases, vol. 66, no. 2, pp. 306–311, 2018.
[7] The People’s Republic of China, Diagnostic criteria for hospital infection (trial), the Ministry of Health of the People’s Republic of China, 2001.
[8] H. P. Loveday, J. A. Wilson, R. J. Pratt et al., “epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England,” Journal of Hospital Infection, vol. 86, Suppl 1, pp. S1–S10, 2014.
[9] A. Kashiha, N. Setayesh, Y. Panahi et al., “Prevalence of candidemia and associated candida subtypes following severe sepsis in non-neutropenic critically ill patients,” Acta Bio-Medica, vol. 89, no. 2, pp. 193–202, 2018.
[10] F. Villanueva, J. Veliz, K. Canasa et al., “Characteristics of fungemia in a peruvian referral center: 5-year retrospective analysis,” Revista Peruana de Medicina Experimental y Salud Pública, vol. 37, no. 2, pp. 276–281, 2020.
[11] P. G. Pappas, M. S. Lionakis, M. C. Arendrup, L. Ostrosky-Zeichner, and B. J. Kullberg, “Invasive candidiasis,” Nature Reviews. Disease Primers, vol. 4, no. 1, article 18026, 2018.
[12] M. Xiao, Z. Y. Sun, M. Kang et al., “Five-year national surveillance of invasive candidiasis: species distribution and azole susceptibility from the China Hospital Invasive Fungal Surveillance Net (CHIF-NET) study,” Journal of Clinical Microbiology, vol. 56, no. 7, article e00577, 2018.
[13] S. G. Whaley, E. L. Berkow, J. M. Rybak, A. T. Nishimoto, K. S. Barker, and P. D. Rogers, “Azole antifungal resistance in Candida albicans and emerging non-albicans Candida species,” Frontiers in Microbiology, vol. 7, p. 2173, 2017.
[14] R. H. Jensen, H. K. Johansen, L. M. Søes et al., “Posttreatment antifungal resistance among colonizing Candida isolates in Candidemia patients: results from a systematic multicenter study,” Antimicrobial Agents and Chemotherapy, vol. 60, no. 3, pp. 1500–1508, 2016.
[15] M. Salehi, Z. Ghomi, R. Mirshahi, S. A. Dehghan Manshadi, and O. Rezahosseini, “Epidemiology and outcomes of candidemia in a referral center in Tehran,” Caspian Journal of Internal Medicine, vol. 10, no. 1, pp. 73–79, 2019.
[16] The Candidemia Study Group, F. Barchiesi, E. Orsetti, R. Gesuita, E. Skrami, and E. Manso, “Epidemiology, clinical characteristics, and outcome of candidemia in a tertiary referral center in Italy from 2010 to 2014,” Infection, vol. 44, no. 2, pp. 205–213, 2016.
[17] S. Vallabhaneni, A. A. Cleveland, M. M. Farley et al., “Epidemiology and risk factors for echinocandin nonsusceptible Candida glabrata bloodstream infections: data from a large multisite population-based candidemia surveillance program, 2008–2014,” Open Forum Infectious Diseases, vol. 2, no. 4, article ofv163, 2015.
[18] C.-f. Ma, F.-q. Li, L.-n. Shi et al., “Surveillance study of species distribution, antifungal susceptibility and mortality of nosocomial candidemia in a tertiary care hospital in China,” BMC Infectious Diseases, vol. 13, no. 1, p. 337, 2013.
[19] P. G. Pappas, C. A. Kauffman, D. R. Andes et al., “Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America,” Clinical Infectious Diseases, vol. 62, no. 4, pp. e1–50, 2016.
[20] S. Iguchi, Y. Itakura, A. Yoshida et al., “Candida auris: a pathogen difficult to identify, treat, and eradicate and its characteristics in Japanese strains,” Journal of Infection and Chemotherapy, vol. 25, no. 10, pp. 743–749, 2019.
[21] M. C. Arendrup, B. Bruun, J. J. Christensen et al., “National surveillance of fungemia in Denmark (2004 to 2009),” Journal of Clinical Microbiology, vol. 49, no. 1, pp. 325–334, 2011.
[22] X. Jia, C. Li, J. Cao, X. Wu, and L. Zhang, “Clinical characteristics and predictors of mortality in patients with candidemia: a six-year retrospective study,” European Journal of Clinical Microbiology & Infectious Diseases, vol. 37, no. 9, pp. 1717–1724, 2018.
[23] H. Kato, Y. Yoshimura, Y. Suido et al., “Mortality and risk factor analysis for Candida blood stream infection: A multicenter study,” Journal of Infection and Chemotherapy, vol. 25, no. 5, pp. 341–345, 2019.
[24] F. Sbrana, E. Sozio, M. Bassetti et al., “Independent risk factors for mortality in critically ill patients with candidemia on Italian Internal Medicine Wards,” Internal and Emergency Medicine, vol. 13, no. 2, pp. 199–204, 2018.
[25] E. Ghrenassia, D. Mokart, J. Mayaux et al., “Candidemia in critically ill immunocompromised patients: report of a retrospective multicenter cohort study,” *Annals of Intensive Care*, vol. 9, no. 1, p. 62, 2019.

[26] J. K. Chow, Y. Golan, R. Ruthazer et al., “Risk factors for albicans and non-albicans candidemia in the intensive care unit,” *Critical Care Medicine*, vol. 36, no. 7, pp. 1993–1998, 2008.

[27] Y. Liu, Y. Bai, Z. Zheng et al., “Epidemiological characteristics and drug resistance of fungemia: a 10-year data analysis in general hospitals,” https://www.researchsquare.com/article/rs-399853/v1.