Infection and Drug Resistance

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ORIGINAL RESEARCH

Distribution and Epidemiological Characteristics of Clinical Isolates of *A. fumigatus* in a Hospital from 2021 to 2023: A Retrospective Study

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Objective: The distribution characteristics of clinical isolates of *A. fumigatus* were analyzed to provide the basis for the prevention and control of *A. fumigatus* infection.

Methods: From January 2021 to December 2023, the First Affiliated Hospital of Nanjing Medical University collected clinical isolates of *A. fumigatus* from hospitalized patients for study. Duplicate strains from the same patient in the same area were eliminated, and community-, hospital-, and colonization infections were grouped.

Results: A total of 561 clinical isolates of *A. fumigatus* were identified, with 402 (82.35%) originating from male patients and 159 (17.65%) from female patients. The percentage of individuals aged 51 to 90 years was 78.97% (443/561). With the exception of surgery, which predominantly involved colonization, other departments mainly exhibited community-acquired infections (CAI) (P=0.002). The length of hospital stay was less than <15–30 days for most cases in the healthcare-associated infection group (HAI) (P<0.001). Lower respiratory tract infection accounted for the main site of infection across all three groups (95.37%), with ventilator-associated pneumonia being most prevalent in the HAI group (P<0.001). The detection rates of *A. fumigatus* from 2021 to 2023 were 3.89‰, 7.15‰, and 12.50‰, respectively. The detection frequencies of *A. fumigatus* throughout the three groups exhibited a year-on-year increase (P<0.001). Sputum samples constituted the main source of clinical isolates for all three groups, accounting for 61 strains (89.71%), 277 strains (78.69%), and 122 strains (86.52%) respectively, followed by bronchoalveolar lavage fluid samples.

Conclusion: The detection rate of *A. fumigatus* has exhibited a consistent upward trend over the past three years, with varying epidemiological characteristics observed across different infection types. It is recommended that medical institutions develop targeted prevention and control measures for *A. fumigatus* infections based on these unique characteristics.

Keywords: community-acquired infections, hospital-acquired infections, *A. fumigatus*, epidemiology

Introduction

Aspergillus fumigatus (*A. fumigatus*) is a prevalent airborne fungus and a significant opportunistic disease in humans. *A. fumigatus* infection is the predominant cause of invasive aspergillosis, resulting in around 14,000 hospitalizations and over 1,200 fatalities annually in the United States.[1,2] *A. fumigatus* exhibits a saprophytic lifestyle and is likely to induce invasive aspergillosis in immunocompromised individuals.[3,4] The extensive utilization of hormones, immunosuppressants, and broad-spectrum antibiotics, along with the rising incidence of malignancies and immunodeficiency, has rendered invasive fungal infections a significant hazard to human health. Annual fatalities attributed to fungal diseases globally have surpassed 1.5 million.[5] Worldwide, there might be around 5 million instances of allergic

Received: 28 November 2024
Accepted: 24 February 2025
Published: 28 February 2025

bronchopulmonary aspergillosis, 3 million instances of chronic pulmonary aspergillosis, and 250,000 to 400,000 instances of invasive aspergillosis annually.[6–10] The prevalence of mold infections has been rising annually, imposing a significant strain on the healthcare system and sufferers. The prevalence of invasive aspergillosis has surged significantly during the last two decades, with a fatality rate ranging from 60% to 90%.[5] A retrospective review of invasive fungal infections across five Asian nations revealed that prevalent species were *A. fumigatus* (71.6%), Mucorales (10.2%), mixed infection molds (8.0%), miscellaneous species (8.0%), and Fusarium (2.3%). The findings further corroborate that *Aspergillus* is the most often identified fungus in clinical settings.[11] A retrospective analysis was undertaken utilizing data from the Chinese Hospital Invasive Fungal Disease Surveillance Network, focusing on patients with fungal infections across several representative units in different areas to examine the epidemiological situation of fungal infections in China. In this investigation, 16,285 fungal strains were identified, with *Aspergillus* representing the largest share at 84.8% (13,806/16,285), of which *A. fumigatus* comprised 49.4% (6,819/16,285); the predominant specimen type was lower respiratory tract specimens, constituting 81.7% (13,305/16,285).[1]

Over 90% of *Aspergillus* infections are attributed to *A. fumigatus*, which significantly affects human and animal health and poses a life-threatening risk.[12,13] *A. fumigatus* has developed resistance to antifungal agents compared to other *Aspergillus* species, and its environmentally resistant populations are proliferating globally, increasing the risk of human infection.[14–16] *A. fumigatus* can invade the lungs of immunocompromised persons.[17]

Recently, there has been a rising incidence of panazole-resistant *A. fumigatus* strains in individuals without prior azole treatment. *Aspergillus* resistance to azoles denotes the capacity of *Aspergillus* species, especially *A. fumigatus*, to proliferate and endure in the presence of azole antifungal agents. Infections caused by azole-resistant *Aspergillus* are linked to increased rates of treatment failure and death.[18] Due to the unpredictability of future developments, it is essential to observe the proliferation of *A. fumigatus* and regulate its increasing prevalence. This study retrospectively gathered and analyzed data from patients infected with clinical isolates of *A. fumigatus* at Jiangsu Provincial People's Hospital over the past three years to enhance understanding of the epidemiological distribution of invasive *A. fumigatus* infections, thereby offering data support for the effective prevention and control of fungal infections in clinical settings.

Methods

Study Site

Clinical isolates of *A. fumigatus*, totaling 561, along with clinical data from hospitalised patients at Jiangsu Provincial People's Hospital (First Affiliated Hospital of Nanjing Medical University) were retrospectively gathered over a three-year period from January 2021 to December 2023. Strains isolated from the same portion of the same patient and incomplete clinical data were eliminated. All isolates were procured from patients at our hospital in accordance with standard hospital protocols, and this work received approval from the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (Ethics Number: 2024-SR-535).

Judgment Criteria

The "Nosocomial Infection Diagnostic Criteria (Trial)" categorises infection origins in patients into three types: hospital-acquired infection (HAI), community-acquired infection (CAI), and colonization.[19] HAI denotes invasive pulmonary *Aspergillus* infection contracted by patients during their hospitalization, encompassing infections that manifest while admitted and those acquired in the hospital but presenting post-discharge. However, it excludes infections that began before to admission or were present at the time of admission. CAI denotes invasive lung *Aspergillus* infection that arises outside of a hospital setting. Colonization denotes the condition in which *A. fumigatus* resides and proliferates in a specific region of the human body without eliciting a clinical illness. All samples were cultured following standard fungal testing protocols utilizing Sabouraud medium, blood agar plate medium, or potato dextrose agar medium for the cultivation of *Aspergillus*. Figures 1 and 2 illustrate the morphology of *A. fumigatus* when cultured in Sabouraud medium and on a blood agar plate, respectively. Each medical record of discovered *A. fumigatus* was meticulously evaluated item by item for assessment, and subsequently double-checked and validated. Patients with lung infections attributable to other bacteria, fungi, or new coronary pneumonia were excluded from the study.

Figure 1 Morphology of *A. fumigatus* cultured on a blood agar plate.

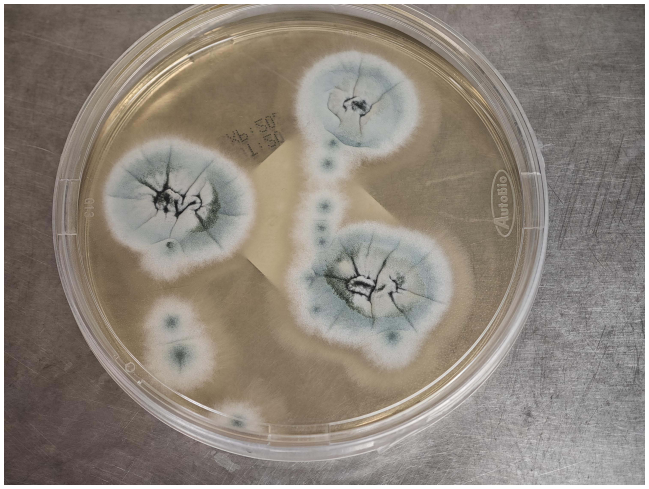

Figure 2 Morphology of *A. fumigatus* cultured in Sabouraud medium.

Data Sources

Specimen types encompass sputum, alveolar lavage fluid, nasal secretions, catheters, ear secretions, stool, ascites, oropharyngeal secretions, pus, skin secretions, wound secretions, pleural effusion, and tissue. Specimen culture was conducted in accordance with the National Clinical Laboratory Operation Procedures [M] 4th Edition.[20] The isolates were identified at the complex or species level following standard hospital protocols, including morphological phenotypic identification, matrix-assisted laser desorption/ionization-time of flight, and/or sequencing.

Statistical Analysis

Data analysis was conducted using SPSS 26.0 statistical software, comparing the clinical distribution of *A. fumigatus* isolates among the community infection group, hospital infection group, and colonisation group during three consecutive years. The count data were represented as percentages (%), and the chi-squared test was employed. The temporal trend of the detection rate was analysed using the trend chi-squared test. A P value of less than 0.05 was deemed statistically significant.

https://doi.org/10.2147/IDR.S507944

Results

Descriptive Results

A total of 561 clinical isolates of *A. fumigatus* were identified, comprising 68 healthcare-associated infections (HAI), 349 community-acquired infections (CAI), and 144 colonization strains (Figure 3). Among the patients, 402 (82.35%) were male and 159 (17.65%) were female. The percentage of individuals aged 51 to 90 years was 78.97% (443/561). The detection departments were mostly focused in the intensive care unit and internal medicine department, comprising 81.11% of the total. With the exception of the surgical department, which was mostly colonised, the remaining departments were primarily CAI (P=0.002). The duration of hospitalisation in the CAI and colonisation groups was mostly less than 15 days, but the HAI group primarily had a hospitalisation period of 15 to 30 days (P<0.001).

The infection locations in the three groups were largely lower respiratory tract infections (accounting for 95.37%), and ventilator-associated pneumonia accounted for the largest proportion in the HAI group (P<0.001) (Table 1).

Trend of A. fumigatus Detection

The detection rates of *A. fumigatus* from 2021 to 2023 were 3.89‰, 7.15‰, and 12.50‰, respectively. The trend analysis indicated that the detection frequencies of *A. fumigatus* in the three groups escalated annually (P<0.001) (Table 2).

Source of A. fumigatus Specimens

The primary sources of clinical isolates of *A. fumigatus* in the three groups were sputum specimens, including 61 strains (89.71%), 277 strains (78.69%), and 122 strains (86.52%), respectively. The second source comprised bronchoalveolar lavage fluid specimens, yielding 5 strains (7.35%), 62 strains (17.61%), and 10 strains (7.09%), respectively (Table 3).

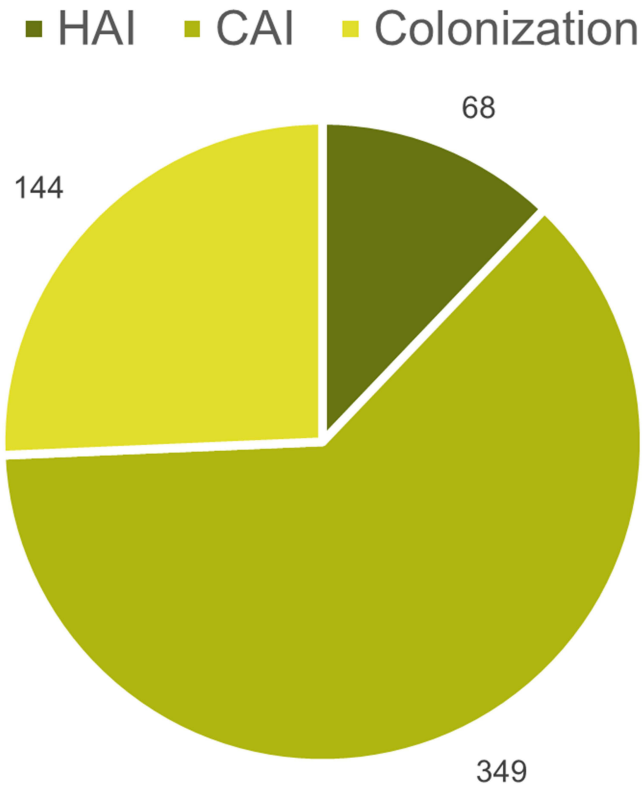

Figure 3 Distribution of *A. fumigatus* clinical isolates (2021–2023): Healthcare-associated infections (HAI), community-acquired infections (CAI), and colonization strains.

Table 1 Basic Distribution of Clinical Isolates of *A. Fumigatus* [n (%)]

	Total	CAI	HAI	Colonisation Group	χ^2	*P*
Gender						
Male	402	245(60.94)	49(16.92)	108(35.82)	1.162	0.559
Female	159	104(65.41)	19(11.95)	36(22.64)		
Age						
<30 yrs	12	7(58.33)	1(8.33)	4(33.33)	4.389	0.820
31–50 yrs	85	53(62.35)	12(14.12)	20(23.53)		
51–70 yrs	236	145(61.44)	31(13.14)	60(25.42)		
71–90 yrs	207	130(62.80)	20(9.66)	57(27.54)		
>90 yrs	21	14(66.67)	4(19.05)	3(14.29)		
Department						
Intensive Care Unit	297	195(65.66)	37(12.46)	65(21.89)	25.083	0.002
Internal Medicine	158	98(62.03)	19(12.03)	41(25.95)		
Surgery	47	19(40.43)	3(6.38)	25(53.19)		
Geriatrics	47	28(59.57)	9(19.15)	10(21.28)		
Emergency Department	12	9(75.00)	0(0.00)	3(25.00)		
Days in hospital						
<15 days	268	194(72.39)	13(4.85)	61(22.76)	34.508	<0.001
15~30 days	200	109(54.50)	34(17.00)	57(28.50)		
≥30 days	93	46(49.46)	21(22.58)	26(27.96)		
Infection site						
Lower respiratory tract	520	339(65.19)	54(10.38)	127(24.42)	111.877	<0.001
Ventilator-associated pneumonia	15	0(0.00)	12(80.00)	3(20.00)		
Upper respiratory tract	2	0(0.00)	1(50.00)	1(50.00)		
Skin and soft tissue	6	2(33.33)	0(0.00)	4(66.64)		
Pleural cavity	3	3(100.00)	0(0.00)	0(0.00)		
Ascites	2	0(0.00)	0(0.00)	2(100.00)		
Tissues in the abdominal (pelvic) cavity	2	2(100.00)	0(0.00)	0(0.00)		
Gastrointestinal tract	1	0(0.00)	1(100.00)	0(0.00)		
Urinary tract	1	0(0.00)	0(0.00)	1(100.00)		
Joint capsule	1	1(100.00)	0(0.00)	0(0.00)		
Endocarditis	1	1(100.00)	0(0.00)	0(0.00)		
Other	7	1(14.29)	0(0.00)	6(85.71)		

Abbreviations: HAI, hospital-acquired infection; CAI, community-acquired infection.

Table 2 The Change of Detection Trend of *A. Fumigatus* Between 2021–2023

Years	Total Number of Patients	Total Cases (‰)	CAI Cases (‰)	HAI Cases (‰)	Colonisation Group Cases (‰)
2021	192854	75 (3.89)	50 (2.59)	9 (0.4)	16 (0.8)
2022	213900	153 (7.15)	89 (4.16)	27 (1.2)	37 (1.7)
2023	266487	333 (12.50)	210 (7.88)	32 (1.2)	91 (3.4)
χ^2		113.009	66.710	7.946	37.420
P		<0.001	<0.001	0.019	<0.001

Abbreviations: HAI, hospital-acquired infection; CAI, community-acquired infection.

Discussion

The findings of this investigation indicated that the incidence of *A. fumigatus* infection in male patients was markedly greater than in female patients, with the 51–90 age demographic representing 78.97% of all identified cases. The disparity in gender and age distribution may be associated with the high-risk behaviors exhibited by male patients

Table 3 Sources of *A. Fumigatus* Specimens

Specimen Source	CAI (%)	HAI (%)	Colonisation Group (%)	Total
Sputum	277 (60.2)	61 (13.2)	122 (26.52)	460
Bronchoalveolar lavage fluid	62 (80.5)	5 (6.49)	10 (12.99)	77
Pleural and abdominal fluid	1 (16.6)	0 (0.00)	2 (33.33)	6
Catheter	4 (80.0)	0 (0.00)	1 (20.00)	5
Wound secretions	3 (60.0)	0 (0.00)	2 (40.00)	5
Ear and pharyngeal secretions	0 (0.00)	0 (0.00)	1 (33.33)	3
Tissue	1 (50.0)	0 (0.00)	1 (50.00)	2
Feces	0 (0.00)	1 (100.00)	0 (0.00)	1
Pus	1 (100.00)	0 (0.00)	0 (0.00)	1

Abbreviations: HAI, hospital-acquired infection; CAI, community-acquired infection.

(such as smoking and occupational exposure) and the diminished immunity of the older demographic.[4,21–24] However, our findings indicate no statistical difference in age and gender within the population; nonetheless, variations in fundamental health condition, behavior, profession, and immune function between men and women may contribute to disparities in the infectivity of *A. fumigatus*. Studies have demonstrated that gender differences have a definite influence on the incidence of many infectious illnesses caused by fungus, and various behavioral features or immunological responses of the host will alter the susceptibility to fungal infections.[25] Despite the absence of research on the correlation between gender and *A. fumigatus* infection in humans, findings from a principal component analysis in an animal disease model indicated that females exhibited significantly elevated levels of immune components against *A. fumigatus* compared to males, implying that host gender may play a crucial role in the development of immune responses.[26] Furthermore, *A. fumigatus* infection predominantly occurred in the critical care unit and internal medicine department, comprising 81.11% of cases, with the surgical department primarily exhibiting colonization, whereas other departments primarily had CAI (P=0.002). This distribution characteristic indicates that *A. fumigatus* infection is significantly associated with exposure to medical environments and high-risk departments, particularly affecting patients in the intensive care unit and internal medicine department, who may be more vulnerable to infection due to compromised immune function or invasive procedures.[25]

Regarding infection locations, the three groups predominantly exhibited infections in the lower respiratory tract (comprising 95.37%), with the HAI group demonstrating the greatest incidence of ventilator-associated pneumonia (P<0.001). This indicates that *A. fumigatus* infection is intimately connected with respiratory medical procedures, such as mechanical ventilation. Moreover, the duration of hospitalization for the CAI and colonization groups was mostly less than 15 days, but the HAI group primarily experienced stays of 15–30 days (P<0.001), further suggesting that hospital-acquired infections may extend patient hospitalization and elevate the medical burden. Between 2021 and 2023, the detection rate of *A. fumigatus* exhibited a notable increase. This trend may be attributed to several factors, including the rise in immunosuppressed patients and the heightened risk of environmental exposure to *A. fumigatus*. This trend indicates that *A. fumigatus* infection has emerged as a significant public health concern that warrants attention, necessitating enhanced monitoring, preventive, and control measures. The primary sources of clinical isolates of *A. fumigatus* throughout the three groups were sputum specimens, succeeded by bronchoalveolar lavage fluid specimens. This outcome further validated the characteristics of *A. fumigatus* mostly affecting the lower respiratory tract and indicated that sputum specimens are a crucial sample type for the clinical diagnosis of *A. fumigatus* infection.[27–29]This study's results indicate an increase in *A. fumigatus* infections in both community and hospital environments, mostly attributed to lower respiratory tract infections. Intensive care units and internal medicine departments are high-incidence areas for infections; thus, emphasis must be directed towards hospital-acquired *A. fumigatus* infections.

A. fumigatus conidia are frequently detectable in interior surroundings, including air, surfaces, and tap water in hospitals.[30–32] *A. fumigatus* conidia are frequently identified in interior settings, such as air, surfaces, tap water, and various hospital situations.[30–32]A study assessing the prevalence of *A. fumigatus* in the indoor air of hospital wards

revealed that *A. fumigatus* spores were found in the pulmonary disease department at concentrations reaching 300 CFU/m^3, whereas the corridors and restrooms in other departments exhibited the highest levels of contamination.[33] While no standard exists for the acceptable number of conidia in the atmosphere, one study suggested that the typical concentration of *Aspergillus* in outdoor air ranges from 0 to 20 CFU/m^3 or more.[34] We can consistently assess the air quality in high-risk departments, including critical care units, internal medicine, and geriatrics, to guarantee that the concentration of *A. fumigatus* spores remains under a safe threshold. Secondly, frequently touched objects in hospitals (such as bed rails, door handles, and medical equipment) can be routinely cleaned and disinfected using potent antifungal agents. Third, filters must be installed in high-risk locations, such as ICUs and transplant wards, to diminish the concentration of *A. fumigatus* spores in the air, guarantee adequate air circulation throughout the hospital, prevent humid environments, and mitigate circumstances conducive to mold proliferation. Moreover, the colonization of *A. fumigatus* may elevate the risk of invasive infections in immunocompromised individuals; therefore, early screening should be enhanced for high-risk patients to promptly identify *A. fumigatus* colonization or infection.

A study examining the thermal adaptation of 89 *A. fumigatus* strains from 12 countries across various climatic regions revealed significant variability in growth at different temperatures among strains, irrespective of geographic origin and genetic divergence. This indicates a robust capacity for *A. fumigatus* populations to adapt to climate change and global warming.[35] Research indicates that *A. fumigatus* conidia may be disseminated by aerosols produced by sick individuals, leading to environmental contamination and potential cross-infection among patients.[36–39] A Spanish investigation corroborates the notion that the hospital environment may facilitate the transmission or colonization of *A. fumigatus* in patients, adversely impacting treatment efficacy and exacerbating the challenges of hospital infection prevention and control.[40] Given the potential increase in hospital-acquired *A. fumigatus* infections due to the admission of patients with community-acquired infections, it is imperative to consider the risk of environmental transmission from these patients. To mitigate this risk, enhancing indoor ventilation and purification conditions is essential to diminish the presence of *A. fumigatus* in indoor environments, thereby reducing the incidence of hospital-acquired infections.

Recent years have witnessed an expansion of vulnerable patient populations and the rise of drug-resistant *A. fumigatus*, resulting in a notable increase in the morbidity and mortality associated with *A. fumigatus* infections in both community and hospital settings. However, the precise mechanisms underlying azole resistance in *A. fumigatus* are inadequately understood, complicating patient treatment.[10,16,37] Despite the global identification of azole-resistant *A. fumigatus*, active surveillance for resistant molds is insufficient or low in the majority of nations. Seventeen countries have now reported clinical isolates exhibiting resistance to azoles, and this strain of *A. fumigatus* has been identified in environmental samples across several more nations.[41] The Dutch investigation, concentrating on high-risk patients, revealed that 20% of those with invasive aspergillosis harbored triazole-resistant bacteria.[42] The extensive application of antifungal agents in human and veterinary medicine, agricultural practices, and timber products may have adverse side effects that might modify both the human microbiome and the natural microbiome. The relationship between the dissemination of *A. fumigatus* and alterations in the environmental microbiome remains uncertain; nevertheless, the presence of azoles that induce resistance in soil has been demonstrated to modify the soil microbiome.[43] Current research indicates that *A. fumigatus* colonization does not invariably correlate with infection; rather, its presence in diverse immunocompromised groups significantly elevates the risk of invasive infection. A study examining cytokines and pathogen recognition in aspergillosis, focusing on human and animal infections, revealed that the immune response to aspergillosis entails a complex interplay of cytokines and chemokines, which are crucial for host defense and disease advancement. Various interactions exist between cytokines and chemokines in aspergillosis. 1. Pathogen-associated molecular patterns and cytokine synthesis; 2. Th1, Th2, and Th17 immune responses; 3. The function of chemokines. The interconnections between cytokines and chemokines in aspergillosis are intricate, and comprehending the host response via human and animal research will facilitate the development of novel treatment techniques and enhance customized therapy.[44]

The management of *Aspergillus* infection is hindered by challenges in diagnosis and a rise in reports of medication resistance.[22,45,46] Despite our hospital doing medication sensitivity studies on *Aspergillus*, the available data is insufficient, and the overall in vitro sensitivity to voriconazole, caspofungin, and amphotericin B is 100%. Consequently, this data has not yet been included in the publication.

Currently, several laboratories in Chinese hospitals lack the capability to identify mold, and there is a scarcity of studies regarding the epidemiological data on mold diseases.[1] Subsequent research ought to investigate the mechanisms of drug resistance and transmission pathways of *A. fumigatus*, while enhancing the utilization of drug sensitivity testing and whole genome sequencing technologies to inform clinical antifungal therapies and strategies for infection prevention and control. Enhancing environmental monitoring, improving hospital ventilation, optimizing the diagnosis and treatment of high-risk patients, and instituting pertinent infection monitoring mechanisms can create an environment for immunosuppressed patients and those with chronic lung disease that minimizes high spore exposure. It is anticipated to diminish the morbidity and mortality associated with *A. fumigatus* infection.

Conclusion

Comprehending the epidemiology of *A. fumigatus* is becoming more vital for the accurate formulation of hospital infection management, control measures, and therapeutic treatment methods in the future. Currently, we can significantly mitigate the danger of *A. fumigatus* infection by environmental management, personal safeguards, medical interventions, and the protection of high-risk populations. The findings of this study can serve as a foundation for high-risk departments to implement effective strategies for managing *A. fumigatus* hospital infections and enhancing clinical and environmental fungal surveillance. In clinical isolation therapy, it is crucial to differentiate between hospital-acquired and community-acquired infections to regulate the proliferation of *A. fumigatus* hospital infections and promote policies for enhanced clinical antifungal management.

Data Sharing Statement

The data used in this paper can be provided by Feng Zang.

Ethics Approval Statement

All isolates were procured from patients at our hospital in accordance with standard hospital protocols, and this work received approval from the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (Ethics Number: 2024-SR-535), and waiver of patient informed consent. The Ethics Committee of the First Affiliated Hospital of Nanjing Medical University does not require patients to consent to review their medical records because ethics, consent to participate, and consent to publish declarations: not applicable. We are committed to abide by the Declaration of Helsinki and to keep data containing patient information confidential.

Acknowledgments

This study was supported by Jiangsu Provincial People's Hospital.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors declare that they have no conflict of interest.

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