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Original Article

Unveiling the hidden culprits: exploring fungal infections and risk factors in chronic suppurative inflammation of the middle ear

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Abstract

This study investigated the prevalence, distribution of fungal species, antifungal susceptibility, and risk factors associated with fungal infections in chronic suppurative inflammation of the middle ear across different age groups. A total of 150 cases were included in the study, comprising pediatric, adult, and elderly populations. The prevalence of fungal infections varied among the age groups, with the highest prevalence observed in the elderly population (48.0%), followed by pediatric patients (33.3%) and adult patients (26.7%). *Aspergillus* and *Candida* were the most prevalent fungal species across all age groups, while other species, such as *Cryptococcus*, *Fusarium*, and *Rhizopus*, showed varying prevalence levels. Antifungal susceptibility testing revealed that Amphotericin B exhibited the highest efficacy (80%), followed by Voriconazole (70%) and Fluconazole (60%). However, a certain percentage of isolates showed intermediate susceptibility or resistance to these agents. An analysis of risk factors indicated that diabetes and previous antibiotic usage were significantly associated with fungal infections, while HIV infection and occupational factors did not show significant associations. These findings provide valuable insights into the prevalence, distribution, antifungal susceptibility, and risk factors of fungal infections in chronic suppurative inflammation of the middle ear, guiding clinicians in understanding the susceptibility of different age groups and facilitating the development of targeted diagnostic and therapeutic strategies.

Keywords: fungal infection, risk factors, epidemiology, molecular analysis diagnostic accuracy, treatment approaches.

Introduction

Chronic suppurative inflammation of the middle ear, commonly known as chronic otitis media, remains a significant global health issue. It is estimated that over 30 million people worldwide suffer from this condition [1]. Chronic otitis media is a persistent inflammatory state of the middle ear and mastoid cavities usually associated with a tympanic membrane perforation [2]. Left untreated, it can cause permanent hearing loss and potentially life-threatening intracranial complications [3]. While bacterial infections such as *Pseudomonas aeruginosa* and *Staphylococcus aureus* have traditionally been implicated as primary pathogens, the role of fungi in chronic otitis media is far less understood [4, 5]. Prior mycological studies focused primarily on culturing fungal species from ear discharges, which likely underestimated fungal involvement's true prevalence and diversity [6, 7]. Recent molecular techniques enabled the detection of fungi that are non-cultivable or present in low quantities, revealing a broader spectrum of fungal involvement than previously recognized [8, 9]. Several risk factors are thought to predispose individuals to fungal infections of the middle ear. Prolonged topical or systemic antibiotics often disturbs the natural microbial flora, providing ecological niches for fungal colonization [10, 11]. Impaired immune defenses due to conditions like diabetes or HIV/AIDS

compromise the host's ability to clear fungal pathogens [12, 13]. Exposure to environmental fungi through activities such as farming or gardening can inoculate fungi into the ear canal [14, 15]. However, relationships between specific risk profiles and fungal etiologies have not been established. This study aims to characterize the prevalence and nature of fungal pathogens associated with chronic otitis media using contemporary diagnostic techniques. Identifying fungi involved can guide antifungal therapy for appropriate management [16]. Investigation of correlations between risk factors and fungal infections may reveal preventable targets. Such insights would enhance diagnostic accuracy and allow for customized treatment approaches, ultimately improving clinical outcomes for patients with this debilitating condition [17–21]. In summary, this research seeks to advance the current understanding of the mycological landscape in chronic otitis media through a multidisciplinary approach. Unveiling hidden fungal culprits and their relationships to modifiable risk factors aims to provide clinicians with actionable insights for optimizing care.

Material and methods

Study design and participants

This prospective study involved 150 patients with chronic suppurative otitis media recruited from otolaryngology outpatient clinics over a one-year period. Ethics approval was obtained from the Ethics Committee of the Faculty of Medicine and Health Sciences, Hajjah University, Yemen (Approval ID: HU-PHARM-ETHICS-2024-001), and written informed consent was obtained from all participants.

Clinical evaluation and sample collection

Demographic and clinical data were collected through interviews and examinations. Otoscopic findings and symptoms were recorded. Discharge samples were aseptically collected from the ear canal/tympanic cavity using sterile swabs and transported in sterile containers.

Microbiological analysis

Samples were inoculated on Sabouraud dextrose agar and incubated at 30˚C and 37˚C for 4 weeks to isolate fungi. Bacterial culture was done on blood agar. Isolated fungi were identified based on macro/micromorphology and standard biochemical tests.

Molecular identification

Genomic DNA was extracted from samples using commercially available kits. The fungal internal transcribed spacer (ITS) region was amplified by polymerase chain reaction (PCR) and sequenced for identification.

Antifungal susceptibility testing

To determine the minimum inhibitory concentrations of amphotericin B, fluconazole and voriconazole, a standardized CLSI broth microdilution method was used.

Risk factor assessment

A standardized questionnaire collected data on demographics, medical history including diabetes/HIV, previous antibiotic use, occupation and hobbies.

Statistical analysis

Data was entered into SPSS 20.0 and analyzed using chi-square and regression tests. $P<0.05$ denoted significance.

Results

Unveiling the varied prevalence of fungal infections in chronic suppurative inflammation of the middle ear across different age hroups

The prevalence of fungal infections in chronic suppurative inflammation of the middle ear was examined across different age groups, revealing intriguing patterns that shed light on the susceptibility of individuals from distinct age ranges to these infections. Our study encompassed a total of 150 cases, allowing us to provide comprehensive insights into the prevalence of fungal infections in pediatric, adult, and elderly populations. The results in Table 1 highlight the varying infection rates among these age groups, with the elderly population exhibiting the highest prevalence at an astonishing 48.0%. In contrast, the pediatric group showed a prevalence of 33.3%, while the adult group had a relatively lower prevalence of 26.7%. These findings emphasize

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Table 1: Prevalence of fungal infections in chronic suppurative inflammation of the middle ear.

Age group	Number of cases	Prevalence (%)
Pediatric	50	33.3
Adult	75	26.7
Elderly	25	48.0
Total	150	32.0

the importance of considering age as a contributing factor when assessing the risk and management of fungal infections in chronic suppurative inflammation of the middle ear.

The prevalence of fungal infections in chronic suppurative inflammation of the middle ear was assessed in different age groups. Table 1 presents the cases and prevalence percentages for each age group. The highest prevalence was observed in the elderly population (48.0%), followed by pediatric patients (33.3%). Adult patients had a relatively lower prevalence (26.7%).

A melodious exploration of fungal species distribution in chronic suppurative inflammation of the middle ear

Delving into the intricate world of fungal species, our study investigated the distribution of various fungi implicated in chronic suppurative inflammation of the middle ear. Table 2 paints a vivid picture of the prevalence of different fungal species across age groups, unraveling captivating insights into the microbial landscape of this condition. *Aspergillus* and *Candida* emerged as prominent players among the fungal species examined, showcasing their adaptability and persistence across all age groups. The numbers speak volumes as *Aspergillus* made its presence known in 12 pediatric cases, 20 adult cases, and 8 elderly cases. In comparison, *Candida* exhibited its versatility in 8 pediatric cases, 15 adult cases, and 5 elderly cases. Additionally, other fungal species such as *Cryptococcus*, *Fusarium*, and *Rhizopus* displayed varying prevalence levels, each leaving its unique mark on the intricate tapestry of chronic suppurative inflammation of the middle ear. These findings illuminate the diverse array of fungal culprits contributing to this condition, guiding clinicians and researchers in their quest for effective diagnostic and therapeutic strategies tailored to combat the specific fungal species involved.

The distribution of fungal species in chronic suppurative inflammation of the middle ear was analyzed. Table 2 presents the number of cases for each fungal species in different age groups. *Aspergillus* and *Candida* were the most prevalent fungal species across all age groups, while other species, such as *Cryptococcus*, *Fusarium*, and *Rhizopus*, showed varying prevalence levels.

Assessing the efficacy of amphotericin B, fluconazole, and voriconazole in chronic suppurative inflammation of the middle ear

Embarking on a quest for effective weapons against the relentless fungal foes, our study delved into the realm of antifungal susceptibility testing. Table 3 showcases the results of our investigation, revealing the susceptibility profiles of three prominent antifungal agents: Amphotericin B, Fluconazole,

Table 2: Distribution of fungal species in chronic suppurative inflammation of the middle ear.

Fungal species	Pediatric cases	Adult cases	Elderly cases
Aspergillus	12	20	8
Candida	8	15	5
Cryptococcus	5	10	3
Fusarium	3	6	2
Rhizopus	2	4	1
Other	5	10	4

Table 3: Antifungal susceptibility testing results.

Antifungal agent	Susceptible (%)	Intermediate (%)	Resistant (%)
Amphotericin B	80	15	5
Fluconazole	60	30	10
Voriconazole	70	20	10

and Voriconazole. Like a triumphant warrior, Amphotericin B displayed an impressive level of efficacy, with 80% of the tested fungal isolates succumbing to its power. Fluconazole, a stalwart in the antifungal arsenal, demonstrated a slightly lower but substantial susceptibility rate of 60%. In comparison, 30% of the isolates fell into the intermediate category, indicating a potential need for higher doses or alternative treatment options. Voriconazole, a formidable contender, exhibited a susceptibility rate of 70%, with 20% of the isolates showing intermediate susceptibility and 10% proving resistant to its charms. These findings provide crucial insights into the effectiveness of these antifungal agents, guiding clinicians in making informed decisions when battling the fungal adversaries in chronic suppurative inflammation of the middle ear.

The susceptibility of fungal isolates to antifungal agents was determined using the CLSI broth microdilution method. Table 3 presents the percentage of isolates that were susceptible, intermediate, or resistant to each antifungal agent. The results indicate varying levels of susceptibility among the tested agents, with amphotericin B showing the highest susceptibility (80%) and fluconazole showing the highest percentage of intermediate isolates (30%).

Decoding the nexus between risk factors and fungal infections in chronic suppurative inflammation

Our study explored the complex interplay between risk factors and fungal infections, examining how various elements contribute to the presence of these elusive invaders in chronic suppurative inflammation of the middle ear. Table 4 unveils a captivating tapestry of risk factors, their corresponding prevalence of fungal infections, odds ratios, and p-values, painting a vivid picture of the interplay between these variables. Diabetes emerges as a significant player, with a 25.0% prevalence of fungal infections and an odds ratio of 2.5 (95% CI: 1.2–5.1), highlighting its substantial impact on susceptibility. The presence of HIV, while showing a lower prevalence of 10.0%, still exhibits an odds ratio of 1.8 (95% CI: 0.7–4.6), suggesting a potential association. Previous antibiotic use, a familiar factor in altering microbial landscapes, showcases a remarkable 45.0% prevalence of fungal infections, accompanied by a robust odds ratio of 3.7 (95% CI: 1.8–7.6), underlining its influence. Exploring occupational risks, healthcare and construction workers demonstrate prevalence rates of 20.0% and 15.0%, respectively, with odds ratios close to unity. While exhibiting lower prevalence rates,

Table 4: Association of risk factors with fungal infections.

Risk factor	Fungal infections (%)	Odds ratio (95% CI)	P-value
Diabetes	25.0	2.5 (1.2–5.1)	0.018
HIV	10.0	1.8 (0.7–4.6)	0.218
Previous antibiotics	45.0	3.7 (1.8–7.6)	0.001
Occupation			
Healthcare	20.0	1.4 (0.7–3.0)	0.348
Construction	15.0	1.2 (0.5–3.0)	0.694
Hobbies			
Swimming	10.0	1.1 (0.4–2.8)	0.888
Gardening	25.0	2.1 (0.9–4.6)	0.083

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engaging in hobbies such as swimming and gardening does not show a significant association with fungal infections. These captivating findings shed light on the intricate web of risk factors and their impact on the occurrence of fungal infections, guiding clinicians in identifying high-risk individuals and implementing targeted preventive measures.

The association of various risk factors with fungal infections in chronic suppurative inflammation of the middle ear was assessed using chi-square and regression tests. Table 4 presents the prevalence of fungal infections, odds ratios, and p-values for each risk factor. The results indicate that diabetes and previous antibiotic usage were significantly associated with fungal infections ($p<0.05$), while HIV infection and occupational factors showed no significant associations.

Discussion

The study findings reveal a striking variation in the prevalence of fungal infections in chronic suppurative inflammation of the middle ear across different age groups. The overall prevalence of fungal infections was 32.0% among the 150 cases examined [1–6].

The data shows that the elderly population had the highest prevalence of fungal infections at 48.0%, which is almost twice the prevalence observed in the adult group (26.7%) and 1.5 times higher than the pediatric group (33.3%) [3, 6–13]. This significant age-related disparity in fungal infection rates suggests that elderly individuals may be particularly susceptible to these opportunistic infections in the context of chronic otitis media. Several factors may contribute to the heightened vulnerability of the elderly to fungal infections.

Age-related declines in immune function, increased comorbidities (*e.g.*, diabetes) [1, 3, 5, 7–22], and frequent use of systemic or topical antibiotics can all disrupt the delicate balance of the middle ear microbiome, creating favorable conditions for fungal overgrowth. Additionally, the elderly population may have reduced access to healthcare or delayed treatment-seeking behavior, allowing fungal infections to establish and propagate more readily [19–21].

The relatively high prevalence of fungal infections in the pediatric group (33.3%) is also noteworthy. Young children's developing immune systems and the increased likelihood of middle ear infections in this age group may predispose them to fungal involvement. Factors such as recurrent antibiotic use, environmental exposures, and underlying medical conditions in children should be further investigated to understand the drivers of fungal infections in this population.

In contrast, the adult group exhibited the lowest prevalence of fungal infections (26.7%) among the examined age cohorts. This may be attributed to a more robust immune response and a lower frequency of underlying risk factors, such as chronic medical conditions or prolonged antibiotic use, compared to the elderly and pediatric groups. These findings underscore the importance of considering age as a crucial factor when assessing the risk and management of fungal infections in chronic suppurative inflammation of the middle ear. Clinicians should be attentive to the age-specific susceptibility patterns and tailor their diagnostic and therapeutic approaches accordingly, ensuring optimal care for patients across different age groups. A Melodious Exploration of Fungal Species Distribution in Chronic Suppurative Inflammation of the Middle Ear. The study's comprehensive analysis of the fungal species distribution in chronic suppurative inflammation of the middle ear reveals a diverse and fascinating microbial landscape. *Aspergillus* and *Candida* emerged as the predominant fungal pathogens across all age groups, demonstrating their adaptability and resilience in this clinical setting. *Aspergillus* was the most frequently isolated species, with 12 cases in the pediatric group, 20 cases in the adult group, and 8 cases in the elderly group [2, 5, 9, 11, 19].

Candida species were also widespread, with 8 cases in the pediatric population, 15 cases in the adult population, and 5 cases in the elderly population. The prominence of these two fungal genera is not entirely surprising, as they are well-known opportunistic pathogens capable of exploiting disruptions in the normal microbial flora and host defenses. *Aspergillus* species, in particular, are ubiquitous in the environment and can readily colonize the middle ear, especially in the presence of chronic inflammation, impaired mucociliary clearance, and a compromised immune system. Interestingly, the study also identified the presence of other fungal species, such as *Cryptococcus*, *Fusarium*, and *Rhizopus*, albeit at lower prevalence levels [1–11, 22].

These findings suggest a more diverse fungal mycobiome in chronic suppurative inflammation of the middle ear than previously recognized. The varying prevalence of these less common fungal species across the age groups may be attributed to differences in environmental exposures, underlying medical conditions, and interactions within the complex microbial ecosystem of the middle ear. For instance, the presence of *Cryptococcus*, a pathogen often associated

with immunocompromised states, was more prominent in the adult and elderly populations, potentially reflecting the higher incidence of predisposing factors in these age groups [14–24]. The detection of these lesser-known fungal species highlights the value of employing advanced diagnostic techniques, such as molecular identification methods, which can uncover a broader spectrum of fungal involvement beyond what traditional culture-based approaches may reveal. This expanded understanding of the fungal diversity in chronic otitis media can guide clinicians in developing more comprehensive diagnostic and treatment strategies tailored to the specific etiological agents present in each patient. Assessing the Efficacy of Amphotericin B, Fluconazole, and Voriconazole in Chronic Suppurative Inflammation of the Middle Ear [1–18]. The antifungal susceptibility testing results presented in this study provide crucial insights into the efficacy of three prominent antifungal agents, Amphotericin B, Fluconazole, and Voriconazole, in the management of fungal infections associated with chronic suppurative inflammation of the middle ear. Amphotericin B demonstrated the highest susceptibility rate, with 80% of the tested fungal isolates exhibiting susceptibility to this broad-spectrum antifungal [1–32].

This finding is particularly significant, as Amphotericin B is considered a cornerstone in the treatment of invasive and life-threatening fungal infections. Its potent activity against a wide range of fungal pathogens, including *Aspergillus* and *Candida* species, makes it a valuable option for clinicians when confronted with severe or recalcitrant fungal infections in the middle ear. Fluconazole, a widely used azole antifungal, exhibited a susceptibility rate of 60% among the tested isolates. While still presenting a substantial level of efficacy, the study also revealed that 30% of the isolates showed intermediate susceptibility to Fluconazole. This finding suggests that clinicians may need to consider higher dosages or alternative antifungal agents, especially in cases where Fluconazole monotherapy may not be sufficient. Voriconazole, another azole antifungal, demonstrated a susceptibility rate of 70%, with 20% of the isolates exhibiting intermediate susceptibility and 10% being resistant. Voriconazole is a broader-spectrum azole that is often used to treat infections caused by *Aspergillus* and other filamentous fungi. The variable susceptibility profile observed in this study highlights the need for clinicians to consider the specific fungal species involved carefully and to potentially employ therapeutic drug monitoring to optimize Voriconazole dosing and efficacy.

The differences in susceptibility patterns among the tested antifungal agents underscore the importance of conducting comprehensive antifungal susceptibility testing in chronic suppurative inflammation of the middle ear. This information can guide clinicians in making informed, evidence-based decisions when selecting the most appropriate antifungal therapy for their patients, leading to improved treatment outcomes and reduced risk of therapeutic failure or the development of antifungal resistance. Decoding the Nexus Between Risk Factors and Fungal Infections in Chronic Suppurative Inflammation The study's exploration of the association between various risk factors and the occurrence of fungal infections in chronic suppurative inflammation of the middle ear provides valuable insights that can inform clinical practice. The analysis revealed that diabetes and previous antibiotic use were significantly associated with an increased risk of fungal infections. Individuals with diabetes had a 2.5-fold higher odds of developing fungal infections compared to those without diabetes. This finding aligns with the well-established link between impaired immune function and susceptibility to opportunistic fungal infections in individuals with diabetes. The compromised host defenses in diabetic patients create a favorable environment for fungal pathogens to thrive and proliferate.

Similarly, the study found that previous antibiotic use was strongly associated with fungal infections, with a 3.7-fold higher odds of infection in those with a history of antibiotic exposure. Antibiotic treatment can disrupt the delicate balance of the middle ear microbiome, eliminating competing bacterial species and creating ecological niches for opportunistic fungal colonization. This finding underscores the importance of judicious and targeted antibiotic use in the management of chronic suppurative inflammation of the middle ear, as indiscriminate or prolonged antibiotic therapy may inadvertently predispose patients to fungal complications. In contrast, the study did not find a significant association between HIV infection and fungal infections in chronic otitis media [3–9, 32–36].

This may be due to the relatively small number of HIV-positive individuals included in the study or the possibility that the impact of HIV on fungal infections in this condition is less pronounced than in other clinical settings, such as invasive fungal diseases. Regarding occupational factors, the analysis did not reveal a significant link between healthcare or construction work and an increased risk of fungal infections. This suggests that environmental exposures through these occupations may not be a major contributory factor in

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the development of fungal infections in chronic suppurative inflammation of the middle ear. However, the study did observe a trend towards an increased risk associated with gardening activities, though the association did not reach statistical significance. These findings highlight the importance of carefully assessing and addressing modifiable risk factors, such as underlying medical conditions and antibiotic usage when managing patients with chronic suppurative inflammation of the middle ear [9–22]. Clinicians should be proactive in identifying high-risk individuals, optimizing the management of comorbidities, and judiciously prescribing antibiotics to mitigate the risk of fungal infections and improve overall clinical outcomes.

Conclusions

In conclusion, our study on the prevalence of fungal infections in chronic suppurative inflammation of the middle ear across different age groups has provided valuable insights into the susceptibility patterns and distribution of fungal species, the efficacy of antifungal agents, and the association of risk factors with fungal infections.

Firstly, we observed varying rates of fungal infections among different age groups, with the elderly population exhibiting the highest prevalence, followed by pediatric patients and adults. These findings highlight the importance of considering age as a contributing factor when assessing the risk and management of fungal infections in chronic suppurative inflammation of the middle ear.

Secondly, our investigation into the distribution of fungal species revealed that *Aspergillus* and *Candida* were the most prevalent fungal species across all age groups. Other species, such as *Cryptococcus*, *Fusarium*, and *Rhizopus*, also showed varying prevalence levels. These findings emphasize the diverse array of fungal culprits involved in this condition, providing guidance for clinicians and researchers in developing targeted diagnostic and therapeutic strategies.

Thirdly, our study assessed the efficacy of three prominent antifungal agents: Amphotericin B, Fluconazole, and Voriconazole. Amphotericin B demonstrated the highest susceptibility rate, followed by Voriconazole and Fluconazole. These results inform clinicians about the effectiveness of these antifungal agents, aiding in informed decision-making for the treatment of fungal infections in chronic suppurative inflammation of the middle ear.

Lastly, our investigation into the association of risk factors with fungal infections revealed significant associations with diabetes and previous antibiotic usage. Diabetes showed a substantial impact on susceptibility, while previous antibiotic usage displayed a remarkable influence on fungal infection prevalence. HIV infection and occupational factors did not show significant associations in our study. These findings help clinicians identify high-risk individuals and implement targeted preventive measures.

Overall, our study provides comprehensive insights into the prevalence of fungal infections in chronic suppurative inflammation of the middle ear, shedding light on the susceptibility patterns, distribution of fungal species, efficacy of antifungal agents, and association of risk factors. These findings contribute to understanding this condition and can guide clinicians in improving diagnosis, treatment, and preventive strategies tailored to individual patients. Further research is warranted to enhance our knowledge and develop more effective interventions.

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Conflict of interest

The authors declare no conflict of interest.

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