

Review

Candida auris: a Multidimensional Overview of a Rising Global Fungal Threat

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Abstract

This review offers a multidimensional analysis of *Candida auris*, a significant fungal pathogen emerging globally, challenging healthcare systems. Discovered recently, *C. auris* draws attention due to its rapid spread, multidrug resistance, and high morbidity and mortality rates, particularly in immunocompromised individuals. Its taxonomic classification within the Metschnikowiaceae family sets it apart from common *Candida* species. We discuss *C. auris*'s phenotypic traits, including its survival in extreme conditions and unique morphology, and delve into genomic insights like ploidy switching and clade-specific variations. Its epidemiology demonstrates adaptability, with environmental isolates found in diverse ecosystems, indicating broader ecological impacts. The review explores *C. auris*'s presence in European healthcare environments, emphasizing its role in nosocomial infections. Diagnosing *C. auris* is challenging; traditional methods are limited, highlighting the need for advanced molecular diagnostics for accurate identification. A key focus is *C. auris*'s antifungal resistance, detailing resistance mechanisms to major antifungal classes and efforts toward developing effective treatments. Finally, the review stresses the importance of infection control and prevention strategies in healthcare settings, underscoring the need for comprehensive measures to mitigate the spread of this formidable pathogen.

Keywords: *Candida auris*, antifungal resistance, nosocomial infections, epidemiology, pathogen genomics, infection control and prevention

Резюме

Този обзор предлага многоизмерен анализ на *Candida auris*, значителен гъбичен патоген, който се появява глобално и предизвиква предизвикателства за здравните системи. Открит наскоро, *Candida auris* привлича внимание със своето бързо разпространение, мултирезистентност към лекарства и високи нива на заболяемост и смъртност, особено при имунокомпрометирани индивиди. Неговата таксономична класификация в семейството Metschnikowiaceae го отличава от обичайните видове *Candida*. Обсъждат се фенотипичните характеристики на *Candida auris*, включително способността му да оцелява в екстремни условия и уникалната му морфология, и разглеждат геномните аспекти като пloidно превключване и специфични за кладата вариации. Неговата епидемиология демонстрира адаптивност, като екологични изолати са намерени в разнообразни екосистеми, което показва по-широки екологични въздействия. Прегледът изследва присъствието на *Candida auris* в европейските здравни среди, подчертавайки ролята му в нозокомиалните инфекции. Диагностицирането на *Candida auris* е предизвикателно; традиционните методи са ограничени, което подчертава необходимостта от усъвършенствани молекулярни диагностични средства за точна идентификация. Основен фокус е антимикотичната резистентност на *Candida auris*, описвайки механизмите на резистентност към основните класове антимикотични средства и усилията за разработване на ефективни лечения. Накрая, обзорът подчертава важноста на стратегиите за контрол и

превенция на инфекциите в здравните заведения, акцентирайки върху необходимостта от ця-

Introduction

Since its discovery in 2009 from a Japanese patient's ear canal (Munoz *et al.*, 2018), *Candida auris* has become a significant concern in infectious diseases and global health due to its severe nosocomial infections and resistance to multiple antifungal drugs (Arensman *et al.*, 2020; Casadevall *et al.*, 2019). Belonging to the Metschnikowiaceae family and distinct from the CTG clade, *C. auris* exhibits diverse phenotypic traits and varied response to antifungal treatments (Chowdhary *et al.*, 2013; Wang and Xu, 2022). It is morphologically unique, aiding in the identification and understanding of its pathogenic mechanisms (Sato *et al.*, 2009). The organism's adaptability is evident in its ability to thrive in various temperatures and its metabolic flexibility mechanisms (Sato *et al.*, 2009).

C. auris's global spread, reported across numerous countries and leading to widespread healthcare-associated outbreaks, raises concerns about its ecological impact and potential environmental reservoirs (Chowdhary *et al.*, 2020; Arota *et al.*, 2021; Rajni *et al.*, 2021). Its resistance to multiple antifungal classes presents significant clinical management challenges (Arensman *et al.*, 2020; Singh *et al.*, 2020). Understanding the genetic and phenotypic factors underlying this resistance is crucial for developing effective treatment strategies (Munoz *et al.*, 2021).

Diagnosis is challenging due to the limitations of traditional culture methods and common misidentification with conventional biochemical techniques (Kathuria *et al.*, 2015). Advanced molecular diagnostic methods offer more accurate identification but are not widely accessible, especially in resource-limited settings (Santos *et al.*, 1993).

Effective infection control and prevention within healthcare settings are vital to combat the spread of *C. auris*. Stringent measures are necessary due to their ability to persist on various surfaces and colonize patients' skin, particularly in intensive care units (Ledwoch and Maillard, 2018).

This review provides a comprehensive overview of *C. auris*, addressing its taxonomy, pathophysiology, global epidemiology, and challenges in diagnosis, treatment, and infection control. It aims to equip healthcare professionals with the essential knowledge to understand and manage this emerging global fungal threat effectively.

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Taxonomic classification, phenotypic traits, and genomic insights

C. auris, an ascomycetous yeast classified in the Saccharomycetes class, occupies a unique taxonomic position within the Metschnikowiaceae family, distinct from the common *Candida* species in the CTG clade (Munoz *et al.*, 2018). This specific phylogenetic placement influences its response to antifungal treatments and environmental conditions. Morphologically, *C. auris* cells are ovoid or elongated, lacking hyphae or germ tubes, with a distinct appearance on CHROMagar TM *Candida* Plus medium (Chowdhary *et al.*, 2013; Chowdhary, 2020; Sasoni *et al.*, 2022).

C. auris is known for its remarkable adaptability, thriving optimally at temperatures between 37–40°C and tolerating higher temperatures and salt concentrations (Sato *et al.*, 2009). Its metabolic profile, including the inability to assimilate certain carbon sources and efficient amino acid metabolism, contributes to its adaptability (Sato *et al.*, 2009; Munoz *et al.*, 2021; Begum *et al.*, 2022). The organism displays phenotypic plasticity, switching between various forms based on environmental conditions (Borman *et al.* 2016; Yue *et al.*, 2018). This plasticity impacts its antifungal resistance and virulence, with aggregated forms showing increased resistance (Fan *et al.*, 2020).

Genetically, *C. auris* features a conserved mating-type locus (MTL), suggesting potential for genetic recombination across its clades (Munoz *et al.*, 2018). Its genome, comprising seven chromosomes with notable plasticity, including chromosomal rearrangements, contributes to its adaptability and pathogenic complexity (Munoz *et al.*, 2021).

C. auris is divided into distinct geographical clades, each with unique sequence and gene content differences, illustrating profound genomic variations contributing to global spread and diversification (Chow *et al.*, 2020). Clade II is associated with ear canal colonization and shows sensitivity to cell wall-disrupting agents, while Clade I is notable for drug-resistant strains (Chow *et al.*, 2019; Heaney *et al.*, 2020; Sexton *et al.*, 2020). The genomic instability observed in certain clades underscores the pathogen's capability to cause severe, drug-resistant infections (Kwon *et al.*, 2019; Munoz *et al.*, 2021).

Epidemiology and global spread

The epidemiology and global spread of *C. auris* present significant questions about its origins and factors influencing its emergence, especially in the context of global warming and climate change (Casadevall *et al.*, 2021). Recent findings have illuminated the environmental adaptability of this pathogen, contributing to a more comprehensive understanding of its ecological resilience.

A pivotal discovery in 2021 was the isolation of wild *C. auris* from a salt marsh and a sandy beach on the Andaman Islands, marking the first confirmation of its environmental niche in a marine ecosystem (Casadevall *et al.*, 2021). Recent findings have illuminated the environment. This not only demonstrates the pathogen's ability to thrive in diverse settings but also its resilience against biotic predators and environmental stressors like high humidity and temperature variation (Casadevall *et al.*, 2021). This finding, coupled with its presence on a sandy beach, potentially influenced by human activities, suggests the role of anthropogenic factors in spreading *C. auris*.

Further insights have been gained from the recovery of *C. auris* in estuaries in northwest Colombia, indicating its adaptability to various aquatic ecosystems (Escandon, 2022). These observations support the hypothesis that aquatic birds or other species may be vectors for its dissemination. Additionally, the detection of *C. auris* in airborne dust samples within healthcare environments suggests air currents as a potential means of spread, emphasizing the need for rigorous infection control measures.

The pathogen's survival and spread in treated wastewater highlight the challenges in containment (Barbet *et al.*, 2023). This aspect underscores the interconnectedness of various environments in the lifecycle of *C. auris* and the resulting public health challenges. The environmental resilience of *C. auris* necessitates an integrated approach to understanding and managing its impact. Recognizing yeast diversity in natural settings and the influence of environmental changes is crucial for developing strategies to address its distribution and interaction with humans.

Case reports and outbreaks of *C. auris* in Europe

In Europe, *C. auris* has become a significant concern within healthcare settings. The first European case was reported in July 2019 at San Martino Hospital in Genoa, Italy (Crea *et al.*, 2019). From July 2019 to May 2020, 10 cases were identified in

the COVID-19 ICU there (Barbet *et al.*, 2023). A surge in cases occurred throughout 2020 and 2021, with 277 cases in eight healthcare facilities in Liguria by February 2022 and 11 more in the Emilia-Romagna region (Sexton *et al.*, 2020). Most cases in Genoa were linked to the South Asian clade. Between July 2021 and March 2022, eight cases were reported in Turin, involving patients with severe COVID-19 complicated by other infections (Corcione *et al.*, 2022).

Spain's first encounter with *C. auris* was between April and June 2016 at La Fe University Hospital in Valencia, mainly in the post-surgical ICU (Gaitan *et al.*, 2017). From April 2016 to January 2017, 140 colonizations and 41 cases of invasive fungemia were recorded there. Phylogenetic analysis linked these to South African and Venezuelan clusters. By August 2019, Spain had reported 786 cases, increasing to 591 new cases from 2020 to 2021, indicating regional endemicity (Kohlenberg *et al.*, 2022).

The UK reported its first *C. auris* cases in 2013 from various locations (Garcia *et al.*, 2020). Between 2013 and 2016, 19 isolates were received from six hospitals (Plachouras *et al.*, 2020). A significant increase was noted between June 2013 and March 2017, with 225 cases across 22 hospitals, including major outbreaks in London and Oxford ICUs (Borman *et al.*, 2016). The first outbreak at the Royal Brompton Hospital in London began in April 2015, with 50 new cases in 16 months (Schelenz *et al.*, 2016). Phylogenetic analysis identified three distinct clades in the UK isolates. Active screening at Oxford University Hospitals from February 2015 to August 2017 identified 70 colonized patients and seven with invasive infections (Eyre *et al.*, 2018). A national study from May 2017 to April 2018 showed rare *C. auris* colonization among ICU patients (Sharp *et al.*, 2021). Early detection and control measures effectively reduced its spread from January 2018 to May 2019 (Plachouras *et al.*, 2020).

Other European countries, including Germany, France, Belgium, Norway, Poland, and the Netherlands, also reported sporadic cases or outbreaks, especially during the COVID-19 pandemic (Theut *et al.*, 2022). Between 2013 and 2021, the European Union recorded 1,812 cases, with 44 imported and 10 locally acquired, mainly from countries in Africa, the Middle East, and South Asia. Turkey reported three cases in Istanbul in 2021, and Romania reported 40 cases in Bucharest in the first eight months of 2022.

Antifungal resistance and treatment challenges

Antifungal resistance in *Candida auris* poses a significant challenge, exacerbated by the excessive use of antifungal agents in agriculture and healthcare. This has led to the emergence of multidrug-resistant *C. auris* strains, complicating effective treatment (Casadevall *et al.*, 2019). Environmental strains of *C. auris*, even from areas without human activity, have shown susceptibility to antifungals, contrasting with clinical strains adapted to higher temperatures, likely influenced by environmental changes and human interactions.

A study from India linked *C. auris* in stored apples treated with antifungals to drug-resistant isolates (Yadev and Heitman, 2016; Yadev *et al.*, 2022). These apple-associated strains shared genetic similarities with strains from patients, hospitals, and marine environments, highlighting the connection between agricultural antifungal use and public health challenges.

Addressing *C. auris* antifungal resistance requires ongoing research and novel antifungal development, given the limited existing drug options and rising bloodstream infections with pronounced resistance (Perfect, 2017). Resistance mechanisms in *C. auris* include mutations in membrane transporters, ergosterol pathway genes, and cell wall synthesis enzymes (Parlin *et al.*, 2017). Clinical isolates often exhibit formidable resistance against all recognized antifungal classes, including azoles, Amphotericin B (AmB), and echinocandins (Ostrowsky *et al.*, 2017).

Azole resistance in *C. auris* stems from genetic diversity, including aneuploidy, chromosome rearrangements, and mutations in the ERG11 enzyme (Bing *et al.*, 2019; Jenull *et al.*, 2021). Fluconazole resistance, indicated by common substitutions and chromosome duplications encompassing ERG11, is particularly concerning (Garcia *et al.*, 2020).

AmB resistance is increasing, with mechanisms like mutations in ERG6 and aneuploidy in specific chromosomes being implicated (Bing *et al.*, 2022). Reduced membrane lipid permeability also contributes to AmB resistance (Sivarathri *et al.*, 2022).

Echinocandin resistance arises from mutations in the FKS1 and FKS2 genes, with variations across clades. These mutations, coupled with efflux pump overexpression, contribute to resistance, though the complete cellular mechanisms are not fully understood.

The cell wall signaling and mitogen-activated protein (MAP) kinase pathways, particularly the

Hog1 MAP kinase pathway, play crucial roles in *C. auris*'s antifungal resistance (Shivarathri *et al.*, 2020). Mutations in these pathways affect drug resistance, stress adaptation, and cell wall biosynthesis.

Pathophysiology

C. auris, a fungus frequently found in medical environments, infects various body regions, including the bloodstream, urinary and biliary systems, wounds, and skin (Jeffery-Smith *et al.*, 2018). Unlike *C. albicans*, it prefers the skin over the gastrointestinal or urinary tracts and struggles in anaerobic environments like the gut (Day *et al.*, 2018). Histatin-5 in saliva inhibits its growth in the oral region (Pathirana *et al.*, 2018).

Clinically, *C. auris* is associated with bloodstream infections and can cause conditions ranging from minor skin issues to severe meningitis (Abastabar *et al.*, 2019). Its prevalence is higher in males and critically ill patients, especially in intensive care units (Schelenz *et al.*, 2016). Although less virulent than *C. albicans*, *C. auris* is more so than *C. glabrata* and *C. haemulonii* (Fakhim *et al.*, 2018). It often leads to nosocomial infections, sharing pathogenic characteristics like tissue invasion with *C. albicans* (Chatterjee *et al.*, 2015).

C. auris strains vary in virulence and enzyme activities, with some capable of forming biofilms (Kumar *et al.*, 2015; Larkin *et al.*, 2017). Non-aggregating strains tend to be more pathogenic and resistant to physical disturbances (Borman *et al.*, 2016). This adaptability in hospital settings necessitates further research into its pathogenic mechanisms. The exact pathogenesis of *C. auris*, however, remains largely unexplored and is a subject of ongoing scientific inquiry.

Diagnosis

Accurate diagnosis is essential for managing and preventing diseases, including candidiasis. The standard diagnostic method involves culture techniques, where fungal cultures from blood, other body fluids (urine, CSF, perineal fluid), or pus, as well as swab samples from various skin areas, are analyzed (Sarma and Upadhyay, 2017). However, cultures have limitations in detecting low yeast cell concentrations, leading to the adoption of non-culture tests like mannan and anti-mannan IgG tests, B.D.G., and PCR-based assays as supplementary tools (Arastehfar *et al.*, 2020).

C. auris identification utilizes a range of methods, including phenotypic/culture, commercial biochemical, and molecular techniques (Osei

Sekyere, 2018). The phenotypic/culture approach is based on the appearance and color of colonies in culture broths (CDC Identification). On Sabouraud dextrose/glucose agar, *C. auris* forms distinctive smooth, white/cream-colored colonies, while on commercial chromogenic candida agar, it produces colonies in shades of pink, beige, red, or pale rose. Despite their effectiveness, these methods often require supplementary techniques for definitive identification (Fasciana *et al.*, 2020).

Traditional biochemical methods like API 20C, Vitek 2, Phoenix, and MicroScan can misidentify *C. auris* as other yeasts. Reliable identification is achieved using techniques such as MALDI-TOF or molecular methods including PCR, sequencing, or A.F.L.P. MALDI-TOF MS, particularly the Bruker biotyperTM platform, offers high specificity for *C. auris*, though its effectiveness depends on the inclusion of *C. auris* in the reference database (Jeffery-Smith *et al.*, 2018; Osei Sekyere, 2018).

Molecular techniques such as conventional PCR, A.F.L.P., W.G.S., and real-time PCR are highly reliable for detecting *C. auris* (Osei Sekyere, 2018). The gold standard involves sequencing the D1–D2 region of the 28 S rDNA or the ITS region, with comparisons made against GEN bank sequences. *C. auris* is typically first identified via MALDI-TOF, with confirmation through molecular amplification and sequencing (Chowdhary *et al.*, 2020).

Diagnosis of *C. auris* poses challenges, particularly in resource-limited settings, where advanced identification technology is scarce, leading to under-recognition of fungal co-infections in COVID-19 patients. Misdiagnosis is common, even in well-equipped facilities, due to automated system errors and difficulties in differentiating fungal from bacterial co-infections (Rudra Murthy *et al.*, 2017). In COVID-19 patients, these diagnostic challenges can lead to misdiagnosis, delayed treatment, and increased mortality risk (Salehi *et al.*, 2020). Studies indicate that fungal co-infections in COVID-19 patients can result in false negative SARS-CoV-2 test results (Lai *et al.*, 2020). The need for a thorough investigation of suspected co-infection cases is vital. Early diagnosis and management of fungal co-infections are crucial for reducing mortality rates, with systematic screening recommended for early detection and public health response (Allaw *et al.*, 2021; Yadav *et al.*, 2021).

Infection control and prevention

In healthcare environments, managing the spread of *C. auris* poses a significant challenge due

to its ability to colonize various surfaces and patients' skin, especially in ICUs and nursing homes (Yadav *et al.*, 2021). This colonization disrupts the normal fungal composition of the skin, making it a key reservoir for the pathogen's transmission. *C. auris*'s resilience is further highlighted by its presence on a wide array of healthcare surfaces, including floors, bed rails, bedsheets, and medical equipment like blood pressure cuffs and dialysis machines (Eyre *et al.*, 2018; Piedrahita *et al.*, 2018).

C. auris demonstrates remarkable survival skills, enduring on plastic surfaces for up to 28 days and on steel surfaces for a week, showing resistance to common disinfectants and insensitivity to quaternary ammonium compounds (Welsh *et al.*, 2017). These features demand a stringent re-evaluation of infection control protocols to effectively combat its spread and ensure patient safety.

A proactive approach, emphasizing prevention, is essential. Healthcare professionals must swiftly recognize and respond to *C. auris* infections or colonization, utilizing appropriate antifungal treatments and infection control strategies (Barantsevich *et al.*, 2019). Laboratories play a critical role in accurately identifying *Candida* species and promptly communicating findings to clinicians and infection control teams.

Education about *C. auris* transmission prevention is vital for healthcare workers (HCWs), with hand hygiene being a key strategy. The use of soap and ethanol-based hand sanitizers, along with chlorhexidine for patients colonized by *C. auris*, is recommended (Ledwoch and Maillard, 2018). Alternative disinfectants like UV-C light and ozone may be as effective as chlorine when used for extended periods.

For effective control of *C. auris* transmission, adherence to guidelines is crucial, given the risk posed by patients colonized for long periods and the pathogen's persistence on surfaces. Key control measures include (Barantsevich *et al.*, 2019):

1. Isolating infected or colonized patients in single rooms and implementing contact precautions.
2. Promptly notifying state or local health departments
3. Enforcing stringent hand hygiene practices using alcohol-based hand rub or soap and water.
4. Regularly cleaning patient rooms and equipment with hospital-grade disinfectants effective against *Clostridium difficile* spores (CDC/EPA).
5. Identifying potential cases through contact

investigation and travel history.

6. Exploring decolonization methods, such as chlorhexidine bathing, while acknowledging the need for further research on their effectiveness.

7. Continuously assessing infection control measures' effectiveness, focusing on hand hygiene, contact precautions, and environmental cleaning and disinfection.

Treatment

Addressing *C. auris* infections, whether in COVID-19 patients or others, involves a range of antifungal treatments. These include polyenes (such as amphotericin B, deoxycholate, and liposomal amphotericin B), triazoles (like fluconazole, voriconazole, and itraconazole), echinocandins (caspofungin, anidulafungin, and micafungin), and flucytosine (Pappas *et al.*, 2015). Echinocandin stands as the primary therapy for *C. auris* infections (CDC Treatment). If initial treatment fails, a combination of echinocandin and liposomal amphotericin B is recommended due to their synergistic efficacy (Ademe *et al.*, 2020). Close monitoring for treatment effectiveness and potential resistance development is necessary, especially with reported resistance to echinocandins in some cases.

The challenge in treating *C. auris* lies in its resistance to multiple drugs. A significant percentage of *C. auris* strains show resistance to fluconazole, amphotericin B, and, in fewer cases, echinocandins. This resistance pattern is echoed globally, as observed in a study where *C. auris* strains from critically ill COVID-19 patients in Italy showed resistance to amphotericin B and azoles but were susceptible to echinocandins (Magnasco *et al.*, 2021). Notably, a small proportion of isolates exhibit resistance to all antifungal classes (Pristov and Ghanoum, 2019).

Given the resistance issues, the development of new antifungals is crucial. Fosmanogepix (APX001), in phase 2 clinical development, shows promise against a range of fungal pathogens, including *Candida*, by targeting the Gwt1 enzyme crucial for fungal cell wall biosynthesis (Chow *et al.*, 2020). Ibrexafungerp (SCY-078), in phase 3 trials, represents a new class of glucan synthase inhibitors effective against various *Candida* strains, including those resistant to echinocandins (Wring *et al.*, 2019). Similarly, Rezafungin, in phase 3 trials, is a novel echinocandin effective against *Candida* and *Aspergillus* species, including echinocandin-resistant *C. auris* strains (Ham *et al.*, 2021).

Preventing *C. auris* transmission in hospitals, particularly among COVID-19 patients, requires

rigorous control measures. These patients, often undergoing broad-spectrum antibacterial treatments and mechanical ventilation, are at increased risk (Peman *et al.*, 2021). The C.D.C. recommends isolating *C. auris* patients, enforcing stringent hygiene practices, and regularly disinfecting patient care environments. Screening patient contacts for colonization is also advised (CDC Infection Prevention). Certain disinfectants, like chlorine and hydrogen peroxide, are effective against *C. auris*, unlike quaternary ammonia compounds (Chow *et al.*, 2020). Adhering to these guidelines has proven effective in controlling *C. auris* spread in health-care settings, as demonstrated in a report by Reimer-McAtee *et al.* on successful transmission control in rehabilitation and ICU settings (Ademe *et al.*, 2020).

Impact of COVID-19 pandemic

The COVID-19 pandemic, caused by SARS-CoV-2, primarily manifests as a respiratory illness with varying symptoms among patients. Common symptoms include fever, cough, fatigue, and shortness of breath, while less common ones are headaches, sore throat, and confusion (Phaller *et al.*, 2020). In severe cases, complications like acute respiratory distress syndrome, cardiac issues, liver dysfunction, and multi-organ failure can occur (Phaller *et al.*, 2021). COVID-19 patients often show lymphopenia, increasing their susceptibility to opportunistic nosocomial infections, including fungal co-infections like those caused by *C. auris* (Phaller *et al.*, 2021).

The pandemic's impact was significantly felt in ICUs where overcrowding with critically ill patients led to a heightened risk of *C. auris* colonization and subsequent candidemia. This has been reported globally, with many healthcare facilities experiencing a surge in *C. auris* outbreaks during the pandemic (Chowdhary *et al.*, 2020; Rajni *et al.*, 2021). Interestingly, *C. auris* infections were noted in countries previously unfamiliar with this yeast, indicating the role of healthcare facility overcrowding in its transmission (Polvi *et al.*, 2016; Lyman *et al.*, 2021).

In patients co-infected with COVID-19 and *C. auris*, the severity of illness often escalates. These patients, requiring intensive care, mechanical ventilation, and prolonged hospital stays, become increasingly vulnerable to *C. auris* colonization and infection (Prestel *et al.*, 2021). Even after recovering from COVID-19, some patients remain critically ill, with cases of cardiorespiratory arrest linked to fungal co-infections. Candidiasis, indicat-

ed by fungal growth in blood cultures, is suspected to contribute significantly to patient debilitation (Prestel *et al.*, 2021).

C. auris is associated with various invasive fungal infections, affecting multiple body parts including the brain, heart, blood, and bones (Proctor *et al.*, 2021). Candidemia, a severe bloodstream infection, is a common and feared complication of invasive candidiasis (Proctor *et al.*, 2021). Additionally, *C. auris* has been linked to respiratory and urinary tract infections, ear canal infections, and pericarditis. Rare cases such as endogenous panophthalmitis and spondylodiscitis have been associated with *C. auris* (Revie and Cowen, 2021; Rudramurthy *et al.*, 2017). Notably, fungal otomastoiditis, a rare condition in immunocompromised patients, has been attributed to this pathogen. Infections like vulvovaginitis, pleuritis, intra-abdominal infections, pericarditis, ventriculitis, surgical wound infections, and osteomyelitis have also been observed in patients with *C. auris* (Rudramurthy *et al.*, 2017; Revie and Cowen, 2021).

Discussion

C. auris, uniquely classified within the Metschnikowiaceae family and distinguished from common *Candida* species in the CTG clade, displays significant phenotypic and genotypic diversity (Wang and Xu, 2022). Its unique morphology, characterized by the absence of hyphae and a specific cell structure, along with specialized metabolic capabilities, demonstrates its adaptability (Faciana *et al.*, 2020; Kohlenberg *et al.*, 2022). This diversity impacts its response to environmental conditions and antifungal treatments, posing challenges in identification and treatment.

The rapid global spread of *C. auris*, particularly during the COVID-19 pandemic, underscores its capacity to exploit healthcare system vulnerabilities (Rajni *et al.*, 2021). Its ability to thrive in various environments, including marine ecosystems, highlights its ecological adaptability (Arora *et al.*, 2021, Casadevall *et al.*, 2021). This complicates epidemiological control and emphasizes the need for enhanced surveillance and infection prevention strategies.

The COVID-19 pandemic has exacerbated the challenges posed by *C. auris*, with overcrowded ICUs facilitating its spread and complicating infection control. The pathogen's colonization and infection of various body sites reveal versatile pathogenic mechanisms capable of causing conditions from minor skin infections to severe illnesses like candidemia (Spivak and Hanson, 2018).

Managing *C. auris* is challenging due to its resistance to major antifungal classes. Genetic mutations contributing to this resistance necessitate novel antifungal agents and new treatment approaches, underlining the importance of ongoing research (Wring *et al.*, 2019).

Diagnosis of *C. auris* infections is hindered by the limitations of traditional methods, making advanced molecular diagnostics like MALDI-TOF MS and PCR essential (Osei Sekyere, 2018). However, the global disparity in access to these technologies affects effective infection management, particularly in resource-limited settings (Jeffery-Smith *et al.*, 2018).

Effective management in healthcare settings requires stringent infection control practices (Fakhim *et al.*, 2018). The pathogen's ability to persist on surfaces and colonize patients necessitates comprehensive environmental cleaning and strict hygiene protocols (CDC Infection Prevention).

Conclusion

This review addresses *C. auris*, a significant global health concern due to its unique taxonomy within the Metschnikowiaceae family, distinct from the CTG clade, and its rapid spread in healthcare and ecological settings. *C. auris*'s unique phenotypic traits contribute to its pathogenicity and environmental resilience. The COVID-19 pandemic has highlighted the need for heightened surveillance and control measures.

C. auris's antifungal resistance poses clinical challenges, with mutations in genes like ERG11 and FKS impacting treatment strategies. This resistance necessitates exploring novel antifungal agents and understanding the pathogen's biology to develop effective treatments.

Diagnosing *C. auris* is difficult due to traditional methods' limitations, underlining the importance of advanced molecular diagnostics like MALDI-TOF MS and PCR. Access disparities to these technologies, especially in resource-limited regions, emphasize the need for improved global diagnostic capabilities.

Infection control and prevention in healthcare settings are crucial. Rigorous environmental cleaning, strict personal hygiene practices, and comprehensive infection control strategies are essential to prevent nosocomial transmission and manage outbreaks. Integrating these measures into routine healthcare practices is vital.

The review advocates for an integrated, multidisciplinary approach to address the challenges posed by *C. auris*. Future research should focus

on its ecological roles, developing new antifungal therapies, and enhancing diagnostic and infection control methods. Staying informed and adopting adaptive strategies are key to managing this fungal threat.

In conclusion, *C. auris* presents complex challenges in infectious disease management. Effective response requires comprehensive understanding, continuous research into treatment and diagnostics, and robust infection control measures. Concerted global health community efforts are needed to mitigate its impact.

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