Candida auris: Biology, Antifungal Resistance, and Clinical Challenges

Punyapat Rittidej[1], Wasich Athasart[2], Apirut Chomchoen[3], Matthew Thaveevudh[4], Punyachat Linkangwarnmongkol[5], Siriporn Shupetchsomboon[6]
King Mongkut's Institute of Technology Ladkrabang International Demonstration School[1]
Samsen Wittayalai School[2], International Community School Udon Thani[3]
Saint Dominic School[4], Thidanukhro School[5], Independent researcher[6]
Email: finpunyapat66@gmail.com[1] , E-mail: SS49821@samsenwit.ac.th[2]
E-mail: foam123chom@gmail.com[3], E-mail: mthaveevudh@gmail.com[4]
E-mail: Pmp12564@gmail.com[5] , E-mail: siriporn.shu@gmail.com[6]

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ABSTRACT

Candida auris has emerged as a major global health threat due to its multidrug resistance, environmental persistence, diagnostic complexity, and propensity for healthcare-associated transmission. This review aimed to synthesize current evidence on the biology, antifungal resistance mechanisms, clinical significance, and emerging epidemiology of Candida auris, with particular emphasis on its implications for healthcare systems and the evolving situation in Thailand. A narrative review of published literature and relevant evidence from global studies and available reports from Thailand was conducted. The reviewed evidence indicates that the emergence of C. auris is driven by the convergence of environmental resilience, biofilm formation, genomic adaptability, and multidrug resistance. High levels of resistance to fluconazole and increasing resistance to amphotericin B and echinocandins substantially limit therapeutic options. The pathogen's ability to persist on healthcare surfaces and colonize human skin facilitates sustained nosocomial transmission and recurrent outbreaks. Recent genomic studies have identified multiple resistance-associated mutations, although the clinical significance of several emerging variants remains uncertain. In Thailand, the detection of antifungal-resistant strains and the limited availability of advanced diagnostic capacity highlight important challenges for surveillance, laboratory identification, and infection prevention. Effective control of C. auris requires an integrated approach combining rapid diagnostics, antifungal stewardship, genomic surveillance, and rigorous infection-prevention measures.

Keywords: Candida auris, Antifungal resistance, Healthcare-associated infections, Genomic surveillance, Infection prevention and control

Introduction

Fungal infections are increasingly recognized as a major global health challenge, particularly among immunocompromised individuals and critically ill patients. The expanding use of immunosuppressive therapies, invasive medical procedures, and broad-spectrum antimicrobials has contributed to a growing burden of opportunistic fungal diseases in healthcare settings (Kullberg & Arendrup, 2015; Oladele et al., 2017). Among emerging fungal pathogens, *Candida auris* has attracted substantial international concern because of its multidrug resistance, high mortality, propensity for nosocomial transmission, and ability to cause large-scale

healthcare-associated outbreaks (Chowdhary et al., 2017; Forsberg et al., 2019).

Since its first description in Japan in 2009, *C. auris* has been reported across multiple continents and has emerged independently in several genetically distinct clades (Lockhart et al., 2016; Rhodes & Fisher, 2019). Unlike most *Candida* species, *C. auris* exhibits remarkable environmental persistence, surviving on healthcare surfaces for prolonged periods and tolerating commonly used disinfectants, thereby facilitating sustained transmission within hospitals (Welsh et al., 2017). Furthermore, widespread resistance to fluconazole, variable resistance to amphotericin B, and the emergence of echinocandin-resistant isolates have substantially limited therapeutic options and complicated clinical management (Chowdhary et al., 2017; Lamoth et al., 2018).

The clinical significance of *C. auris* extends beyond antifungal resistance. Invasive infections, particularly candidemia, are associated with considerable morbidity and mortality, especially among patients requiring intensive care, central venous catheters, or prolonged hospitalization (Forsberg et al., 2019). These biological and clinical characteristics have led the World Health Organization to classify *C. auris* as a "critical priority fungal pathogen," highlighting the urgent need for improved surveillance, diagnostic capacity, infection prevention, and therapeutic development (World Health Organization, 2022).

In Thailand, the emergence of *C. auris* has raised concerns regarding laboratory detection, antifungal resistance surveillance, and infection control preparedness. Accurate identification remains challenging because conventional phenotypic methods may misidentify *C. auris* as closely related species, including *Candida haemulonii*, emphasizing the need for advanced diagnostic approaches such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and molecular techniques (Chowdhary et al., 2017). Although published epidemiological data from Thailand remain limited, the detection of *C. auris* in Thai healthcare settings underscores the importance of strengthening surveillance systems and preparedness strategies to prevent further dissemination.

This review summarizes current evidence on the biology, pathogenicity, antifungal resistance, and clinical significance of *Candida auris*, with particular emphasis on its implications for healthcare systems and the emerging situation in Thailand.

The Biology and Antifungal Resistance of Candida auris

Candida auris (Fig. 1) is an emerging multidrug-resistant yeast that exhibits several biological characteristics distinguishing it from other clinically important *Candida* species. Since its first description in 2009, the pathogen has attracted considerable attention because of its remarkable ability to persist in healthcare environments, colonize human skin, and rapidly acquire resistance to multiple antifungal agents (Du et al., 2020; Kim et al., 2024). Unlike *Candida albicans*, which primarily colonizes mucosal surfaces, *C. auris* demonstrates a pronounced affinity for skin colonization, facilitating patient-to-patient transmission and healthcare-associated outbreaks (Du et al., 2020).

Morphology and Environmental Adaptation

Microscopically, *C. auris* appears as oval to elongated budding yeast cells that occur either singly or in aggregates. Colonies are typically smooth, white to cream-colored on conventional fungal media, although colony morphology may vary under different environmental conditions (Satoh et al., 2009; Forsberg et al., 2019). Diagnostic identification remains challenging because conventional biochemical systems frequently misidentify *C. auris* as members of the *Candida haemulonii*

complex, highlighting the importance of matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) or molecular methods for accurate detection (Lockhart et al., 2017; Ahmad & Alfouzan, 2021).

A defining feature of *C. auris* is its exceptional tolerance to environmental stress. Unlike most fungal pathogens, it can grow at temperatures exceeding 40°C and survive in environments containing high salt concentrations (>10% NaCl), properties that are rarely observed among closely related species (Du et al., 2020; Kim et al., 2024). These adaptations are believed to contribute to its prolonged survival on human skin, medical devices, and hospital surfaces, thereby facilitating nosocomial transmission. The ability of *C. auris* to tolerate thermal and osmotic stress has also been cited as evidence supporting the hypothesis that environmental adaptation may have contributed to its recent emergence as a human pathogen (Ahmad & Alfouzan, 2021).

Phenotypic Plasticity and Virulence

Although *C. auris* lacks the robust yeast-to-hypha transition characteristic of *C. albicans*, it retains substantial phenotypic plasticity. Under conditions of genotoxic stress, elevated salinity, or heat stress, some isolates develop elongated or pseudohyphal-like morphologies (Kim et al., 2024). Emerging evidence suggests that these morphological transitions may contribute to environmental adaptation rather than serving as direct virulence determinants.

Biofilm formation represents one of the most clinically relevant virulence traits of *C. auris*. Unlike *C. albicans*, whose biofilms contain extensive hyphal networks, *C. auris* biofilms are predominantly composed of densely packed yeast cells embedded within an extracellular matrix (Kim et al., 2024; Ahmad & Alfouzan, 2021). Biofilm-associated cells exhibit substantially reduced susceptibility to antifungal agents and disinfectants, contributing to persistent environmental contamination and recurrent healthcare-associated outbreaks. Several adhesin-associated genes, including *IFF4*, *CSA1*, *PGA26*, *PGA52*, and *HYR3*, are upregulated during biofilm development, suggesting an important role in colonization and persistence.

Genetic Diversity and Population Structure

Whole-genome sequencing has revealed substantial genetic diversity within the species and identified five major phylogeographic clades: South Asian (Clade I), East Asian (Clade II), African (Clade III), South American (Clade IV), and a recently described Iranian clade (Clade V) (Du et al., 2020; Kim et al., 2024). The near-simultaneous emergence of genetically distinct clades across multiple continents suggests that the global spread of *C. auris* cannot be explained solely by dissemination from a single ancestral source (Du et al., 2020).

The species possesses conserved mating-type loci, although population genomic studies indicate that clonal expansion remains the dominant mode of transmission. Nevertheless, the coexistence of different mating types and increasing global circulation of strains raise the possibility of future genetic recombination events that could facilitate adaptive evolution (Du et al., 2020).

Biological Basis of Persistence and Clinical Relevance

The success of *C. auris* as a healthcare-associated pathogen appears to result from the convergence of several biological attributes, including thermotolerance, osmotolerance, biofilm formation, prolonged environmental persistence, and genomic adaptability. Unlike many fungal pathogens that are primarily opportunistic colonizers of mucosal surfaces, *C. auris* is uniquely adapted for survival in healthcare environments, where it can persist on surfaces and medical equipment for prolonged periods and spread efficiently between vulnerable patients (Ahmad & Alfouzan, 2021; Kim et al., 2024). These

biological characteristics not only explain the increasing frequency of healthcare-associated outbreaks but also complicate infection control efforts and contribute to the growing global public health threat posed by this pathogen.

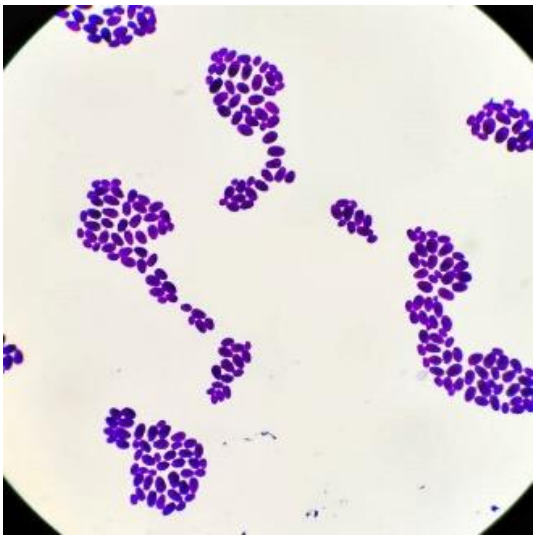


Figure 1 Candida auris (Wellington & Price, 2023)

Infections and Emergence of *Candida auris* in Thailand

The emergence of *Candida auris* in Thailand reflects the broader global expansion of this multidrug-resistant pathogen and presents significant challenges for clinical management and infection prevention. Although *C. auris* was first identified in Japan in 2009 (Satoh et al., 2009), subsequent reports have documented its rapid dissemination across Asia, Europe, Africa, and the Americas, largely driven by healthcare-associated transmission (Chowdhary et al., 2017; Lockhart et al., 2017). The detection of *C. auris* in Thai healthcare facilities confirms that Thailand has become part of this expanding epidemiological landscape and highlights the need for strengthened surveillance and diagnostic capacity.

A major concern associated with *C. auris* is its ability to persist within healthcare environments. Unlike many other *Candida* species, *C. auris* can survive for prolonged periods on hospital surfaces and medical equipment and exhibits reduced susceptibility to several commonly used disinfectants (Welsh et al., 2017; Kean et al., 2018). These characteristics facilitate nosocomial transmission through contaminated environments, healthcare workers, and shared medical devices, contributing to healthcare-associated outbreaks reported worldwide (Chowdhary et al., 2017). Consequently, the introduction of *C. auris* into Thai hospitals raises concerns regarding sustained institutional transmission, particularly in high-dependency units where vulnerable patients are concentrated.

Clinical manifestations reported in Thailand are broadly consistent with international observations. Invasive bloodstream infection remains the most frequently reported and clinically significant presentation, particularly among critically ill patients, individuals with prolonged intensive care unit stays, central venous catheterization, broad-spectrum antibiotic exposure, or underlying immunosuppressive conditions (Lockhart et al., 2017; Chakrabarti & Sood, 2021). The substantial mortality associated with *C. auris* infection is often attributable not only to fungal virulence but also to delays in

diagnosis, severe underlying comorbidities, and limited therapeutic options resulting from multidrug resistance (Rudramurthy et al., 2017; Chakrabarti & Sood, 2021).

Recent genomic investigations of Thai clinical isolates have provided important insights into local resistance mechanisms. Whole-genome sequencing of *C. auris* strains isolated in Bangkok confirmed the presence of the well-established *ERG11* Y132F mutation among fluconazole-resistant isolates and identified additional candidate mutations potentially associated with echinocandin resistance, including alterations in *CDC10*, *BLM3*, and fungal-specific Zn(II)2-Cys6 transcription factor-related genes (Opassathian et al., 2025). Notably, a novel *FKS1* I1361T substitution was identified in a caspofungin-resistant isolate, suggesting that resistance mechanisms in Thai strains may extend beyond the classical *FKS1* hotspot mutations reported previously. These findings emphasize the ongoing evolution of antifungal resistance and highlight the importance of genomic surveillance in monitoring emerging resistance determinants.

The public health implications of *C. auris* extend beyond individual patient outcomes. Healthcare-associated outbreaks require extensive infection-control measures, including patient isolation, environmental decontamination, contact tracing, and enhanced laboratory screening, all of which increase healthcare resource utilization. Furthermore, the frequent occurrence of resistance to first-line antifungal agents complicates treatment decisions and may necessitate the use of broader-spectrum or more toxic alternatives. Consequently, *C. auris* represents both a clinical and economic burden for healthcare systems, particularly in resource-constrained settings.

In response to these challenges, Thai healthcare institutions have increasingly adopted enhanced surveillance strategies, environmental monitoring programs, and advanced diagnostic technologies such as matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) and molecular identification methods. Early and accurate detection is particularly important because conventional biochemical systems frequently misidentify *C. auris*, potentially delaying implementation of appropriate infection-control interventions (Lockhart et al., 2017; Ahmad & Alfouzan, 2021).

Overall, the emergence of *C. auris* in Thailand illustrates the convergence of multidrug resistance, environmental persistence, and healthcare-associated transmission. Current evidence suggests that sustained investment in diagnostic infrastructure, genomic surveillance, antifungal stewardship, and infection-prevention programs will be essential to limit the establishment and further dissemination of this pathogen within Thai healthcare settings.

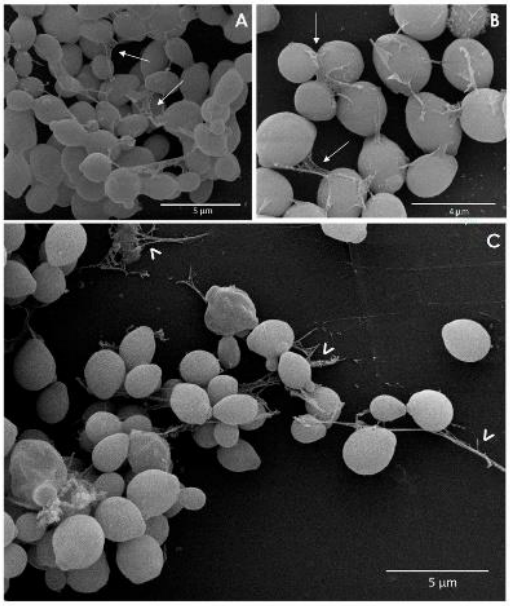


Figure 2 Relationship between *Candida auris* and closely related species within the *Candida haemulonii* complex (Ramos et al., 2020).

Discussion

This review examined the biological characteristics, antifungal resistance mechanisms, clinical significance, and emerging epidemiology of *Candida auris*, with particular consideration of its implications for Thailand. Collectively, the evidence indicates that the global success of *C. auris* is not attributable to a single virulence trait but rather to the convergence of environmental resilience, multidrug resistance, efficient healthcare-associated transmission, and remarkable genomic adaptability. These interconnected characteristics distinguish *C. auris* from most other clinically important *Candida* species and help explain its rapid emergence as a major global public health concern.

A central finding of the reviewed literature is that the epidemiological expansion of *C. auris* appears to be closely linked to its unique ecological and biological adaptations. Unlike *Candida albicans*, which is primarily associated with endogenous colonization and opportunistic infection, *C. auris* demonstrates an unusual capacity to persist on human skin, medical devices, and healthcare surfaces for prolonged periods (Kim et al., 2024; Ahmad & Alfouzan, 2021). This environmental persistence likely contributes to sustained nosocomial transmission and recurrent outbreaks. Although observational studies consistently demonstrate associations between environmental contamination and healthcare-associated spread, the relative contribution of specific transmission pathways remains incompletely understood. Consequently, current infection-control recommendations are largely derived from epidemiological investigations rather than direct experimental evidence, highlighting an important limitation of the existing literature.

The review further demonstrates that antifungal resistance represents one of the defining characteristics of *C. auris*. Across geographic regions, resistance to fluconazole is highly prevalent, while resistance to amphotericin B and echinocandins has increasingly been reported (Chowdhary et al., 2023; Kim et al., 2024). Recent genomic studies suggest that resistance is mediated

through multiple molecular pathways involving *ERG11*, *TAC1B*, *FKS1*, efflux pump regulation, and biofilm-associated mechanisms. However, much of the current evidence originates from genomic association studies and in vitro susceptibility testing. Although these approaches have identified plausible resistance determinants, relatively few studies have experimentally validated the functional consequences of newly identified mutations. Consequently, caution is warranted when inferring causality between specific genetic alterations and clinical treatment failure. The growing complexity of resistance mechanisms suggests that reliance on a limited number of antifungal classes may become increasingly unsustainable, reinforcing the need for continued therapeutic innovation.

Another important observation is the growing recognition that *C. auris* pathogenicity cannot be fully explained by conventional virulence paradigms developed for *C. albicans*. Experimental studies have demonstrated comparatively modest filamentation yet substantial capacity for biofilm formation, environmental persistence, and immune evasion. This finding suggests that adaptation to healthcare environments may be as important as classical host-invasive virulence factors in determining the clinical success of the organism. However, much of the mechanistic evidence regarding virulence originates from laboratory investigations, animal models, and transcriptomic analyses. While these studies provide valuable biological insights, their direct translation to human disease remains uncertain. Additional longitudinal clinical studies are needed to clarify how specific virulence traits influence colonization, transmission, and patient outcomes in real-world healthcare settings.

The emergence of *C. auris* in Thailand should be interpreted within this broader global context. Current evidence confirms the presence of genetically diverse and antifungal-resistant strains within Thai healthcare facilities, including isolates harboring established resistance-associated mutations such as *ERG11* Y132F and potentially novel mutations affecting echinocandin susceptibility. Nevertheless, the available Thai literature remains limited compared with evidence from South Asia, Europe, and North America. Most published reports are derived from case studies, laboratory investigations, or small-scale genomic analyses, restricting the ability to estimate national disease burden, transmission dynamics, and long-term epidemiological trends. Consequently, the true prevalence of *C. auris* in Thailand may be underestimated, particularly in healthcare facilities lacking access to advanced diagnostic methods such as MALDI-TOF MS or molecular identification platforms.

Several limitations of the current evidence base should be acknowledged. First, substantial heterogeneity exists across studies with respect to diagnostic methods, antifungal susceptibility testing protocols, and outbreak investigation strategies, complicating direct comparison between regions. Second, much of the literature is observational, limiting causal inference regarding transmission pathways, environmental reservoirs, and determinants of adverse clinical outcomes. Third, publication bias may favor reporting of large outbreaks, unusual resistance phenotypes, or severe infections, potentially overestimating the perceived threat in some settings. Finally, important gaps remain regarding environmental ecology, community reservoirs, host-pathogen interactions, and the long-term evolutionary consequences of antifungal selection pressure.

These limitations highlight several priorities for future research. Greater emphasis should be placed on prospective multicenter surveillance studies capable of

generating robust epidemiological data across diverse healthcare settings. Whole-genome sequencing integrated with clinical and environmental sampling may improve understanding of transmission networks and resistance evolution. Further investigation of environmental reservoirs, including wastewater and healthcare infrastructure, may clarify potential sources of emergence and dissemination. Equally important is the development of novel antifungal agents targeting pathways distinct from those affected by existing drug classes, as well as studies evaluating combination therapies and immunomodulatory approaches against multidrug-resistant strains. In Thailand and other Southeast Asian countries, regional genomic surveillance networks and harmonized reporting systems could facilitate earlier detection of emerging resistance patterns and strengthen outbreak preparedness.

From a clinical and public health perspective, the findings of this review suggest that effective control of *C. auris* will require an integrated strategy combining rapid diagnostics, antifungal stewardship, genomic surveillance, and rigorous infection-prevention measures. The pathogen's success appears to arise from the interaction between biological adaptability and healthcare-associated transmission opportunities rather than from any single pathogenic mechanism. Consequently, interventions targeting only antifungal treatment are unlikely to be sufficient. Sustained investment in laboratory infrastructure, surveillance systems, and translational research will be essential to mitigate the growing threat posed by *C. auris*. As evidence continues to accumulate, a more comprehensive understanding of its ecology, evolution, and resistance mechanisms may provide the foundation for more effective prevention and therapeutic strategies in Thailand and globally.

Conclusion

Candida auris has emerged as a clinically important fungal pathogen because it combines multidrug resistance, environmental persistence, diagnostic difficulty, and efficient healthcare-associated transmission. The evidence reviewed here suggests that its threat is not driven by a single biological feature, but by the interaction of genomic adaptability, antifungal selection pressure, and gaps in infection-control infrastructure. For Thailand, the detection of resistant clinical isolates underscores the need for stronger laboratory capacity, routine species-level identification, antifungal susceptibility testing, and genomic surveillance. Although current Thai data remain limited, early investment in coordinated surveillance and infection-prevention systems will be essential to prevent *C. auris* from becoming an entrenched nosocomial pathogen. Future research should prioritize multicenter epidemiological studies, functional validation of resistance mechanisms, and regionally appropriate control strategies.

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