



## Review of *Candida auris* – An Emerging Global Threat

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Ganguli SC, Edirisinghe VT, Dasanayaka PN, Wijendra WAS 2024 – Review of *Candida auris* – An Emerging global threat. Current Research in Environmental & Applied Mycology (Journal of Fungal Biology) 14(1), 133–145, Doi 10.5943/cream/14/1/8

### Abstract

*Candida auris* has emerged as a significant global health threat due to its unique characteristics and challenges in management. This literature review aims to provide an overview of why *C. auris* is a current topic of interest, its distinct features compared to other *Candida* species, its morphology, clinical symptoms, molecular detection methods, and the factors contributing to its pathogenicity in human infections. The review also discusses the challenges in controlling *C. auris* infections, including its high prevalence and multidrug resistance. Additionally, it examines the epidemiology and global spread of *C. auris*, highlighting the need for effective prevention strategies. Furthermore, the review explores the interaction between *C. auris* and COVID-19, emphasizing the importance of understanding this relationship in the context of the ongoing pandemic. Finally, the review outlines future research directions and potential strategies for combating *C. auris* infections.

**Keywords** – Antifungal resistance – COVID-19 – prevalence – superbug – virulence factors

### Introduction to *Candida* sp.

*Candida* is a genus of yeasts, specifically classified within the kingdom Fungi, phylum Ascomycota, class Pichiomycetes, order Serinales and family Debaryomycetaceae (Schoch et al. 2020, Wijayawardene et al. 2022, ACIR Community 2024). They are one of the most common causes of fungal infections worldwide. Most *Candida* species coexist peacefully as endosymbionts with their hosts, including humans. However, they may invade and result in opportunistic infections when mucosal barriers are disrupted, or the immune system is weakened (Basmacıyan et al. 2019, Romo & Kumamoto 2020). In addition to the skin, *Candida* can be found on most mucosal surfaces, primarily in the gastrointestinal tract (Spampinato & Leonardi 2013). Although, most members of the *Candida* genus can undergo a reversible morphological switch from yeast to hypha. This switch occurs under adverse environmental conditions or during pathogenic infection in the human host (Gabaldón 2019, Chow, Pang & Wang 2021).

Infection caused by *Candida* is known as candidiasis (Naureen & Rafiq 2024). If the conditions within the mouth, throat, vagina, or esophagus shift in a way that promotes fungal growth, *Candida* may proliferate and result in an infection. Oral candidiasis typically presents as white pseudomembranes, while vulvovaginal candidiasis causes intense pruritus and edema (McCort 2021). Invasive candidiasis is a dangerous infection, rather than vaginal yeast infections or *Candida* infections of the mouth and throat (commonly known as “thrush”). Invasive candidiasis can affect the blood, heart, brain, eyes, bones, and other organs of the body (Koundal & Cojandaraj 2020,

McCarty White & Pappas 2021). Invasive candidiasis can have mortality rates reaching 40% even with antifungal treatment (Kullberg & Arendrup 2019).

As of the latest records in Index Fungorum, approximately 902 species of *Candida* have been documented (Index Fungorum 2024). However, only a few of these species are of medical importance, including whereas only a few numbers of these species are of medical importance such as, *Candida albicans*, *Candida krusei*, *Candida guilliermondii*, *Candida lusitanae*, *Candida kefyr* (pseudotropicalis), *Candida rugosa*, *Candida famata*, *Candida inconspicua*, *Candida norvegensis*, *Candida dubliniensis*, *Candida lipolytica*, *Candida zeylanoides*, *Candida pelliculosa*, *Candida nivariensis*, *Candida albicans* var *Africana*, *Candida glabrata*, *Candida tropicalis* (Nasirian 2017) and *Candida auris*.

This review focuses on *Candida auris*, a multidrug-resistant fungal pathogen that poses a significant public health threat, particularly in hospital settings (Imtiaz et al. 2022).

### **Why is *Candida auris* a current topic of interest, and how does it differ from other *Candida* species?**

*Candida auris* is the first fungal pathogen to pose a threat to public health worldwide, which has recently emerged (Johnson et al 2018). This section reviews why *C. auris* is of particular interest, how it differs from other *Candida* species, and the implications for public health and clinical management.

The most isolated species in patients with invasive fungal infection (IFI) are *Candida albicans*, *Candida dubliniensis*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, and *Candida tropicalis* (Guinea 2014, Pfaller et al. 2014). However, since its initial description in 2009 (Satoh et al. 2009), *Candida auris*, a novel species of *Candida* that has simultaneously emerged on all five inhabited continents as a significant and novel public health hazard, has ended up being responsible for most *Candida* isolates and IFI in certain regions. (Garcia-Bustos et al. 2021)

One of the key distinctions of *Candida auris* is that it distinguishes itself from other *Candida* species through its extensive resistance to antifungal drugs and reduced susceptibility to azoles, polyenes, and echinocandins (Sarma & Upadhyay 2017, Worku & Girma 2020, Sanyaolu et al. 2022). Therefore, *Candida auris* infections have elevated mortality rates due to poor response to therapy (Kaki 2023).

Additionally, unlike many other species of *Candida*, *Candida auris* is not usually found as a resident commensal organism in the human gastrointestinal tract (Jackson et al. 2019, Nett 2019, Sikora & Zahra 2021).

Furthermore, *Candida auris* is distinguished from other *Candida* species by its ability to easily colonize both the human body and the environment (Iguchi et al.2019) and its high rate of transmission (Shyni & Lavanya 2021).

In terms of transmissibility when shed from infected or colonized patients, contaminated surfaces, and objects (fomites) can facilitate the spread of *Candida auris* from person to person. According to research, *C. auris* can be found in a variety of patient rooms as well as public areas such as windowsills, counters, chairs, beds, blood pressure cuffs, infusion pumps, and hallways. Commonly used medical devices with multiple uses, like pulse oximeters and temperature probes, could potentially act as reservoirs for *C. auris* (Biswal et al. 2017).

Because of its resistance to drugs and ability to persist in healthcare settings, *Candida auris* has been referred to as a "superbug" fungus that presents difficulties in its eradication.

Unlike other *Candida* species, *Candida auris* poses a significant identification challenge due to its potential for misidentification as other fungi and the need for specialized testing or molecular techniques for accurate detection. *Candida auris* can be mistaken for a variety of different organisms when using traditional phenotypic methods for yeast identification, such as VITEK 2 YST, API 20C, BD Phoenix yeast identification system, and MicroScan, leading to diagnostic delays and mismanagement (Forsberg et al. 2018, www.cdc.gov 2020).

These distinct characteristics not only make *Candida auris* a formidable pathogen but also highlight the urgent need for improved diagnostic methods, effective treatment strategies, and rigorous infection control practices.

### **Morphology of *Candida auris*.**

On Sabouraud-dextrose agar, it is described as white to cream colonies with a smooth edge, which are germ tube test negative. On CHROMagar *Candida* medium, they produce pale to dark pink or rarely beige colonies (Iguchi et al. 2019). The yeast *Candida auris* is capable of growing at 42°C, a key distinguishing feature that helps differentiate it from other *Candida* species, which cannot grow at this elevated temperature (Kathuria et al. 2015, Casadevall et al. 2019).

Under a microscope, they can be observed individually, in pairs, or groups (Iguchi et al. 2019). However, *Candida auris* can exhibit various morphological phenotypes depending on the culture conditions, including round, ovoid, elongated, and pseudohyphal forms. For example, high concentrations of sodium chloride can induce the formation of pseudohyphal-like structures. Conversely, cycloheximide at concentrations of 0.1% and 0.01% inhibits its growth (Cortegiani et al. 2018).

*Candida auris* reproduce by budding, just like other *Candida* species. It has an oval form and measures 2.5–5.0 µm (Iguchi et al. 2019). *Candida auris* exhibits two distinct phenotypes: an aggregative form in which some isolates retain daughter cells after budding, forming large aggregates that cannot be separated by physical disruption even after vigorous vortexing for several minutes, and a non-aggregative form in which yeast cells are arranged as isolated or coupled cells like other *Candida* species (Garcia-Bustos et al. 2021).

Pseudohyphae are not produced in *Candida auris* therefore the germ tube test is negative. However, the formation of pseudohyphae can happen in the presence of high salt concentrations and depletion of heat shock protein, suggesting that stress may also be the cause of this morphological alteration (Bidaud et al. 2018).

However, none of the morphological characteristics of *Candida auris* are sufficient for definitive identification. Therefore, other methods, such as molecular techniques are needed to accurately distinguish *Candida auris* from closely related *Candida* species (Forsberg et al. 2018).

### ***Candida auris* symptoms and molecular detection**

Symptoms of a *Candida auris* infection depend on the location and severity of the infection. There is not a common set of symptoms specific to *Candida auris* infections (CDC 2024). Commonly these infections are associated with a range of symptoms, including fever, weakness, and respiratory issues (Konjengbam et al. 2022). Some patients may develop severe symptoms due to *Candida auris* infection, while others may harbor *C. auris* without exhibiting any symptoms (asymptomatic), a condition known as colonization. Patients who are colonized with *Candida auris* have the same potential to spread the organism as those who are symptomatic. Therefore, early detection of *Candida auris* is crucial in preventing and controlling outbreaks in healthcare facilities, as it helps identify both symptomatic and asymptomatic (colonized) patients who can spread the pathogen (CDC 2024).

Moreover, the pathogen's rapid emergence and high mortality rate underscore the need for early diagnosis in order to implement effective infection prevention measures (Navalkele et al. 2017). Delays in early and accurate identification of *Candida auris* lead to significant setbacks in applying appropriate infection control principles (Fasciana et al. 2020). Prompt identification enables timely intervention and effective management strategies, crucial for controlling the spread and minimizing the impact of *C. auris* in healthcare settings (Vallabhaneni et al. 2019).

However, the accurate identification of *C. auris* can be challenging, with misidentification as other *Candida* species being common (Mahmoudi et al. 2019). This underscores the need for reliable and cost-effective diagnostic tools, such as DNA-based tests and matrix-assisted laser desorption ionization-time of flight mass spectrometry (Mahmoudi et al. 2019). Early and accurate detection using molecular techniques is crucial for preventing the spread of *C. auris* in healthcare settings, where it often causes outbreaks (Caceres et al. 2019).

Various molecular detection methods have been developed for *Candida auris*, a multidrug-resistant pathogen. Kordalewska (2017) and Ruiz-Gaitán (2018) designed PCR assays targeting specific nucleotide sequences and GPI protein-encoding genes to identify *C. auris* and related species accurately. Sattler (2021) compared the performance of two commercially available qPCR kits, AurisID and Fungiplex *Candida auris* RUO Real-Time PCR, and found that both could detect *C. auris*, with the former showing a lower limit of detection but also a higher rate of false positives. Walchak (2020) developed a real-time PCR assay for the direct detection of *C. auris* from surveillance swabs, blood, and urine, demonstrating its ability to differentiate *C. auris* from closely related species. These studies collectively highlight the potential of molecular methods for accurate and rapid detection of *C. auris*.

### **Unveiling the menace: Dangerous Factors of *Candida auris* in Human Infections.**

*Candida auris* has become a major fungal pathogen due to its ability to cause invasive infections and outbreaks in healthcare facilities that have proven difficult to control and treat. It is also often resistant to medications. Recently, there have been significant outbreaks in numerous countries due to *C. auris*' remarkable capacity to easily contaminate the environment around colonized patients and persist for extended periods (Ahmad & Alfouzan 2021).

Possibly because it forms resilient “dry” biofilms on plastic surfaces, in hospital environments, and on medical devices, *Candida auris* is difficult to eradicate through standard cleaning and decontamination methods (Welsh et al. 2017).

Additionally, they increase the risk of death, especially in people with compromised immune systems or pre-existing medical conditions. The information that is currently available suggests that the risk factors for developing an infection with *Candida auris* are comparable to those for other species of *Candida*. The immune system suppressors include diabetes mellitus, cancer, chemotherapy, central line catheterization, the use of broad-spectrum antibiotics, neutropenia, total parenteral nutrition, hemodialysis, blood transfusion, major surgery within a month, critical care, concurrent bacteremia or candidemia, candiduria, indwelling urinary catheter, and chronic kidney diseases (Raiesi et al.2019).

### **Challenges in controlling *Candida auris* infections: insights into the high prevalence of *Candida auris*.**

*Candida auris* can lead to various infections, with candidemia or bloodstream infection being the most common manifestation. Other infections associated with intravascular devices, such as central catheters, as well as endocarditis, urinary tract infections (candiduria), central nervous system infections, respiratory tract infections, intra-abdominal infections, skin and soft tissue infections, external otitis, otomastoiditis, panophthalmitis, and even osteomyelitis and spondylodiscitis, have also been described (Garcia-Bustos et al.2021)

*Candida auris* demonstrates thermotolerance, thriving best at 37°C and remaining viable up to 42°C. Moreover, it exhibits salt tolerance, and its cells tend to aggregate into large, resilient clusters that are challenging to disperse, potentially aiding its persistence in hospital settings (Rossato & Colombo 2018)

Also, their high prevalence is associated with factors like adherence and the ability to form biofilms. *C. auris* has two growth characteristic phenotypes, i.e., aggregative and non-aggregative. In aggregate form, it does not release its daughter cells after budding. This characteristic leads to the formation of large cell aggregates with high physical resistance, potentially providing the cells with increased resilience in tissues and the environment (Borman et al. 2016). Additionally, the non-aggregated form of *Candida auris* can create more robust biofilms with greater thickness and higher rates of cell death compared to the aggregated form. This ability to form diverse biofilms contributes to *C. auris* being a challenging pathogen to eradicate and capable of causing hospital epidemics of invasive and persistent infections (de Cássia Orlandi Sardi et al. 2018) Due to these characteristics, *C. auris* is resilient on the environmental surfaces despite disinfection.

Recognized worldwide as a significant health concern, *Candida auris* is an invasive fungal pathogen known for its broad innate and acquired resistance to antifungal medications. There is a rising number of reported cases of *C. auris* that are resistant to standard antifungal treatments such as azoles, echinocandins, and polyenes, posing challenges in treatment. Their antifungal resistance plays an important role in their prevalence. (Sanyaolu et al. 2022)

It has been discovered that the fungal pathogen *Candida auris* can evade the immune response in several ways. Both Horton et al. 2021 and Johnson et al. 2018 discovered that *C. auris* poorly recruits neutrophils and evades immune attack, the latter suggests that this is because of the pathogen's cell wall mannosylation. In patients with invasive candidiasis, Kernien (2020) showed that the inhibition of neutrophil extracellular traps (NETs) formation increases this evasion. Also, *Candida auris* employs metabolic strategies to evade the immune system and kill macrophages, as demonstrated by Weerasinghe et al. 2023. These results provide insight into the immune-evading mechanisms that *C. auris* uses to maintain its virulence and high mortality rates.

Overall, *Candida auris* is a dangerous pathogen that is difficult to control because of its capacity to cause severe infections, high tolerance, environmental persistence, multidrug resistance, and ability to elude the immune system.

### **Epidemiology and Global Spread of *Candida auris*.**

Since the first reported in 2009 which isolated from a patient's ear canal in Japan, *Candida auris* has emerged as a major human fungal pathogen (Satoh et al. 2009). Since then, this species has become a "serious threat" in healthcare settings, according to the United States Centers for Disease Control (CDC), and is now listed as a "most wanted" critical pathogen by the World Health Organization (WHO).

Estimating the global incidence rates of *C. auris* colonization and infection has been challenging, as this fungus may not be included in surveillance programs in many countries, and some jurisdictions may have limited laboratory detection capacity. However, available data suggest an increasing trend over the last decade, with outbreaks occurring in numerous countries. The number of cases has also been reported to increase during the COVID-19 pandemic.: (Main conclusions and options for response 2022) *Candida auris* has emerged as a global concern, with reported cases in at least 50 countries across six continents (Vaseghi et al. 2022, Ahmad & Asadzadeh 2023).

Between 2013 and 2021, a total of 1,812 cases of *Candida auris* were identified in the European Union. Sporadic cases of *C. auris* have been detected in all European countries, with hospital outbreaks reported in the UK, Denmark, France, Germany, Greece, Italy, and Spain. In Canada, from 2012 to 2022, there were 43 individuals known to test positive for *C. auris*, with 19 (44.2%) identified in the last three years (Geremia et al. 2023).

In the United States, in the most recent 12 months (January 2022 - December 2022), there were 2,377 clinical cases and 5,754 screening cases reported (Anon 2019). Some studies have also reported *C. auris* infections in over 50 countries and territories worldwide. These include countries/territories in Asia such as Bangladesh, China, India, Iran, Israel, Japan, Kuwait, Lebanon, Malaysia, Oman, Pakistan, Qatar, Saudi Arabia, Singapore, South Korea, Taiwan, Thailand, the United Arab Emirates, and Vietnam; in Europe such as Austria, Belgium, Britain, Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Poland, Russia, Spain, and Switzerland; in the Americas including the Brazil, Canada, Chile, Colombia, Costa Rica, Guatemala, Mexico, Panama, Peru, the USA, and Venezuela; in Africa such as Algeria, Egypt, Kenya, Nigeria, South Africa, and Sudan; and in Oceania including Australia (Oladele et al. 2022, Ahmad & Asadzadeh 2023).

The spread of *Candida auris* around the globe is influenced by various factors, including environmental, and host immunity.

Environmental factors play a crucial role in *C. auris* spreading throughout the world, with the pathogen able to survive harsh environments (Chakrabarti & Sood 2021). Some studies suggest that climate change may have contributed to the spread of *Candida auris* as well (Ellwanger & Chies, 2022, Thakur. 2022, Garcia-Bustos et al. 2023)

The global rise in *Candida auris* infections is also significantly linked to the increasing number of immunocompromised patients (Sanyaolu et al. 2022, Cristina et al. 2023). *C. auris* primarily affects immunocompromised individuals, such as ICU patients, organ transplant recipients, and cancer patients (Sanyaolu et al. 2022). Prolonged hospitalization, mechanical ventilation, and broad-spectrum antibiotic use contribute to increased *C. auris* colonization and infection rates among patients (Khojasteh et al. 2022).

### **Multidrug resistance in *Candida auris*.**

Since *Candida auris* has shown resistance to common antifungal medications, treatment can be challenging (Sanyaolu et al. 2022). In general, antifungal agents target similar mechanisms in *Candida auris* as they do in other fungal species. Azole, echinocandin, polyene, and flucytosine are the antifungal drug classes that are used against *Candida auris* (Frías-De-León et al. 2020). Many fungal processes, including the synthesis of ergosterol, cell walls, nucleic acids, microtubules, mitochondrial function, and protein synthesis, are impacted by these drugs. The effectiveness of these medications against *C. auris* may be restricted, due to the pathogen's special traits and propensity to evolve resistance mechanisms (Bhattacharya Sae-Tia & Fries 2020, Frías-De-León et al. 2020).

Determinative epidemiological cutoff values for antifungal susceptibility and clinical breakpoints for treating *C. auris* infections have not been established due to a lack of available epidemiological data and clinical experience. To assist healthcare providers, the CDC has suggested provisional breakpoints based on clinical and susceptibility data for *C. auris* that are currently available (Anon 2019). The estimated frequency of *Candida auris* resistance to fluconazole, amphotericin B, and echinocandins exceeds 90%, 30%, and roughly 5%, respectively, based on CDC tentative breakpoints. Echinocandins are now the first-line treatment for *C. auris* infections due to the growing resistance to azoles and amphotericin B (Cortegiani et al. 2018).

Fluconazole and other triazole antifungals act by competitively inhibiting sterol demethylase, a key enzyme of the ergosterol-biosynthesis pathway in fungi. Fluconazole has limited effectiveness against *C. auris* because the majority of clinical isolates of the pathogen are resistant to it. The mutation of the gene encoding the sterol-demethylase enzyme (ERG11) is one mechanism of fluconazole resistance that has been repeatedly found in *C. auris*, another common contributor to clinical triazole resistance among multiple species of *Candida* is increased expression of efflux-pump-encoding genes, another is mutations in genes encoding zinc-cluster transcription factors (ZCF), such as TAC1B and MRR1A, can lead to increased expression of efflux pump-encoding genes and contribute to fluconazole resistance, Aneuploidy (An increase in ERG11 copy number as a result of aneuploidy can amplify the effects of mutations in ERG11), Additional, less common mutations in ERG11 and other genes have been reported in *C. auris* isolates, particularly among isolates from specific genetic clades. Some of these mutations have been shown to increase fluconazole MIC. Overall, fluconazole resistance in *C. auris* is likely the result of a combination of multiple resistance mechanisms and mutational stacking in single isolates. The specific mechanisms may vary among isolates from different genetic clades of *C. auris*. (Rybak et al. 2022).

The echinocandins work by inhibiting the synthesis of 1,3-beta-glucan, a major component of the fungal cell wall. Approximately 5% of *C. auris* clinical isolates are resistant to echinocandins, and in many cases, this resistance emerges during therapy. The most observed mutations in echinocandin-resistant isolates of *C. auris* involve substitutions at the amino acid position S639, including S639F, S639P, and S639Y (Biagi et al. 2019) Additional mutations in both hot-spot regions one (D642Y, S639T, F635L/Y, and F635del substitutions) and two (R1354S/H substitutions) have been reported less frequently (Al-Obaid et al. 2022).

Amphotericin B exerts its antifungal activity by directly binding it to ergosterol, the predominant fungal membrane sterol. This binding leads to the formation of pores in the cell membrane and/or sequestration of ergosterols. In *Candida* species, mutations in ergosterol biosynthesis genes such as ERG2, ERG3, ERG5, ERG6, and ERG11 can reduce susceptibility to amphotericin B, likely due to reduced ergosterol levels in the cell membrane. While amphotericin B resistance is uncommon among clinically common *Candida* species, approximately 50% of all *C.*

*auris* isolates are amphotericin B resistant according to tentative breakpoints proposed by the CDC. However, the specific mechanism(s) by which *C. auris* becomes resistant to amphotericin B are poorly understood (Rybak et al. 2022).

Also, biofilm formation enables drug sequestration within the extracellular matrix, leading to antifungal tolerance seen in numerous *Candida* species. A study revealed that *C. auris* isolates with biofilms displayed no susceptibility to any antifungal agent, including fluconazole, echinocandins, and polyenes, unlike planktonic (free-living) *C. auris* isolates, which were only resistant to fluconazole. (Romera et al. 2019).

### ***Candida auris* and Covid -19**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; generally known as Covid 19) has emerged as a major global health crisis, reminiscent of the Spanish influenza pandemic of the early 20<sup>th</sup> century (Hu et al. 2021). The mortality rate associated with COVID-19 in hospitals ranges from 15% to 20% and can increase to 40% among patients requiring intensive care unit (ICU) admission (Wiersinga et al. 2020). Sever patients often require intensive medical interventions, such as mechanical ventilation, extracorporeal membrane oxygenation, continuous renal replacement therapy, glucocorticoids, and intravenous immune-globulin therapy. These interventions can increase the risk of co-infections with various microorganisms, including fungi like *Candida auris* (Villanueva-Lozano et al. 2021, Khojasteh et al. 2022, Nazari et al. 2022). This co-infection has been associated with high mortality rates, even with appropriate antifungal therapy (Villanueva-Lozano et al. 2021).

*Candida auris* is particularly concerning due to its ability to persist on hospital surfaces and its high resistance to antifungal drugs.

The COVID-19 pandemic has created an environment conducive to such fungal infections, especially among ICU patients (Villanueva-Lozano et al.2021). In the latter 2020, several countries, including Brazil, Colombia, India, Italy, Guatemala, Lebanon, Mexico, Panama, Peru, and the United States, reported cases or outbreaks of co-infection with *C. auris* in COVID-19 patients. This highlights the importance of studying and understanding the characteristics of these co-infections (Khojasteh et al. 2022). In 2021 in a COVID-19 specialty care unit in Florida, an outbreak of *C. auris* was reported, highlighting the need for aggressive measures to limit its spread (Prestel 2021). The comprehensive review on *Candida* by Khojasteh et al. (2022) has identified 27 studies, 14 of which provided data on COVID-19-associated *C. auris* infections. These infections have been reported in various regions, including the Americas, Europe, and Asia, suggesting a global concern (Khojasteh et al. 2022)

### **Prevention strategies for *Candida auris* infections.**

Primary infection control measures for preventing the transmission of *Candida auris* in healthcare settings include adherence to hand hygiene practices, ensuring the appropriate use of Transmission-Based Precautions based on the setting, and regular cleaning and disinfection of the patient care environment and reusable equipment using recommended products (Special attention should be given to shared mobile equipment, such as glucometers and blood pressure cuffs), Communication about a patient's *C. auris* status is essential when transferring them to another facility, screening contacts of newly identified case patients to identify any *C. auris* colonization and to conduct laboratory surveillance of clinical specimens to detect additional cases promptly. (CDC. 2021).

When it comes to hand hygiene, alcohol-based hand sanitizer (ABHS) is the recommended method for hand hygiene when hands are not visibly soiled due to *C. auris*. However, if hands are visibly soiled, it is important to wash them with soap and water. It's crucial to keep in mind that good hand hygiene cannot be replaced by wearing gloves. (CDC 2019).

Transmission-based precautions, including contact precautions, must be adhered to for individuals with confirmed hospital-acquired infections such as *C. auris*. Contact precautions entail

wearing specific personal protective equipment (PPE) such as gowns, gloves, and possibly eyewear when caring for individuals with *C. auris* infections. (CDC 2020).

Since *C. auris* live on surfaces for weeks, it is critical to clean and disinfect surfaces and medical equipment continuously throughout the day (CDC 2024). Cleaning surfaces in rooms with *C. auris*-positive patients twice or three times daily using chlorine-based or other sporicidal disinfectants is highly effective in controlling cross-transmission of infection. To streamline cleaning procedures, it is advisable to use single-use items such as pillows, bedding material, and fiber cloth wipes for cleaning, as well as single-use equipment like thermometers and blood pressure cuffs for *C. auris*-positive patients. Less expensive items that are difficult to clean should be discarded (Ahmad & Asadzadeh 2023). CDC recommends using an Environmental Protection Agency (EPA)–registered hospital-grade disinfectant effective against *C. auris* (EPA’s list (US EPA 2020).

Also, Patients under contact precautions should ideally be accommodated in single or private rooms to reduce the risk of spreading the infection to other patients (Isler 2023).

According to the CDC, Screening for *C. auris* colonization involves swabbing the armpits and groin area and is recommended for close healthcare contact with newly diagnosed patients, those who stayed in non-U.S. healthcare facilities in the past year, patients needing higher care levels like mechanical ventilation, and individuals in facilities suspected of ongoing transmission. (www.cdc.gov 2020).

Rapid and accurate detection of *C. auris* is crucial for preventing its transmission. Delayed recognition of infection or colonization and delayed implementation of infection control practices can lead to the rapid spread of *C. auris* among hospitalized patients who share space, facilities, and equipment (Kenters et al.2019, Ahmad & Alfouzan 2021).

Advances in molecular diagnostic procedures now enable the rapid identification of invasive *C. auris* infections within a few hours, with high sensitivity and specificity (Lockhart et al. 2022). Upon identifying a *C. auris*-positive case, hospitals should immediately inform their infection control team to implement transmission-based precautions (TBPs) to prevent the spread of the fungus to other patients in the facility. (Ahmad & Asadzadeh, 2023).

## **Future work**

*Candida auris* has emerged as a significant global health threat due to its multidrug resistance and ability to cause severe infections in healthcare settings. Unlike *Candida albicans*, which has been extensively studied, *Candida auris* presents unique challenges in terms of diagnosis, treatment, and infection control.

The pathogen's resistance to multiple antifungal classes complicates treatment regimens and necessitates a deeper understanding of its underlying mechanisms. Despite the growing recognition of *Candida auris* as a critical pathogen, research into this species lags behind that of other *Candida species*. However, with ongoing outbreaks of *Candida auris* worldwide, there is a pressing need for more information, particularly in areas such as new diagnostic methods and treatment approaches for this multidrug-resistant superbug.

Additionally, molecular characterisation and understanding of the immunometabolism changes induced by the host immune system in response to *Candida auris* infection is crucial. These studies could provide valuable insights and approaches to better control and manage *C. auris* infection. Currently, there are numerous ongoing research projects focusing on these areas, aiming to enhance our understanding and develop effective strategies against *Candida auris*.

In addition to the infection mechanisms, further studies on comprehensive genomic and transcriptomic studies to understand the genetic diversity, evolution, and gene expression of different *Candida auris* strains, including those resistant to antifungal drugs. Investigating the virulence factors of *Candida auris* and conducting epidemiological studies to determine the global prevalence, distribution, and risk factors associated with *Candida auris* infections, as well as improving surveillance systems for early detection and containment of outbreaks.



## Acknowledgements

We would like to extend our heartfelt thanks to our families and friends for their unwavering support throughout the writing of this review.

## References

- ACIR Community. 2024 – [acir.aphis.usda.gov](https://acir.aphis.usda.gov/s/cird-taxon/aOut0000002i7V8AAI/candida-albicans). Available at: <https://acir.aphis.usda.gov/s/cird-taxon/aOut0000002i7V8AAI/candida-albicans>
- Ahmad S, Alfouzan W. 2021 – Candida auris: Epidemiology, Diagnosis, Pathogenesis, Antifungal Susceptibility, and Infection Control Measures to Combat the Spread of Infections in Healthcare Facilities. *Microorganisms*, 9(4), 807
- Ahmad S, Asadzadeh M. 2023 – Strategies to Prevent Transmission of Candida auris in Healthcare Settings. *Current Fungal Infection Reports*, 17(1)
- Al-Obaid I, Asadzadeh M, Ahmad S, Alobaid K et al. 2022 – Fatal Breakthrough Candidemia in an Immunocompromised Patient in Kuwait Due to Candida auris Exhibiting Reduced Susceptibility to Echinocandins and Carrying a Novel Mutation in Hotspot-1 of FKS1. *Journal of Fungi*, 8(3), 267
- Anon. 2019 – Antifungal Susceptibility Testing and Interpretation. Available at: <https://cdc.gov/fungal/candida-auris/c-auris-antifungal.html>
- Anon. 2019 – Tracking Candida auris. [online] Available at: <https://cdc.gov/fungal/candida-auris/tracking-c-auris.html>
- Basmaciyan L, Bon F, Paradis T, Lapaquette P et al. 2019 – Candida Albicans Interactions with the host: Crossing the intestinal epithelial barrier. *Tissue Barriers*, 7(2), 1612661
- Bhattacharya S, Sae-Tia S, Fries BC. 2020 – Candidiasis and Mechanisms of Antifungal Resistance. *Antibiotics*, 9(6),312
- Biagi MJ, Wiederhold NP, Gibas C, Wickes B.L et al. 2019 – Development of High-Level Echinocandin Resistance in a Patient With Recurrent Candida auris Candidemia Secondary to Chronic Candiduria. *Open Forum Infectious Diseases*, 6(7)
- Bidaud AL, Chowdhary A, Dannaoui E. 2018 – Candida auris: An emerging drug resistant yeast – A mini-review. *Journal de Mycologie Médicale*, 28(3), 568–573
- Biswal M, Rudramurthy SM, Jain N, Shamanth AS et al. 2017 – Controlling a possible outbreak of Candida auris infection: lessons learnt from multiple interventions. *Journal of Hospital Infection*, 97(4),363–370
- Borman AM, Szekely A, Johnson EM. 2016 – Comparative Pathogenicity of United Kingdom Isolates of the Emerging Pathogen Candida auris and Other Key Pathogenic Candida Species. *mSphere*, 1(4)
- Caceres DH, Forsberg K, Welsh RM, Sexton DJ et al. 2019 – Candida auris: A Review of Recommendations for Detection and Control in Healthcare Settings. *Journal of Fungi*, 5(4).
- Casadevall A, Kontoyiannis DP, Robert V. 2019 – On the Emergence of Candida auris: Climate Change, Azoles, Swamps, and Birds. *mBio*. Edited by J.W. Kronstad, 10(4). Available at: Doi 10.1128/mbio.01397-19.
- CDC. 2019 – Infection Prevention and Control for Candida auris. [online] CDC. Available at: <https://cdc.gov/fungal/candida-auris/c-auris-infection-control.html>
- CDC. 2020 – Information for Infection Preventionists | Fact Sheets | Candida auris | Fungal Diseases | CDC. [online] Available at: <https://cdc.gov/fungal/candida-auris/fact-sheets/cdc-message-infection-experts.html>
- CDC. 2021 – Infection Prevention and Control for Candida auris | Candida auris | Fungal Diseases | CDC. [online] Available at: <https://cdc.gov/fungal/candida-auris/c-auris-infection-control.html#transmission>
- CDC. 2024 – About C. auris, Candida auris (C. auris). Available at: <https://cdc.gov/candida-auris/about/index.html>

- Chakrabarti A, Sood P. 2021 – On the emergence, spread and resistance of *Candida auris*: host, pathogen and environmental tipping points, *Journal of Medical Microbiology*, 70(3)
- Chow EWL, Pang LM, Wang Y. 2021 – From Jekyll to Hyde: The Yeast–Hyphal Transition of *Candida albicans*. *Pathogens*, 10(7), 859
- Cortegiani A, Misseri G, Fasciana T, Giammanco A et al. 2018 – Epidemiology, clinical characteristics, resistance, and treatment of infections by *Candida auris*. *Journal of Intensive Care*, 6(1)
- Cortegiani A, Misseri G, Fasciana T, Giammanco A et al. 2018 – Epidemiology, clinical characteristics, resistance, and treatment of infections by *Candida auris*. *Journal of Intensive Care*, 6(1)
- Cristina ML, Spagnolo AM, Sartini M, Carbone A et al. 2023 – An Overview on *Candida auris* in Healthcare Settings. *Journal of Fungi*, 9(9), 91
- de Cássia Orlandi Sardi J, Silva DR, Soares Mendes-Giannini MJ, Rosalen PL. 2018 – *Candida auris*: Epidemiology, risk factors, virulence, resistance, and therapeutic options. *Microbial Pathogenesis*, 125, 116–121
- Ellwanger JH, Chies JAB. 2022 – *Candida auris* emergence as a consequence of climate change: Impacts on Americas and the need to contain greenhouse gas emissions. *The Lancet Regional Health – Americas*, 11
- Fasciana T, Cortegiani A, Ippolito M, Giarratano A et al. 2020 – *Candida auris*: An Overview of How to Screen, Detect, Test and Control This Emerging Pathogen. *Antibiotics*, 9(11), 778
- Forsberg K, Woodworth K, Walters M, Berkowet EL et al. 2018 – *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Medical Mycology*, 57(1), 1–12
- Frías-De-León MG, Hernández-Castro R, Vite-Garín T, Arenas R et al. 2020 – Antifungal Resistance in *Candida auris*: Molecular Determinants. *Antibiotics*, 9(9), 568
- Gabaldón T. 2019 – Recent trends in molecular diagnostics of yeast infections: from PCR to NGS. *FEMS Microbiology Reviews*, 43, 517–547
- Garcia-Bustos V, Cabanero-Navalon M.D, Ruiz-Saurí A, Ruiz-Gaitán AC et al. 2021 – What Do We Know about *Candida auris*? State of the Art, Knowledge Gaps, and Future Directions. *Microorganisms*, 9(10), p. 2177. Doi 10.3390/microorganisms9102177
- Garcia-Bustos V, Cabañero-Navalon MD, Ruiz-Gaitán A, Salavert M et al. 2023 – Climate change, animals, and *Candida auris*: insights into the ecological niche of a new species from a One Health approach. *Clinical Microbiology and Infection*, 29(7), 858–862
- Geremia N, Brugnaro P, Solinas M, Scarparo C et al. 2023 – *Candida auris* as an Emergent Public Health Problem: A Current Update on European Outbreaks and Cases. *Healthcare*, 11(3), 425
- Guinea J. 2014 – Global trends in the distribution of *Candida* species causing candidemia. *Clinical Microbiology and Infection*, 20, 5–10
- Horton MV, Johnson CJ, Zarnowski R, Andes BD et al. 2021 – *Candida auris* Cell Wall Mannosylation Contributes to Neutrophil Evasion through Pathways Divergent from *Candida albicans* and *Candida glabrata*. *mSphere*, 6(3)
- Hu B, Guo H, Zhou P, Shi ZL. 2021 – Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol*. 19(3),141–54
- Iguchi S, Itakura Y, Yoshida A, Kamada K et al. 2019 – *Candida auris*: A pathogen difficult to identify, treat, and eradicate and its characteristics in Japanese strains. *Journal of Infection and Chemotherapy*, 25(10), 743–749
- Imtiaz Fauzia, Tariq Moez, Hasan, Syed Noor Ul. 2022 – *Candida auris* case in Karachi, a public health threat ahead. *Journal of the Pakistan Medical Association*
- Index Fungorum. 2024 – ‘Search Page, [Indexfungorum.org](https://indexfungorum.org). Available at: <https://indexfungorum.org/names/Names.asp?pg=2>
- Isler A. 2023 – How to Prevent a *Candida Auris* Infection. [Online] Verywell Health. Available at: <https://verywellhealth.com/candida-auris-is-it-preventable-7373121>
- Jackson BR, Nancy Chow, Kaitlin Forsberg, Anastasia P et al. 2019 – On the Origins of a Species: What Might Explain the Rise of *Candida auris*?. *Journal of Fungi*, 5(3), 58.

- Johnson C, Davis JM, Huttenlocher A, Kernien J et al. 2018 – Emerging Pathogen *Candida auris* Evades Neutrophil Attack. *Open Forum Infectious Diseases*, 5(suppl\_1), 37–37
- Johnson Chad J, Davis JM, Huttenlocher A, Kernien JF et al. 2018 – Emerging Fungal Pathogen *Candida Auris* Evades Neutrophil Attack. *MBio*, 9(4)
- Kathuria S, Singh PK, Sharma C, Prakash A et al. 2015 – Multidrug-Resistant *Candida auris* Misidentified as *Candida haemulonii*: Characterization by Matrix-Assisted Laser Desorption Ionization–Time of Flight Mass Spectrometry and DNA Sequencing and Its Antifungal Susceptibility Profile Variability by Vitek 2, CLSI Broth Microdilution, and Etest Method. *Journal of Clinical Microbiology*. Edited by D.W. Warnock, 53(6),1823–1830
- Kenters N, Kiernan M, Chowdhary A, Denning DW et al. 2019 – Control of *Candida auris* in healthcare institutions: Outcome of an International Society for Antimicrobial Chemotherapy expert meeting. *International Journal of Antimicrobial Agents*, 54(4), 400–406
- Kernien JF, Johnson CJ, Bayless ML, Chovanec JF et al. 2020 – Neutrophils from patients with invasive candidiasis are inhibited by *Candida albicans* biofilms. *Front. Immunol.* 11.
- Khojasteh S, Jafarzadeh J, Hosseini AS, Haghani I et al. 2022 – *Candida auris* and COVID-19: A health threatening combination. *Current Medical Mycology*, 8(3), 44–50
- Konjengbam O, Khuraijam R, Ningthoujam P, Acharjee A et al. 2022 – P223 First case of *Candida auris* candidemia in Manipur, Northeast India. *Medical Mycology*, 60(Supplement\_1).
- Kordalewska M, Zhao Y, Lockhart S.R, Chowdhary A et al. 2017 – Rapid and Accurate Molecular Identification of the Emerging Multidrug–Resistant Pathogen *Candida auris*. *Journal of Clinical Microbiology*, 55(8), 2445–2452
- Koundal S, Cojandaraj L. 2020 – *Candida* species-morphology, medical aspects and pathogenic spectrum. *European Journal of Molecular & Clinical Medicine*, 07(7), 2020
- Kullberg BJ, Arendrup MC. 2019 – Invasive Candidiasis. *New England Journal of Medicine*. Edited by E.W. Campion, 373(15), 1445–1456
- Lockhart SR, Lyman MM, Sexton DJ. 2022 – Tools for Detecting a “Superbug”: Updates on *Candida auris* Testing. *Journal of Clinical Microbiology*, 60(5)
- Mahmoudi S, Agha Kuchak Afshari S, Aghaei Gharehbolagh S, Mirhendi H et al. 2019 – Methods for identification of *Candida auris*, the yeast of global public health concern: A review. *Journal de Mycologie Médicale*, 29(2), 174–179
- Main conclusions and options for response. 2022 – Available at: <https://ecdc.europa.eu/sites/default/files/documents/RRA-candida-auris-Feb2022.pdf>
- McCarty TP, White CM, Pappas PG. 2021 – Candidemia and Invasive Candidiasis. *Infectious Disease Clinics of North America*, 35(2), 389–413. McCort ME. 2021 – Oropharyngeal and Vulvovaginal Candidiasis. Elsevier eBooks, 726–729.
- Nasirian H. 2017 – Contamination of cockroaches (Insecta: Blattaria) to medically fungi: A systematic review and meta-analysis. *Journal of Medical Mycology*, 27, 427–448
- Naureen B, Arya NR, Rafiq NB. 2024 – Candidiasis, PubMed. Treasure Island (FL): StatPearls Publishing
- Navalkele BD, Revankar S, Chandrasekar P. 2017 – *Candida auris*: a worrisome, globally emerging pathogen. *Expert Review of Anti-infective Therapy*, 15(9), 819–827
- Nazari T, Sadeghi F, Izadi A, Sameni S et al. 2022 – COVID-19-associated fungal infections in Iran: A systematic review. *PLOS ONE*, 17(7), p.e0271333
- Nett JE. 2019 – *Candida auris*: An emerging pathogen “incognito”, *PLOS Pathogens*. Edited by D.A. Hogan, 15(4), p. e1007638
- Oladele RO, Jessica Nnena Uwanibe, Olawoye IB, Abdul-Wahab Omo-ope Ettu et al. 2022 – Emergence and Genomic Characterization of Multidrug Resistant *Candida auris* in Nigeria, West Africa. *Journal of Fungi*, 8(8), 787–787
- Pfaller MA, Andes DR, Diekema DJ, Hornet DL et al. 2014 – Epidemiology and Outcomes of Invasive Candidiasis Due to Non-*albicans* Species of *Candida* in 2,496 Patients: Data from the Prospective Antifungal Therapy (PATH) Registry 2004–2008. *PLoS ONE*. Edited by N. Chauhan, 9(7), p. e101510

- Prestel C. 2021 – *Candida auris* Outbreak in a COVID-19 Specialty Care Unit – Florida, July–August 2020. *MMWR. Morbidity and Mortality Weekly Report*, 70
- Raiesi O, Shabandoust H, Getso M, Raissi V et al. 2019 – *Candida auris*: A New Emerging Fungal Monster. *Archives of Clinical Infectious Diseases*, In Press (In Press)
- Reham Kaki 2023 – Risk factors and mortality of the newly emerging *Candida auris* in a university hospital in Saudi Arabia. *Mycology*, 14(3), 256–263
- Romera D, Aguilera-Correa JJ, Gadea I, Viñuela-Sandoval L et al. 2019 – *Candida auris*: a comparison between planktonic and biofilm susceptibility to antifungal drugs. *Journal of Medical Microbiology*
- Romo JA, Kumamoto CA. 2020 – On Commensalism of *Candida*, *Journal of Fungi*, 6(1)
- Rossato L, Colombo AL. 2018 – *Candida auris*: What Have We Learned about Its Mechanisms of Pathogenicity? *Frontiers in Microbiology*, 9
- Ruiz-Gaitán AC, Fernández-Pereira J, Valentin E, Tormo-Mas et al. 2018 – Molecular identification of *Candida auris* by PCR amplification of species-specific GPI protein-encoding genes. *International Journal of Medical Microbiology*, 308(7), 812–818
- Rybak JM, Cuomo CA, David Rogers P. 2022 – The molecular and genetic basis of antifungal resistance in the emerging fungal pathogen *Candida auris*. *Current Opinion in Microbiology*, 70, 102208
- Sanyaolu A, Okorie C, Marinkovic A, Abbasi AF et al. 2022 – *Candida auris*: An Overview of the Emerging Drug-Resistant Fungal Infection. *Infection and Chemotherapy*, 54(2), 236
- Sarma S, Upadhyay S. 2017 – Current perspective on emergence, diagnosis and drug resistance in *Candida auris*, *Infection and Drug Resistance*, Volume 10, 155–165
- Satoh K, Makimura K, Hasumi Y, Nishiyama Y et al. 2009 – *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. *Microbiology and Immunology*, 53(1), 41–44
- Sattler J, Noster J, Brunke A, Plum G et al. 2021 – Comparison of Two Commercially Available qPCR Kits for the Detection of *Candida auris*. *Journal of fungi*, 7(2), 154–154
- Schoch CL, Ciufo S, Domrachev M, Hotton CL et al. 2020 – NCBI Taxonomy: a comprehensive update on curation, resources and tools, *Database*, 2020
- Shyni UK, Lavanya R. 2021 – A study on transmission dynamics of the emerging *Candida Auris* infections in Intensive Care Units: Optimal control analysis and numerical computations. *Physica A: Statistical Mechanics and its Applications*, 561, 125253
- Sikora A, Zahra F. 2021 – *Candida Auris*. [online] PubMed. Available at: <https://ncbi.nlm.nih.gov/books/NBK563297/>
- Spampinato C, Leonardi D. 2013 – *Candida* infections, Causes, Targets, and Resistance Mechanisms: Traditional and Alternative Antifungal Agents. *BioMed Research International*, 1–13
- Thakur S. 2022 – The state of the globe: *Candida auris*-a global healthcare threat. *Journal of Global Infectious Diseases*, 14(4), 129.
- US EPA O. 2020 – EPA’s Registered Antimicrobial Products Effective Against *Candida auris* [List P]. [online] [www.epa.gov](https://www.epa.gov/pesticide-registration/epas-registered-antimicrobial-products-effective-against-candida-auris-list). Available at: <https://www.epa.gov/pesticide-registration/epas-registered-antimicrobial-products-effective-against-candida-auris-list>
- Vallabhaneni S, Zahn M, Epton E, ODonnell K et al. 2019 – 2449. Early Detection of *Candida auris* is Essential to Control Spread: Four Effective Active Surveillance Strategies. *Open Forum Infectious Diseases*, 6 (Supplement\_2), 846–847
- Vaseghi N, Sharifisooraki J, Khodadadi H, Nami S et al. 2022 – Global Prevalence and Subgroup Analyses of Coronavirus Disease (COVID-19) Associated *Candida auris* infections (CACa): A Systematic Review and Meta-Analysis. *Mycoses*
- Villanueva-Lozano H, Treviño-Rangel R. de J, González GM, Ramírez-Elizondo MT et al. 2021 – Outbreak of *Candida auris* infection in a COVID-19 hospital in Mexico. *Clinical Microbiology and Infection*, 27(5), 813–816

- Walchak RC, Buckwalter SP, Zinsmaster NM, Henn KM et al. 2020 – *Candida auris* Direct Detection from Surveillance Swabs, Blood, and Urine Using a Laboratory-Developed PCR Method. *Journal of Fungi*, 6(4), 224–224
- Weerasinghe H, Simm C, Djajawi T.M, Tedja I et al. 2023 – *Candida auris* evades innate immunity by using metabolic strategies to escape and kill macrophages while avoiding antimicrobial inflammation. *bioRxiv* (Cold Spring Harbor Laboratory)
- Welsh RM, Bentz ML, Shams A, Houston H et al. 2017 – Survival, Persistence, and Isolation of the Emerging Multidrug-Resistant Pathogenic Yeast *Candida auris* on a Plastic Health Care Surface. *Journal of Clinical Microbiology*, 55(10), 2996–3005
- WHO fungal priority pathogens list to guide research, development and public health action. Geneva: World Health Organization; 2022
- Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ et al. 2020 – Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA*, [online] 324(8), 782–793
- Wijayawardene NN, Hyde KD, Dai DQ1, Sánchez-García M5 et al. 2022 – Outline of fungi and fungus-like taxa-2021. *Mycosphere*, 13(1), 53-453.
- Worku M, Girma F. 2020 – *Candida auris*: From Multidrug Resistance to Pan-Resistant Strains. *Infection and Drug Resistance*, 13, 1287–1294
- www.cdc.gov. 2020 – Identification of *Candida auris* *Candida auris* | Fungal Diseases | CDC. [online] Available at: <https://cdc.gov/fungal/candida-auris/identification.html>