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Candida auris: an emerging life-threatening fungal pathogen of global public health concern

Abstract

The multidrug-resistant yeast *Candida auris* has in recent times emerged to be known as an alarming threat to global health. Since it was first discovered in Japan in 2009, the virus has spread to more than 50 nations, resulting in significant epidemics in health care facilities throughout the world. It is currently endemic in several regions of Asia and Africa, where infection death rates have been estimated to reach up to 72% in some cases. Treatment for this infection is complicated by its resistance to numerous antifungal drugs, and its threat level is increased by its ability to elude normal laboratory identification techniques. Due to its ability to colonize skin and other surfaces, *Candida auris* is especially harmful in healthcare settings as it can spread throughout hospitals as well as between them. Its simultaneous emergence on multiple continents in genetically diverse clades highlights the complexity of its epidemiology and the difficulties in controlling it. Although the exact origins of this virus are still unknown, theories indicate that bird migration and global warming may have had a role in its spread. Making a diagnosis of *Candida auris* is still difficult. Because of its multidrug resistance and persistent transmission, *Candida auris* requires innovative therapeutic and preventive approaches for effective management. To combat *Candida auris,* this paper discusses its epidemiology, diagnostic methods, treatment choices, and preventative and control measures.

Keywords: *Candida auris,* emerging pathogen, health care settings, multidrug-resistant, public health

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Introduction

A major global health threat is the newly discovered, multidrug-resistant yeast *Candida auris*. From its initial discovery in Japan in 2009,[1] *Candida auris* has spread to more than 50 countries and caused significant outbreaks in healthcare facilities across the globe.[2] According to Hinrichs et al.,[3] it is now considered to be endemic in several African and Asian regions. Its tolerance to several antifungal drugs makes this infection particularly dangerous as it makes treatment efforts more difficult. Multiple drug-resistant strains of *C. auris* have been found worldwide by researchers. As per Chow et al.,[4] the five main clades of *C. auris* are found in various regions, namely I (southern Asia), II (eastern Asia), III (Africa), IV (South America), and V (Iran). Geographic locations exhibit dramatically different mortality rates for *C. auris* infections. According to Chow et al.,[4] the five main clades of *C. auris* are found in the following geographical locations: I (southern Asia), II (eastern Asia), III (Africa), IV (South America), and V (Iran). Geographically, *C. auris* infection mortality rates vary greatly; some data indicate that rates might reach 72%.[5] *C. auris's* multidrug resistance and capacity to elude standard laboratory identification further compound the threat that it poses.

Candida auris has been recognized by the Centers for Disease Control and Prevention (CDC) as a pathogen that can result in rapid outbreaks and high mortality rates. The pathogen infects patients even when there is no visible infection and lingers in the surroundings of medical equipment and healthcare facilities, which can lead to hospital outbreaks.[6] There are theories that this pathogen may have originated because of global warming and that birds, with their high body temperatures, may have helped spread the infection throughout the world.[7] The origins of this pathogen are still unknown. *C. auris* is a persistent danger in healthcare facilities due to its tendency for horizontal transmission, regardless of its source.[8]

Candida auris does not colonize the gastrointestinal system or mucosal surfaces like other harmful species of the yeast. Rather, it has a distinct affinity for human skin and can remain on it for a long time.[9] Long-term survival of *C. auris o*n human skin and mucosal surfaces in healthcare settings facilitates intra- and inter hospital clonal transmission, which can result in large outbreaks in medical facilities.[9,10] Easy skin-to-skin transmission, especially in medical environments, contributes to the spread of *C. auris*.[10]

According to Chowdhary et al,[11] it has developed resistance to frontline antifungal medications, which highlights the critical need for innovative treatment and preventive measures. Because of its rapid worldwide spread, difficult microbiological diagnosis, high death rate, and ongoing transmissions, *Candida auris* poses a severe threat to human health.[12] This study is to investigate strategies for controlling the rapid global spread of *C. auris.* Thus, the focus of this study is on infection control and preventive measures, treatments, diagnostic tools, and epidemiology.

Epidemiology

Emergence and global spread

The spread and appearance of *C. auris* have posed serious problems for public health around the world. This pathogen was first identified in 2009[1] and has subsequently spread to healthcare facilities across the globe, causing epidemics of invasive diseases that can be fatal.[13] *C. auris* is especially concerning because of how rapidly it inhabits the skin, how readily it transmits among patients, and how long it survives in healthcare environments in spite of infection control procedures. Moreover, it has grown resistant to every class of antifungal medication, making treatment extremely challenging.[14]

C. auris has been identified as a "stealthy pandemic" since it was discovered and is currently known to have spread to every continent

except Antarctica. Presumably, *C. auris* was present as a human pathogen before its official discovery in 2009, as it was commonly mistaken as *C. haemulonii*.[14,15] Misidentified isolates from as far back as 1996 in South Korea,[16] 1997 in Japan,[17] and 2008 in Pakistan[18] have been found by retrospective studies, suggesting an earlier undiscovered presence.

In addition to being recognized as a novel species by 2009, *C. auris* was also the subject of reports of invasive infections and hospital outbreaks. Europe reported its first outbreak in 2013; between April 2013 and April 2017, a London cardio-thoracic facility reported 50 cases.[19] Twelve patients' samples from 2009 to 2012 were analyzed in the first epidemic in India, which was reported in 2013. Genetically related strains also made their way to Pakistan.[19] The first epidemic in the Americas was documented in Venezuela by 2012,[20] and Colombia by the same year.[21] According to Govender et al.[22] and Okinda et al.,[23] the first solitary cases and outbreaks in Africa occurred in 2010 in Kenya and South Africa. The first reports of cases were from Saudi Arabia, Kuwait, and Oman in the Gulf region; later reports came from the United Arab Emirates.[19]

The simultaneous yet independent development of genetically diverse clades on several continents is a noteworthy aspect of the rapid emergence of *C. auris*.[24] Four primary clades have been identified through *whole*-genome sequencing of clinical isolates: clade I is South Asian, clade II is East Asian, clade III is South African, and clade IV is South American. Iran *was* the site of the 2018 discovery of the Iranian clade, the fifth clade.[4] According to Rhodes and Fisher,[15] molecular epidemiological research has revealed groups of closely related isolates within outbreaks, suggesting local and continuous transmission. Moreover, it has been noted that there have been several introductions into countries including the US, UK, and Germany, followed by local transmission.[25] For *C. auris*, clonal proliferation appears to have occurred in every clade. Only one of the two fungal mating forms is found in each given clade, even though *C. auris* genomes still contain conserved meiosis and mating genes. According to Muñoz et al.,[26] MTLa is specifically found in clades I and IV, whereas MTLα, the opposite mating type, is found in clades II and III.

Diagnostic techniques

According to De Gaetano et al.,[27] *C. auris's* phenotypic similarities to other species, including *C. duobushaemulonii, C. haemulonii, C. famata, and C. lusitaniae*, make diagnosis difficult and frequently result in misidentification in regular laboratory settings. Advanced techniques like genetic sequencing, advanced mass spectrometry, or upgraded VITEK 2 versions are necessary for precise identification.[28,29] The internal transcribed spacer (ITS) of rDNA and the D1/D2 region of the 28S rDNA are two loci that can be sequenced specifically to help distinguish between distinct regional clades of *C. auris*.[30] Due to a lack of a thorough database for species identification, earlier versions of VITEK 2 (bioMérieux, Marcy-l'Étoile, France) misdiagnosed *C. auris*; however, the current version 8.01 can differentiate it from other Candida species.[30]

According to Jeffery-Smith et al.,[5] *C. auris* can be separated from closely related species using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) when it is fitted with a specific spectrum. However, misidentification is prevalent in places with limited resources where such technology is unavailable, which results in the underreporting of *C. auris* infections.[30] Infections with *C. auris* often present with an uncertain clinical presentation akin to other systemic infections. When severe, disseminated intravascular coagulation, shock, oliguria, and renal failure can all be symptoms of bacterial sepsis.[31] Fever is one of the symptoms of candidemia. Systemic therapy is required for positive cultures from sterile locations such as biopsy tissue, cerebral fluid, blood or pericardial fluid. Serum beta-glucan testing assists in diagnosis but may produce misleading results.[31] Although the principal diagnostic technique is still culturing blood or body fluids, *C. auris* is more challenging to identify than other *Candida* species. New chromogenic mediums have been developed to help identify *Candida auris* and optimize the speed and accuracy of culture-based diagnostics.[32] In addition to promoting the growth of *Candida albicans*, *C. tropicalis,* and several other *Candida* species, the Pal sunflower seed medium was initially developed in 1980 for the early diagnosis and epidemiological study of *Cryptococcus neoformans*, a potentially fatal mycotic agent in humans and animals.[33–37] Therefore, *C. auris* can be isolated from clinical specimens in microbiology and public health laboratories across the globe by employing this easily accessible and affordable media.

Public health significance

A severe bloodstream infection brought on by the species *Candida*, candidemia is a serious threat to the public's health, especially for those who are immunocompromised or have significant underlying medical conditions like solid tumors, hematological malignancies, HIV infection, neutropenia, diabetes mellitus, or chronic kidney disease. It is noteworthy that infants are also vulnerable.[38] In hospital settings, where even individuals without underlying medical conditions may be vulnerable to intra-hospital epidemics, especially in certain wards, these infections are especially alarming. Septic shock is a life-threatening condition that affects around one-third of individuals with candidemia.[39] According to Sikora and Zahra,[40] invasive candidiasis, which includes *C. auris* infections, carries a high mortality rate of up to 30–40%. Infections with *C. auris* have the potential to result in even greater mortality rates of up to 70%. According to CDC data, bloodstream infections caused by *C. auris* have a 39% 30-day fatality rate and a 58% 90-day mortality rate.[41]

Risk factor and transmission

Numerous risk factors can impact the onset and spread of *candidemia.* Advanced age and infections originating in the abdomen are important intrinsic factors directly linked to the onset of septic shock in patients with candidemia.[39] Five extrinsic factors were found to be the most prevalent in a global retrospective analysis of *C. auris* infections from 2009 to 2020: invasive medical procedures (such as surgery, urinary catheters, and central venous catheters), prolonged hospital stays, living in high-acuity skilled nursing facilities, and exposure to both acute and long-term healthcare environments.[42] No other factors were found to be as common. Amongst healthcare settings, *C. auris* in particular has demonstrated a considerable tendency for patient-to-environment-to-patient transmission. Research has documented extensive contamination of equipment and surfaces in the environment that lasts for months, with *C. auris* infection developing in patients as little as four hours after contact. According to reports, *C. auris i*nfestations can also be disseminated by ventilators in clinical care units.[43] The complete scope of *C. auris* pathogenicity and invasive capacity is yet unknown, despite its propensity for transmission and resistance.[40] This presents challenges for effective control and containment techniques.

Therapeutics

C. auris exhibits a clade-specific pattern of antifungal susceptibility, with this species displaying 70% global resistance to fluconazole and

5% global resilience to echinocandins.[44] Furthermore, 23% of the isolates are resistant to amphotericin B, an antifungal that usually causes relatively minimal resistance in *Candida* isolates. There are pan-resistant isolates with high minimum inhibitory concentrations (MIC) for all of the antifungal classes that are currently accessible, and about 20% of *Candida* isolates demonstrate resistance to two antifungal classes.[19] Since the majority of *C. auris* species are resistant to azoles and amphotericin B, echinocandins are the first-line treatment for infections caused by this pathogen. Nevertheless, a number of investigations have also documented *C. auris* resistance to echino candins. In order to track the effectiveness of treatment and the emergence of resistance, patients should therefore get frequent follow-ups and reevaluations by microbiological culture investigations.[19]

Control and prevention strategies

The growth and persistence of *Candida auris* in medical facilities pose significant challenges to infection control and prevention efforts. Remarkably, certain strains of *Candida auris* may form biofilms on both biotic and abiotic surfaces.[45] This ability results in the permanent colonization of patients, mainly on the nares, skin and other body sites. Regretfully, no effective decolonization method is currently available, and colonization may continue for months before becoming incurable and spreading further.[28] It is speculated that infected medical equipment, long-term environmental contamination, and other variables play a significant role in nosocomial *C. auris* transmission. The bacteria can also survive in the environment for extended periods.[46]

Due to the growing concern over *C. auris* infections, the 2018 Council for State and Territorial Epidemiologists (CSTE) Annual Conference declared these as nationwide required to notify.[47] Isolation in distinct wards with stringent preventative measures is crucial for patients with proven or suspected infections, and all cases should be reported to provincial or state departments of health.[47] Strict precautions should be taken against close contacts of infected individuals, especially healthcare personnel until they display negative results in confirmatory diagnostic testing. Furthermore, it is advised to thoroughly clean shared medical equipment and wards to stop additional transmission.[48]

Forsberg et al.[28] state that further efficient infection control strategies include healthcare personnel cleaning medical instruments properly and practicing good hand sanitation by applying soap and water, alcohol-based hand cleaners, or chlorhexidine hand rubs. To avert the spread of *C. auris*, patients should be divided into separate rooms, and contact tracing should be done to identify any more potential exposures. Those who have been exposed should be screened for asymptomatic colonization.[28] Sodium hypochlorite and topical hydrogen peroxide-based treatments should be utilized for disinfecting sick patients' rooms and equipment, even if commercial cleaning solutions and white distilled vinegar have not been proven to be effective against *C. auris*.[28] According to Maslo and co-workers,[49] there is potential for new technologies like pulsed-xenon UV light to reduce *C. auris* contamination. However, more research is necessary to determine their effectiveness in hospital environments.[50]

Conclusion

Due to its antibiotic resistance, tenacity in medical settings, and quick continental spread, *Candida auris* represents a significant threat to worldwide health concerns. This disease has caused major outbreaks in healthcare facilities across the globe since it was first discovered in 2009. Its ability to avoid normal laboratory identification increases the hazard, and its resistance to certain antifungal medicines complicates treatment. Because *C. auris* can linger on skin and other surfaces and facilitate transmission both within and between hospitals, it is especially dangerous in healthcare settings. The simultaneous appearance of genetically diverse clades on several continents emphasizes the complexity of the disease's epidemiology and control difficulties. The following suggestions are offered on the basis of these findings:

a) To improve early detection and infection control, medical practitioners should be trained on the perils of *C. auris* transmission and its treatment.

b) In medical facilities, employ thorough and frequent environmental cleaning protocols.

c) Adherence to infection control procedures to the letter is crucial.

d) To prevent misidentification, advanced diagnostic tools ought to be available, particularly in environments with limited resources.

Contribution of authors

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Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Satoh K, Makimura K, Hasumi Y, et al. *Candida auris*-a novel *ascomycetous* yeast isolated from the external ear canal of an inpatient in a Japanese hospital. *Microbiol Immunol*. 2009;53(1):41–44.
2. Fungal priority pathogens list to guide research, development and public health action. *World Health Organization*. 2022.
3. Hinrichs C, Wiese-Posselt M, Graf B, et al. Successful control of *Candida auris* transmission in a German COVID-19 intensive care unit. *Mycoses*. 2022;65(6):643–649.
4. Chow NA, de Groot T, Badali H, et al. Potential fifth clade of *Candida auris*, Iran, 2018. *Emerg Infect Dis.* 2018;25(9):1780.
5. Jeffery–Smith A, Taori SK, Schelenz S, et al. *Candida auris*: a review of the literature. *Clin Microbiol Rev.* 2018;31(1):1110–1128.
6. Egger NB, Kainz K, Schulze A, et al. The rise of *Candida auris*: from unique traits to co–infection potential. *Microbial Cell*. 2022;9(8):141.
7. Sanyaolu A, Okorie C, Marinkovic A, et al. *Candida auris*: an overview of the emerging drug-resistant fungal infection. *Infect Chemother*. 2022;54(2):236.
8. Watkins RR, Gowen R, Lionakis MS, et al. Update on the pathogenesis, virulence, and treatment of *Candida auris*. *Pathogens and Immunity*. 2022:7(2):46.
9. Huang X, Hurabielle C, Drummond RA, et al. Murine model of colonization with fungal pathogen *Candida auris* to explore skin tropism, host risk factors and therapeutic strategies. *Cell Host Microbe.* 2021;29(2):210–221.
10. Alanio A, Snell HM, Cordier C, et al. First patient–to–patient intra hospital transmission of clade I *Candida auris* in France revealed after a two–month incubation period. *Microbiology Spectrum*. 2022;10(5):e01833–e01922.

11. Chowdhary A, Jain K, Chauhan N. *Candida auris* genetics and emergence. *Ann Rev Microbiol.* 2023;77:583–602.
12. Pallotta F, Viale P, Barchiesi F. *Candida auris*: the new fungal threat. *Le Infezioni in Medicina*. 2023;31(3):323.
13. Casadevall A, Kontoyiannis DP, Robert V, et al. On the emergence of *Candida auris*: climate change, azoles, swamps, and birds. *M Bio*. 2019;10(4):10–1128.
14. Cortegiani A, Misseri G, Giarratano A, et al. The global challenge of *Candida auris* in the intensive care unit. *Critical Care*. 2019;23:1–3.
15. Rhodes J, Fisher MC. Global epidemiology of emerging *Candida auris*. *Curr Opin Microbiol*. 2019;52:84–89.
16. Lee WG, Shin JH, Uh Y, et al. First three reported cases of nosocomial fungemia caused by *Candida auris*. *J Clin Microbiol.*2018;49(9):3139–3142.
17. Sekizuka T, Iguchi S, Umeyama T, et al. Clade II *Candida auris* possess genomic structural variations related to an ancestral strain. *PLoS One*. 2019;14(10):e0223433.
18. Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. *Clin Infect Dis*. 2017;64(2):134–140.
19. Cortegiani A, Misseri G, Fasciana T, et al. Epidemiology, clinical characteristics, resistance, and treatment of infections by *Candida auris*. *J Intensive Care.* 2018;6:1–13.
20. Calvo B, Melo AS, Perozo–Mena A, et al. First report of *Candida auris* in America: clinical and microbiological aspects of 18 episodes of candidemia. *J Infect*. 2016;73(4):369–374.
21. Calvo B, Melo AS, Perozo–Mena A, et al. First report of *Candida auris* in America: clinical and microbiological aspects of 18 episodes of candidemia. *J Infect*. 2016;73(4):369–374.
22. Govender NP, Magobo RE, Mpembe R, et al. *Candida auris* in South Africa, 2012–2016. *Emerg Infect Dis.* 2018;24(11):2036.
23. Okinda N, Kagotho E, Castanheira M, et al. Candidemia at a referral hospital in sub-Saharan Africa: emergence of *Candida auris* as a major pathogen. *Europe Congress of Clin Microbiol Infect Dis*. 2014:10–13.
24. Ahmad S, Alfouzan W. *Candida auris*: epidemiology, diagnosis, pathogenesis, antifungal susceptibility, and infection control measures to combat the spread of infections in healthcare facilities. *Microorganisms*. 2021;9(4):807.
25. Chow NA, Muñoz JF, Gade L, et al. Tracing the evolutionary history and global expansion of *Candida auris* using population genomic analyses. *mBio.* 2018;11:e03364–e03419.
26. Muñoz JF, Gade L, Chow N, et al. Genomic insights into multidrug-resistance, mating and virulence in *Candida auris* and related emerging species. *Nature Communications*. 2018;9(1):5346.
27. De Gaetano S, Midiri A, Mancuso G, et al. *Candida auris* outbreaks: current status and future perspectives. *Microorganisms.* 2024;12(5):927.
28. Caceres DH, Forsberg K, Welsh RM, et al. *Candida auris*: a review of recommendations for detection and control in healthcare settings. *J Fungi*. 2019;5(4):111.
29. Fernandes L, Ribeiro R, Henriques M, et al. *Candida auris*, singular emergent pathogenic yeast: its resistance and new therapeutic alternatives. *Europe J Microbiol Infect Dis.* 2022;41(12):1371–1385.
30. Forsberg K, Woodworth K, Walters M, et al. *Candida auris*: The recent emergence of a multidrug–resistant fungal pathogen. *Med Mycol*. 2019;57(1):1–12.
31. Cristina ML, Spagnolo AM, Sartini M, et al. An overview on *Candida auris* in healthcare settings. *J Fungi*. 2023;9(9):913.
32. CDC. Increasing threat of spread of antimicrobial-resistant fungus in healthcare facilities. 2023.
33. Pal M. Use of Pal's sunflower seed medium for an early diagnosis of cryptococcosis. *The Antiseptic*. 1997;95:175.
34. Pal M. Veterinary and medical mycology. *India Council Agri Res*. 2007.
35. Pal M. Candidiasis: an important opportunistic mycosis of global public health concern. *Res Infect Dis Trop Med*. 2020:2(1);49–51.
36. Pal M, Hofmeister M. Gutama KP, et al. Growing role of *Candida albicans* as an important cause of nosocomial infection. *J Adv Microbiol Res*. 2022;3(1):47–52.
37. Pal M. Cryptococcus neoformans and cryptococcosis. *J Bacteriol Mycol Open Access*. 2024:12(1):23–29.
38. Sears D, Schwartz BS. *Candida auris*: an emerging multidrug-resistant pathogen. *Intl J Infect Dis*. 2017;63:95–98.
39. Bassetti M, Vena A, Meroi M, et al. Factors associated with the development of septic shock in patients with candidemia: a post hoc analysis from two prospective cohorts. *Critical Care*. 2020;24:1–9.
40. Sikora A, Zahra F. Nosocomial infections. *StatPearls Publishing*. 2022:16.
41. Clinical alert to U.S. healthcare facilities–June 2016. *Candida auris*. Fungal diseases. CDC. 2019.
42. Hu S, Zhu F, Jiang W, et al. Retrospective analysis of the clinical characteristics of *Candida auris* infection worldwide from 2009 to 2020. *Front Microbiol*. 2021;12:658329.
43. Ademe M, Girma F. *Candida auris*: from multidrug resistance to pan-resistant strains. *Infect Drug Res.* 2020;1287–1294.
44. Arthisari NN, Budayanti, NN, et al. *Candida auris* as a pathogen that can cause emerging infectious disease: a literature review. *Intisari Sains Medis*. 20223;14(1):394–400.
45. Larkin E, Hager C, Chandra J, et al. The emerging pathogen *Candida auris*: growth phenotype, virulence factors, activity of antifungals, and effect of SCY–078, a novel glucan synthesis inhibitor, on growth morphology and biofilm formation. *Antimicrobial Agent Chemother*. 2017;61(5):1110–1128.
46. Shackleton J, Schelenz S, Rochon M, et al. The impact of environmental decontamination in a *Candida auris* outbreak. *J Hospital Infect*. 2016;94(Suppl 1):S24–S134.
47. CDC. *Candida auris*: a drug–resistant germ that spreads in healthcare facilities. 2020.
48. Schelenz S, Hagen F, Rhodes JL, et al. First hospital outbreak of the globally emerging Candida auris in a European hospital. *Antimicrobial Resist Infect Control*. 2016;5:1–7.
49. Maslo C, Plooy M, Coetzee J. The efficacy of pulsed-xenon ultraviolet light technology on *Candida auris*. *BMC Infect Dis*. 2019;19:1–3.
50. CDC. Recommendations for treatment of *Candida auris* infections. 2021.