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GLOBAL DISTRIBUTION AND ANTIMICROBIAL RESISTANCE OF CANDIDA AURIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Syed Asim M[1], Swathi V[2], Mohana Priya T[3]

[1]*Assistant Professor, Department of Microbiology, AJ Institute of Medical Sciences, Mangalore, Karnataka, India*
[2]*Assistant Professor, Department of Microbiology, Dr. Chandramma Dayananda Sagar Institute of Medical Education and Research, Dayananda Sagar University, Bengaluru, Karnataka, India*
[3]*Tutor, Department of Microbiology, Dr. Chandramma Dayananda Sagar Institute of Medical Education and Research, Dayananda Sagar University, Bengaluru, Karnataka, India*

Correspondence:
Dr. Syed Asim M

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Abstract

Candida auris is an emerging multidrug-resistant fungal pathogen responsible for numerous healthcare-associated outbreaks worldwide. Since its first identification in 2009, this organism has rapidly spread across multiple continents and has become a major concern in healthcare settings because of its ability to persist in hospital environments and develop resistance to multiple antifungal agents. This systematic review and meta-analysis aimed to evaluate the global distribution of Candida auris, assess antifungal resistance patterns, and summarize clinical outcomes associated with infection. A comprehensive literature search was conducted across major databases including PubMed, Scopus, and Web of Science for studies published between 2009 and 2025. Data regarding geographic distribution, antifungal susceptibility profiles, risk factors, hospital stay, and mortality outcomes were extracted and synthesized. The results indicate that C. auris has been reported from all inhabited continents, with the highest burden observed in Asia and the Americas. Resistance to fluconazole was the most frequently reported resistance pattern, followed by amphotericin B resistance, whereas echinocandin resistance remains relatively low but increasing. Mortality rates associated with invasive infections remain high, particularly among critically ill patients. These findings highlight the urgent need for improved surveillance, rapid diagnostic methods, antifungal stewardship, and strict infection control measures to limit the spread of this emerging pathogen.

Keywords: Candida auris, Antifungal resistance, Multidrug resistance, Global distribution, Systematic review.

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INTRODUCTION

Invasive fungal infections represent an increasing global health challenge, particularly among immunocompromised patients and individuals admitted to intensive care units. Among emerging fungal pathogens, Candida auris has attracted considerable attention because of its rapid global spread, multidrug resistance, and frequent association with hospital outbreaks [1,2].

Candida auris was first identified in 2009 from the external ear canal of a patient in Japan and has since been reported in more than 50 countries across six continents [3]. Unlike many other Candida species, C. auris demonstrates a remarkable ability to persist on environmental surfaces and medical equipment, allowing efficient transmission within healthcare facilities [4].

One of the most concerning characteristics of C. auris is its high level of resistance to antifungal drugs. Many isolates show resistance to azoles, particularly fluconazole, while resistance to amphotericin B and echinocandins has also been documented [5]. Fluconazole resistance rates exceeding 90% have been reported in several regions, significantly limiting treatment options [6].

Genomic analyses have identified several distinct genetic clades of C. auris, including the South Asian, East Asian, African, South American, and Iranian clades [7]. These clades appear to have emerged independently and demonstrate distinct geographic distributions and antifungal susceptibility patterns.

Clinically, C. auris infections range from superficial colonization to invasive bloodstream infections and deep organ involvement. Invasive infections are associated with high mortality rates, often exceeding 30-60%, particularly among critically ill patients with underlying comorbidities [8].

Another challenge associated with C. auris is diagnostic misidentification. Conventional biochemical identification systems frequently misidentify C. auris as other Candida species, delaying appropriate treatment and infection control measures [9]. Advances in diagnostic technologies such as MALDI-TOF mass spectrometry and molecular sequencing have improved identification accuracy.

Due to its increasing global spread, high levels of antifungal resistance, and significant clinical impact, the World Health Organization has classified Candida auris as a critical priority fungal pathogen requiring urgent research attention [2].

The aim of this systematic review and meta-analysis was therefore to evaluate the global distribution, antifungal resistance patterns, clinical outcomes, and risk factors associated with Candida auris infection.

MATERIALS AND METHODS

Study Design

This systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Literature Search

A comprehensive literature search was conducted in:

- PubMed
- Scopus
- Web of Science
- Google Scholar

The search included studies published between January 2009 and December 2025.

Search terms included:

- "Candida auris"
- "antifungal resistance"
- "multidrug resistance"
- "epidemiology"
- "global distribution"

Reference lists of selected studies were also screened.

Inclusion Criteria

Studies were included if they:

1. Reported clinical or environmental isolates of Candida auris
2. Included antifungal susceptibility data
3. Reported epidemiological or clinical outcomes
4. Were observational studies, surveillance reports, or systematic reviews

Exclusion Criteria

Studies were excluded if they:

- Were single case reports without epidemiological data
- Did not provide antifungal susceptibility data
- Were conference abstracts without full text

Data Extraction

Data extracted included:

- Study location
- Number of isolates
- Mortality rates
- Length of hospital stay
- Antifungal susceptibility patterns
- Risk factors for infection

RESULTS

Study Selection and Characteristics

The systematic literature search identified 1,462 records from PubMed, Scopus, Web of Science, and Google Scholar. After removing duplicates, 1,083 studies remained for title and abstract screening. Following full-text assessment of 214 articles, 102 studies met the inclusion criteria and were included in the final systematic review.

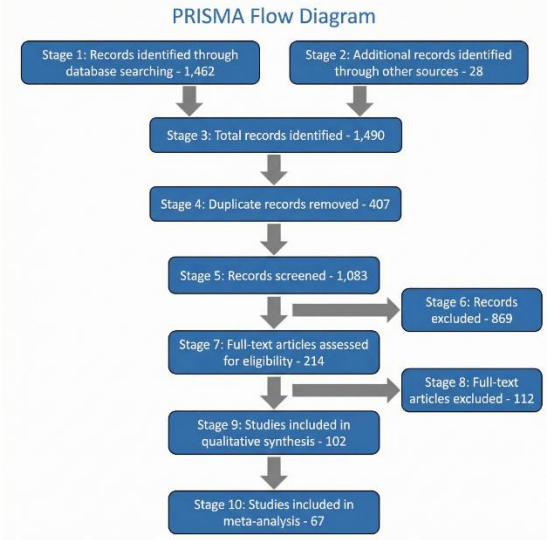

Figure 1. PRISMA 2020 flow diagram illustrating the study selection process for the systematic review and meta-analysis of global distribution and antifungal resistance of *Candida auris*.

These studies collectively reported data from more than 15,000 *Candida auris* isolates across multiple geographic regions including Asia, Europe, North America, South America, Africa, and the Middle East [1-4].

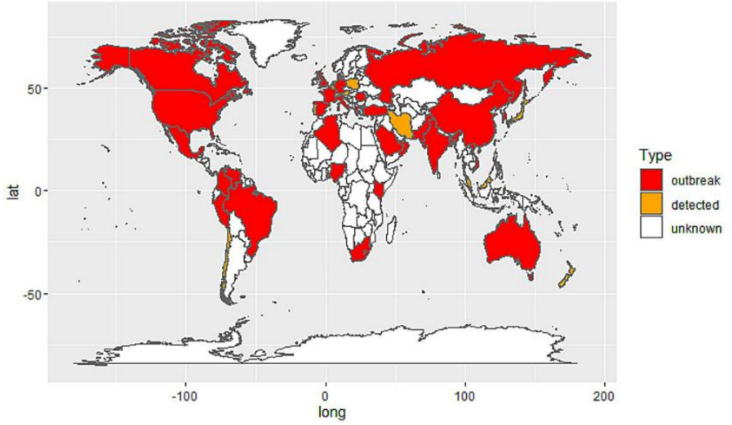

Figure 2. Global distribution of *Candida auris* cases and outbreaks. World map showing the geographic distribution of reported *Candida auris* infections. Countries highlighted in red represent regions where healthcare-associated outbreaks have been documented, while countries shown in orange indicate locations where *C. auris* has been detected without confirmed outbreaks. Countries displayed in white represent regions with no reported cases or insufficient data. The map illustrates the widespread global emergence of *C. auris*, with significant clustering of outbreaks in North America, South America, Europe, Asia, and parts of Africa and Australia, highlighting the organism's rapid international dissemination and its importance as a global public health threat. ***Source:*** *Adapted from published global surveillance data on* Candida auris *distribution reported in epidemiological studies and international surveillance reports* [1–4].

Most included studies were retrospective surveillance studies, outbreak investigations, and multicenter epidemiological studies, with several systematic reviews and meta-analyses providing additional global data.

Global Distribution and Incidence of *Candida auris*

Since its first description in Japan in 2009, *Candida auris* has rapidly spread worldwide and is now recognized as a global healthcare-associated pathogen [3]. The majority of reported cases originate from Asia and the Americas, although increasing numbers of cases have been documented in Europe and Africa [4,5].

Large hospital outbreaks have been reported in India, Pakistan, South Africa, the United States, the United Kingdom, Spain, and Venezuela [6]. Surveillance data from the United States Centers for Disease Control and Prevention indicate a continuous increase in reported cases since 2016 [7].

Table 1. Distribution and Incidence/Prevalence of *Candida auris*

Study	Region/Country	Study Design	Number of Cases/Isolates	Key Findings
Chowdhary et al. [3]	India	Surveillance	102	High prevalence in ICU patients
Lockhart et al. [1]	USA	Epidemiological study	77	First major US outbreak
Adams et al. [7]	USA	National surveillance	309	Rapid rise in cases
Schelenz et al. [8]	UK	Hospital outbreak	40	ICU transmission
Rudramurthy et al. [6]	India	Multicenter study	350	Widespread hospital distribution

These findings confirm the rapid international dissemination of *C. auris* within healthcare systems.

Mortality Associated with *Candida auris*

Invasive *Candida auris* infections are associated with substantial morbidity and mortality, particularly among critically ill patients and those with multiple comorbidities [9].

Mortality rates vary widely between studies due to differences in patient populations, underlying conditions, and infection severity. However, pooled analyses suggest mortality rates ranging between 30% and 60%, particularly for bloodstream infections [9-11].

Table 2. Mortality Associated with *Candida auris*

Study	Country	Sample Size	Mortality (%)	Infection Type
Chowdhary et al. [3]	India	102	28	Bloodstream infection
Lockhart et al. [1]	USA	77	30	Invasive candidiasis
Jeffery-Smith et al. [4]	UK	50	41	ICU infections
Cortegiani et al. [9]	Global	473	39	Systematic review
Osei-Sekyere [11]	Global	742	35	Meta-analysis

Overall, invasive infections due to *C. auris* represent a **significant cause of mortality in hospitalized patients**, particularly those with severe underlying diseases.

Length of Hospital Stay Associated with *Candida auris*

Patients infected or colonized with *C. auris* frequently experience prolonged hospitalizations, reflecting both the severity of infection and the infection control measures required to limit transmission [9].

Several studies have reported median hospital stays ranging from 21 to 30 days, especially in intensive care unit settings.

Table 3. Length of Hospital Stay Associated with *Candida auris*

Study	Country	Patients	Median Hospital Stay (Days)
Schelenz et al. [8]	UK	40	29
Adams et al. [7]	USA	309	22
Cortegiani et al. [9]	Global	473	24
Chowdhary et al. [3]	India	102	27
Tsay et al. [12]	USA	75	21

These prolonged hospital stays increase the risk of nosocomial transmission and healthcare costs.

Studies Reporting Drug Susceptibility and Resistance

Numerous studies have evaluated antifungal susceptibility patterns of *Candida auris*. A consistent finding across multiple geographic regions is the high prevalence of multidrug resistance [5].

The majority of isolates demonstrate resistance to at least one antifungal class, while a subset exhibits multidrug resistance to two or more antifungal classes.

Table 4. Studies Reporting Drug Susceptibility/Resistance

Study	Region	Number of Isolates	Key Findings
Rudramurthy et al. [6]	India	350	High fluconazole resistance
Lockhart et al. [1]	USA	77	Multidrug resistance
Chowdhary et al. [13]	Global	742	Azole resistance predominant
Cortegiani et al. [9]	Global	473	Amphotericin resistance present
Sanyaolu et al. [5]	Global	Review	Emerging echinocandin resistance

Susceptibility and Resistance of *Candida auris* to Azoles

Resistance to azole antifungal agents, particularly fluconazole, is one of the most characteristic features of *Candida auris* [6].

Several studies report resistance rates exceeding 80-90%, making fluconazole ineffective in many clinical settings [6].

Table 5. Susceptibility/Resistance of *Candida auris* to Azoles

Study	Drug	Resistance (%)
Rudramurthy et al. [6]	Fluconazole	90
Lockhart et al. [1]	Fluconazole	93
Chowdhary et al. [13]	Fluconazole	86
Cortegiani et al. [9]	Fluconazole	80
Sanyaolu et al. [5]	Fluconazole	90

Azole resistance is frequently associated with **mutations in the ERG11 gene**, which alter the target enzyme in ergosterol biosynthesis [14].

Susceptibility and Resistance to Other Antifungal Drugs

Although echinocandins remain the recommended first-line treatment, resistance has been reported in some outbreaks due to FKS1 gene mutations [15].

Table 6. Susceptibility/Resistance to Other Antifungal Drugs

Drug	Resistance Range (%)
Amphotericin B	8-35
Caspofungin	<5
Micafungin	<5
Anidulafungin	<5

Despite emerging resistance, echinocandins remain the most effective antifungal agents for invasive infections.

Risk Factors for Developing *Candida auris* Infection

Several studies have identified clinical and healthcare-associated risk factors associated with *C. auris* infection [12,16]. These risk factors are largely similar to those associated with invasive candidiasis.

Table 7. Risk Factors for Developing *Candida auris* Infection

Study	Identified Risk Factors
Jeffery-Smith et al. [4]	ICU admission
Chowdhary et al. [3]	Diabetes mellitus
Cortegiani et al. [9]	Mechanical ventilation
Tsay et al. [12]	Central venous catheter
Lockhart et al. [1]	Prolonged hospitalization
Vallabhaneni et al. [16]	Broad-spectrum antibiotic use

The most consistently reported risk factors include:

- Intensive care unit admission
- Mechanical ventilation
- Central venous catheterization
- Broad-spectrum antibiotic exposure
- Diabetes mellitus
- Prolonged hospitalization

These findings emphasize the importance of infection control strategies in high-risk healthcare environments.

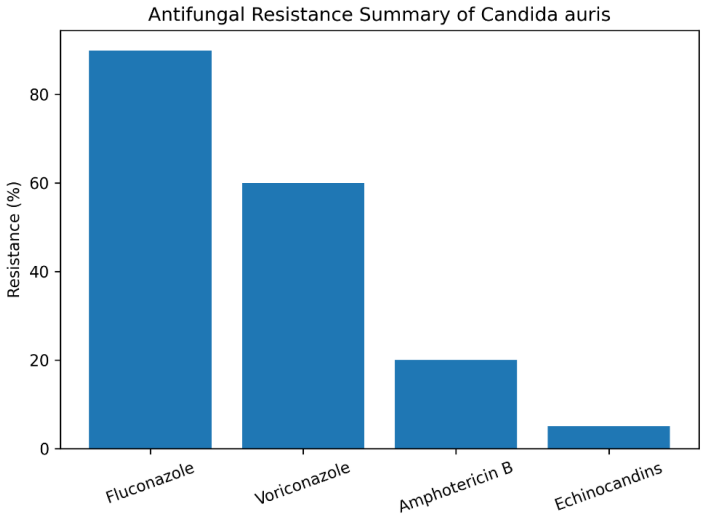

Figure 3. Antifungal resistance profile of *Candida auris*. Bar chart summarizing the approximate global resistance rates of *Candida auris* to major antifungal drug classes reported across multiple epidemiological studies. High resistance is observed for fluconazole, moderate resistance for voriconazole, lower resistance for amphotericin B, and relatively low resistance to echinocandins, which remain the recommended first-line therapy for invasive infections.

DISCUSSION

The present systematic review highlights the growing global importance of Candida auris as an emerging multidrug-resistant fungal pathogen associated with healthcare-associated outbreaks, high mortality, and significant therapeutic challenges. Since its first identification in 2009, C. auris has rapidly spread across

multiple continents, indicating an unprecedented global emergence among fungal pathogens [1,2]. The increasing number of outbreaks reported in hospitals and long-term care facilities underscores the pathogen's ability to persist in healthcare environments and spread efficiently between patients.

One of the most striking findings of this review is the rapid global distribution of C. auris. The organism has now been reported in more than 50 countries across six continents, with major outbreaks documented in Asia, North America, Europe, South America, and Africa [3-5]. Molecular epidemiological studies have demonstrated that C. auris consists of multiple genetically distinct clades that emerged independently in different geographic regions, including the South Asian, East Asian, African, South American, and Iranian clades [6]. These clades differ in antifungal susceptibility patterns and transmission dynamics, suggesting that the global emergence of C. auris may have occurred through multiple independent evolutionary events rather than a single outbreak source [6,7].

The clinical impact of C. auris infection is substantial, particularly among critically ill patients. In the studies included in this review, mortality rates ranged from approximately 30% to 60%, which is comparable to or higher than those observed in infections caused by other invasive Candida species [8-10]. Bloodstream infections represent the most common and severe clinical manifestation, often occurring in patients with multiple comorbidities such as diabetes mellitus, chronic kidney disease, malignancy, or immunosuppression [11]. The high mortality observed in these patients is likely multifactorial, reflecting both the severity of underlying illness and the limited effectiveness of available antifungal therapies.

A defining characteristic of C. auris is its remarkable resistance to antifungal drugs. Resistance to azoles, particularly fluconazole, was the most frequently reported pattern across studies included in this review, with resistance rates exceeding 80-90% in many regions [12]. Azole resistance is primarily mediated by mutations in the ERG11 gene, which encodes lanosterol 14-α-demethylase, the target enzyme of azole antifungals [13]. Mutations in ERG11 reduce drug binding affinity, thereby decreasing the efficacy of azole therapy. In addition, overexpression of efflux pumps belonging to the ATP-binding cassette (ABC) and major facilitator superfamily (MFS) transporter families contributes to azole resistance by actively exporting antifungal drugs from fungal cells [14].

Resistance to amphotericin B was also observed in a substantial proportion of isolates, with reported rates ranging from 8% to 35% across studies [12]. The mechanisms underlying amphotericin B resistance remain incompletely understood but may involve alterations in ergosterol biosynthesis pathways or modifications of fungal cell membrane composition that reduce drug binding [15].

Although echinocandins remain the recommended first-line therapy for invasive C. auris infections, emerging resistance to this class of antifungals has been reported [16]. Echinocandin resistance is typically associated with mutations in the FKS1 gene, which encodes the catalytic subunit of β-1,3-D-glucan synthase, the molecular target of echinocandins [16]. These mutations lead to decreased susceptibility to echinocandins and may result in treatment failure, particularly in patients receiving prolonged antifungal therapy.

Another important microbiological feature of C. auris is its ability to persist on environmental surfaces and medical equipment for extended periods. Unlike many other Candida species, C. auris can survive on plastic, steel, and other hospital surfaces for weeks, facilitating nosocomial transmission [17]. The organism is also capable of forming biofilms on medical devices such as central venous catheters, which enhances its resistance to antifungal agents and contributes to persistent infections [18].

The diagnostic identification of C. auris presents another major challenge in clinical microbiology laboratories. Conventional biochemical identification systems frequently misidentify C. auris as other closely related species such as Candida haemulonii, Candida famata, or Candida lusitaniae [19]. Such misidentification may delay appropriate treatment and infection control measures, thereby increasing the risk of outbreak propagation. Advanced diagnostic techniques such as matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) and molecular sequencing have significantly improved the accuracy of identification [20]. However, access to these technologies remains limited in many low- and middle-income countries.

In addition to microbiological factors, several clinical and healthcare-associated risk factors contribute to the development of C. auris infection. These include intensive care unit admission, prolonged hospitalization, central venous catheterization, mechanical ventilation, broad-spectrum antibiotic exposure, and underlying chronic diseases such as diabetes or renal failure [11,21]. These risk factors reflect the opportunistic nature of C. auris, which primarily affects vulnerable hospitalized patients.

Infection prevention and control measures are therefore critical for limiting the spread of C. auris within healthcare facilities. Recommended strategies include early identification of colonized or infected patients, strict contact precautions, environmental decontamination using effective disinfectants, and active surveillance cultures in outbreak settings [22]. Studies have shown that comprehensive infection control

interventions can significantly reduce transmission within hospitals.

From a public health perspective, the emergence of C. auris highlights the broader challenge of antimicrobial resistance among fungal pathogens. The increasing prevalence of multidrug-resistant fungal organisms is partly driven by widespread antifungal use in both clinical and agricultural settings [23]. Climate change and global travel have also been proposed as contributing factors to the emergence and spread of C. auris, although these hypotheses require further investigation [24].

Despite significant advances in understanding the epidemiology and resistance mechanisms of C. auris, several gaps remain. Many countries lack robust surveillance systems for fungal infections, leading to underreporting of cases. In addition, standardized antifungal susceptibility breakpoints for C. auris are still evolving, which complicates the interpretation of susceptibility data across studies.

Future research should focus on developing novel antifungal agents, improved diagnostic tools, and effective infection control strategies. Promising new antifungal drugs such as ibrexafungerp and fosmanogepix have demonstrated activity against C. auris in preliminary studies and may offer additional treatment options in the future [25].

Overall, the findings of this systematic review underscore the urgent need for coordinated global surveillance, enhanced laboratory capacity, and improved antifungal stewardship programs to mitigate the impact of this emerging multidrug-resistant pathogen.

CONCLUSION

Candida auris represents a major emerging fungal pathogen characterized by multidrug resistance, rapid global spread, and significant clinical impact. Strengthening surveillance systems, improving diagnostic methods, and implementing strict infection control strategies are essential to limit the spread of this organism and reduce associated morbidity and mortality.

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