

AN EMERGING MULTI-DRUG RESISTANT YEAST LIKE FUNGUS *CANDIDA AURIS* INFECTIONS IN ICUs

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The incidence of fungal infections in recent years is increasing rapidly and there is an emergence of newer fungal pathogens and anti-fungal drug resistance due to multiple predisposing reasons such as prolonged and indiscriminate use of antibiotic therapy, immunosuppressive corticosteroid therapy, aggressive use of anti-cancer drugs, bone marrow and organ transplantation procedures, and underlying conditions like immunodeficiency diseases (e.g. AIDS) and metabolic disorders such as diabetes mellitus.¹

A recent and most prominent clinical problem is the emergence of multi-drug resistant fungal pathogen *Candida auris* outbreaks of severe blood stream and invasive diseases world-wide, in hospitalized patients in Intensive Care Units (ICUs) associated with high mortality, posing a challenge in the management of patients admitted to ICUs. It does not respond to commonly used antifungal drugs, and associated with high level of anti-fungal drug resistance, making failure in treatment. About 90% of *Candida auris* strains are intrinsically resistant to fluconazole, and some strains of *Candida auris* are resistant to all the available major classes of antifungal drugs. This type of multi-drug resistance has not been seen before in other species of *Candida*.²

Candida auris was first isolated in 2009, as an infectious agent from a 70-year-old woman's external ear discharge at Tokyo Metropolitan Geriatric Hospital in Japan, identified as yeast-like fungus and placed in the genus *Candida* due to similar biological features and named *Candida auris* (*auris* means "ear" in Latin).³ Subsequently, it was recovered from 15 ear discharge samples from five South Korean hospitals and identified as a causative agent of otitis media.⁴ Later it was isolated from the blood of three South Korean patients with septicemia in 2011.⁵ Around the same time, 15 isolates of *Candida auris* were recovered from 15 patients in a tertiary care hospital in Northern India. Further reports have been published regularly from hospitals in India, Middle East, South Africa, South America, North America and Europe. In a relatively short period of less than 10 years, *Candida auris* was able to spread all over the world, mainly in hospitals. *Candida auris* is the first fungus to behave like an epidemic nosocomial bacterial pathogen. No one has an idea where it's coming from, and never heard of it. It's just spread like wildfire, and emerged as an important nosocomial pathogen with clonal transmission within and between the hospitals and nursing homes.⁶

At present, *Candida auris* is separated into four geographic clades: South Asian, South African, South American, and East Asian clades, and according to DNA analysis research, this divergence in evolution took place 4,000 years ago. These strains are quite similar to one another within each region, but different across regions, suggesting that *Candida auris* has emerged independently, and almost at the same time in different regions.⁵ This relatively old species causing a new invasive disease among hospitalized patients world-wide is incompletely understood. It may probably relate to changes in the natural environmental niche of the organism, changes in health care environments, changing antifungal prophylaxis and treatment, or changing approaches to diagnosis and to the identification of species.^{3,6}

In 2016, CDC sounded the alarm in the USA about *Candida auris*, and this is the first emerging fungal pathogen categorized as a serious global public health threat by CDC for three main reasons:⁷

1. It is resistant to multiple anti-fungal drugs commonly used to treat *Candida* infections. Some strains are resistant to all anti-fungal drugs.
2. It is difficult to identify with standard laboratory methods; and its misidentification leads to inappropriate patient management.
3. Since it causes nosocomial outbreaks, it is very important to quickly identify *Candida auris*, so that hospitals can take special precautions to prevent its spread.

The clinical spectrum associated with *Candida auris* ranges from colonization to invasive diseases. It causes bloodstream, wound, and ear infections. The fungus can spread throughout the body from blood stream, causing serious invasive infections with a high death rate (about 57%).⁶ *Candida* species cause oral or esophageal diseases more frequently, whereas *Candida auris* is not frequently reported at these sites. A study on activity of a salivary cationic peptide, histatin 5, against *Candida auris* revealed that majority of isolates were highly sensitive, particularly those exhibiting antifungal resistance.⁸ Clinical symptoms of *Candida auris* infection include fever and chills while on antibiotic therapy; sepsis, coma, organ failure (due to spread of infection to multiple organs), no patient improvement with conventional antifungal

DOI: <http://doi.org/10.3126/jucms.v8i02.34096>

drug therapy, and may be fatal.²

The major risk factors for nosocomial acquisition of *Candida auris* infection are hospitalization in ICUs, underlying respiratory disease, surgical procedures including vascular surgery, mechanical ventilation, vascular catheterization, gastrostomy tube placement and antifungal drug therapy. Neutropenia, a common risk factor for invasive candidiasis caused by other *Candida* spp. has not been seen with *Candida auris* infection, which suggests that the host neutrophil response may not be adequate for control of *Candida auris* infections. Infections have been found in patients of all ages, from preterm infants to the elderly. Healthy people usually don't get infected, but they should clean their hands with soap and water or hand sanitizer when they come in contact with a patient who has the disease or with surfaces or equipment in the hospital.⁹

Unlike other *Candida* species, *Candida auris* has emerged as a nosocomial threat, and primarily detected in patients with a long period of hospitalization in ICUs, and impaired immune systems exhibiting rapid person-to-person transmission and causing serious invasive disease. *Candida auris* has the ability to colonize the skin of patients, and contaminate hospital environments and persist on the surfaces of hospital rooms and on medical devices, and spread rapidly among patients and staff (Nurses and doctors). Some people may be carriers of this fungus for many months. The fungus was isolated from patient's mattresses, windowsills, chairs, and countertops. In areas where *Candida auris* first emerged, now it accounts for nearly 20% of *Candida* blood stream isolates, surpassing that of *Candida albicans*, which is the most common species. In some hospitals in Asia, *Candida auris* is the second most common isolated species from blood cultures.⁶

Many diagnostic laboratories and institutions do not identify *Candida* to the species level. The emergence of *Candida auris* as a nosocomial pathogen stresses the need for the identification of *Candida* to the species level and its public health relevance. The main difficulty faced by many researchers are the misidentification of *Candida auris* by conventional methods in clinical laboratories. *Candida auris* is usually misidentified as *Candida haemulonii*, *C. famata*, *C. guilliermondii*, and *C. sake* by commercially available biochemical tests.³ Some commonly used disinfectants such as quaternary ammonium compounds and other cationic surface active agents are ineffective against *Candida auris*. Chlorine disinfectants, and hydrogen peroxide can kill *Candida auris*.^{3,10} Echinocandins are the first-line therapy used for *Candida auris* infections, however the drug of choice will depend on the drug susceptibility report of the isolate. Some clinicians prefer multi-antifungal drug therapy to treat *Candida auris* infections.¹¹

It is believed that *Candida auris* multi-drug resistant strains may continue to emerge independently and simultaneously throughout the world in forthcoming years, and become a major concern for healthcare and scientific community. Hence there is a need to alert hospitals to be on the lookout for *Candida auris* infections in their patients, particularly in ICUs. High level of knowledge and alertness by physicians and healthcare workers, especially in ICUs, would help to prevent the spread of *Candida auris* infections.

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