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Act Now: The Global Threat of *Candida Auris* and the Urgent Need for Effective Countermeasures

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Since its discovery in 2009, the multidrug-resistant yeast *Candida auris* has been causing invasive infections with high co-morbidities and mortality rates.¹ Alarmingly, this pathogen can be found in clinical environments such as air and bedding, and remains present even in patients undergoing antifungal treatment. Its close phylogenetic relationship to other multidrug-resistant organisms contributes to its inherent resistance to various antifungal drugs. Amidst the COVID-19 pandemic, hospitals have experienced major outbreaks of multidrug-resistant organisms, including *C. auris*, though its infection prevalence has not increased.²

Cases of *Candida auris* have been reported across the globe, with the exception of Antarctica. The majority of cases have been isolated in India (n ≥ 243), the United States (n ≥ 232), and the United Kingdom (n ≥ 103), according to Seykere et al.'s review, which covers data up until 2017. Interestingly, more isolates were found in men (64.76 %) than women (35.24 %).

Risk factors have remained consistent worldwide, with colonized or infected patients typically presenting with catheters, arterial lines, or having undergone surgery. Comorbidities such as diabetes, hypertension, renal failure, transplants, and other causes of immunosuppression or malignancy also contribute to a significant 29.75 % crude mortality rate.³ As data from 2019 to 2023 continues to emerge, it is pertinent to monitor news articles and research for the latest information on this global health concern.

The history of *Candida auris* traces back to potentially misidentified cases in South Korea as early as 1996, where it was mistaken for *C.*

haemulonii.⁴ The first confirmed case was reported in 2009 by Satoh et al., involving a 70-year-old female Japanese patient.⁵ Interestingly, no further cases have been reported in South Korea since 2013.

India experienced the largest recorded number of *C. auris* candidemia cases until 2015, with the first cases reported in 2013. These cases were clonally different from those in Japan and South Korea, suggesting an independent emergence.⁶ However, the strains found in India were similar to those in Pakistan, the UK, and the USA, raising concerns due to the high mortality rates and resistance.⁷ The first European cases emerged in the UK in 2013, involving three unrelated patients at distant locations, followed by a significant outbreak among 50 patients at a London cardiothoracic center.⁸ The isolates belonged to two different phenotypes with varying virulence. The earliest incidence in continental Europe occurred in Spain in 2017, where two of the four colonized patients succumbed to the infection.⁹

In South America, the first cases of *Candida auris* emerged in Colombia and Venezuela, affecting patients with similar risk factors as previously mentioned. In 2017, 17 patients were identified across six different hospitals in Colombia. Unfortunately, misidentification and delayed diagnosis led to a 35.2 % mortality rate.¹⁰ A subsequent outbreak in Venezuela resulted in *C. auris* becoming the sixth most common cause of fungemia, with isolates closely related to those from Illinois, USA, raising concerns about cross-contamination between hospitals.¹¹ However, Lockhart et al. demonstrated that the strains in Venezuela emerged independently.⁷

North America experienced the second-highest number of *C. auris* cases, as reported by the CDC,

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with incidents occurring across nine states since 2013. The first case was identified in New York,¹² and most isolates within the same states were closely related. It is believed that these cases were acquired abroad as patients returned from the Middle East or other regions.¹³ Isolates from New York and New Jersey shared similarities with those from the Middle East and South Asia, as also noted in Illinois and South America by Lockhart et al. In Canada, only a single isolate was identified in a patient initially admitted to a hospital in India, with no further reports.¹⁴ A study conducted across 22 hospitals estimated 15 cases per 100,000 patients.¹⁵

Between 2019 and 2021, the CDC reported a substantial increase in *C. auris* cases across the United States, rising from 44 % to 95 %, with 17 states encountering their first cases during this period.¹⁶ In

2022, the CDC estimated 2377 *C. auris* infections compared to 1471 in 2021, a number that may grow more rapidly as post-pandemic PPE restrictions continue to be lifted.¹⁷ Four primary clades of the organism have been identified worldwide, with specific geographical regions predominantly having certain clades or subclades. However, this pattern is evolving, particularly in Canada, Kenya, and the United States, where a mix of clades is now seen, possibly due to global travel.¹⁸

In the absence of a definitive management protocol and the presence of multi-drug resistances, researchers have been examining pharmacokinetic and pharmacodynamic data to determine optimal dosages based on similar species.^{19,20} Several new antifungals are being developed, while step-down therapy, early administration of echinocandins, and

Preventive Model for Combating *Candida Auris*

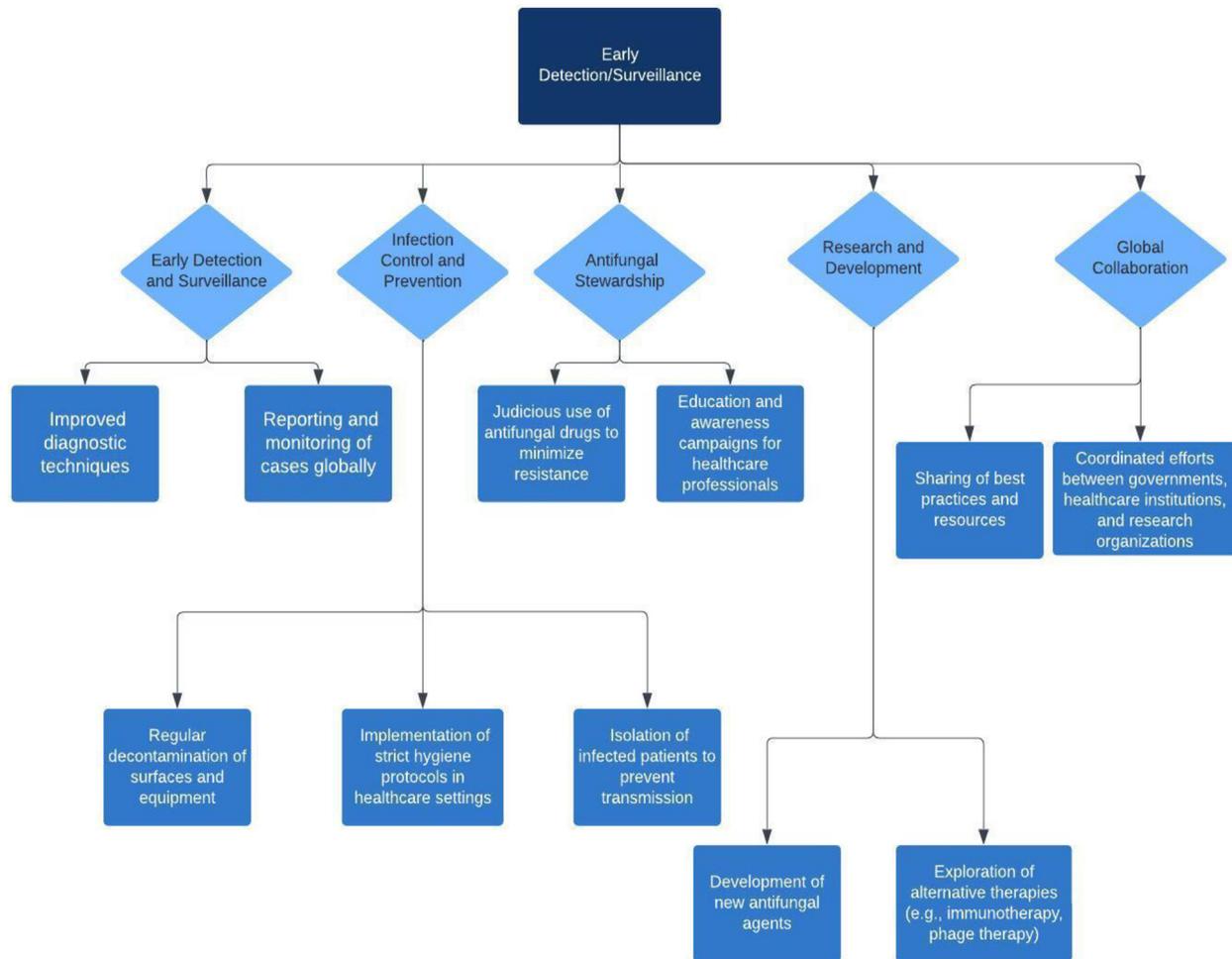


Fig. 1. Preventive model for combating *Candida auris*.

other methods are utilized for patient management.²¹ Yet, challenges such as misidentification, cross-transmission, and inadequate treatment options continue to exacerbate the situation. The high virulence and crude mortality rates, ranging from 33 to 72 %, could further worsen the current post-COVID-19 pandemic landscape,²² raising concerns about the world's readiness to confront another infectious disease crisis.

In order to effectively manage *C. aureus* infections in the face of these challenges, a combination of preventative measures and targeted treatment is required. Prevention is better than cure, and prevention is essential, as it is easier to avoid infections than to treat them once they occur. This can be achieved through basic practices, such as hand hygiene, limiting or avoiding contact with infected individuals. For the infected individuals, antifungals are the mainstay of treatment. However, the overuse has led to the development of antifungal-resistant strains of *C. aureus*, which are not only difficult to treat but are also fatal. To address this issue, healthcare providers must follow strict infection control protocols, appropriate use of medications and isolation of infected patients to prevent the spread (Fig. 1).

In addition to above practices; research into development of new antifungal drugs and innovative diagnostic techniques are also the dire need of time. Furthermore, it is imperative that a coordinated global effort is implemented to monitor and prevent its spread. This calls for heightened surveillance and vigilance, as well as increased collaboration and swift action among healthcare providers, researchers, and stakeholders, similar to the global response to the COVID-19 pandemic.

In conclusion, *C. aureus* is an emerging fungal pathogen that can cause a range of infections, from mild infections to life-threatening. The emergence of this antifungal-resistant strain of *Candida* highlights the need for improved infection control measures and new treatment options. As researchers continue to study this pathogen and its mechanisms of virulence, it is imperative that new insights and approaches should be developed to combat and reduce the burden of disease associated with this pathogen. Researchers, medical fraternity, and stakeholders should not delay in implementing the strategies, the need for finding better diagnostic techniques, and new antifungal drugs given the potential consequences of another infectious disease crisis. As the world has not yet fully recovered from the impact of one pandemic, action needs to be taken now to prevent another in the form of *C. aureus*.

Conflict of interest

The authors declare they have no conflict of interest.

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