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Popular Article

Candida auris: yet another global threat post COVID-19

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Introduction

While *Candida auris* was first reported from a patient with external ear infection in 2009 in Japan, the fungus soon emerged as a multi-drug resistant nuisance pathogen after the advent of COVID-19 [1]. However, the initially reported cases originated primarily as ear infections, sooner the symptoms progressed to those evident in invasive blood infections. The fatal outcomes led to the declaration of *C. auris* as a clinical alert in health care facilities in the year 2016 by the U.S Centers for Disease Control and Prevention (CDC) [2]. However, the fungus garnered the maximum attention of clinicians and health authority in the advent of COVID-19, with *C. auris* being announced as the first fungus among urgent antimicrobial resistance threats by the CDC. The genus *Candida* comprises of approximately 200 species and therefore is the largest of all medically important yeast [3]. They are generally commensals of the host mucosal membranes, while *C. auris* colonizes gastrointestinal tract apart from the mucosal membranes, making its person-to person transmission easier [1]. Additionally, it possesses the potential to infect the vital internal organs *viz.,* respiratory tract, muscles and even central nervous system via entry into the systemic circulation causing candidemia, which is associated with 30-70% case fatality rate (CFR) [4].

Epidemiology

The geographical distinction of *C. auris* isolates enables their grouping into four major clades, with the isolates in the same clade sharing a genetic similarity however, those belonging to

different clades differing by tens or thousands of single nucleotide polymorphism (SNP) [5]. The four geographical clades are namely, clade I (South Asia), clade II (East Asia), clade III (South Africa), and clade IV (South America) [6], and a probable fifth clade originating from Iran [4]. While, initially isolates were restricted to certain geographical boundaries; around fifty countries including India have reported the infections so far [7].

Reservoirs and transmission

Although the epidemiological research promulgates the fact that *C. auris* isolates were mostly found in hospitalized patients on anti-fungal therapy which implies that the infections were a result of failure of anti-fungal treatment and thereby development of resistant isolates.

However, current reports suggest that the initial origin of the isolate is yet to be elucidated, while speculations also suggest the role of global warming in its species selection [8]. The probable transmission so far suggested involves warm blooded animals *viz.,* birds which could facilitate spread of fungus in urban settings, which would eventually infect humans [9].

Pathogenicity

The pathogenicity of *Candida* species is attributed to number of virulence factors *viz.,* proteases and lipases, mannosyl transferases, oligopeptide, siderophore-based iron transporters, and biofilm formation [10]. These virulence factors are responsible for pathogen invasion and colonization and acquisition of nutrition [4]. The pathogenic potential of the organism makes it a global cause of concern accounting for nosocomial outbreaks primarily in patients admitted in intensive care units (ICUs). While the most common risk factors for the fungal infections are diabetes mellitus (DM), senility, neutropenia, prolonged ICU stays, cardiovascular diseases, pulmonary diseases, kidney diseases (KD), medical implants such as catheters and endotracheal tubes, extended usage of broad-spectrum antibiotics and anti-fungals and immunosuppressive drugs. Furthermore the exact mechanism of how *C. auris* invades the epithelial layer without hyphae formation is still not well understood. The recent findings also suggest that evasion of immune system could be due to non-aggregative phenotypes of the fungus.

Afflictions and survival instincts

Apart from the plethora of virulence factors that *C. auris* possesses, certain characteristic features like high heat (37 – 42°C) and salt endurance augments its survival in extremes of environmental conditions. These features thus facilitate its colonization in environment and human reservoirs, which further aid in disease transmission. Apart from the clinical specimens, the fungus

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has also been previously isolated from sterile non-biological samples *viz.,* urine thus illustrating its presence in sterilized hospital settings as well.

Drug resistance

The specialty of C. auris to transform into a persistent yeast capable of withstanding extremely harsh physical and chemical conditions helps it to resist the three major anti-fungal drugs *i.e.,* azoles, echinocandins and polyenes making drug resistance as one of the major problems linked with this fungus [11]. The magnitude of multi-drug resistance could be estimated with the fact that while ≥40.0% of *C. auris* have been resistant to at least two anti-fungal classes and approximately 4.0% displayed resistance to all three classes of drugs [11]. The genetic factors such as polyploidy, aneuploidy, and chromosome rearrangements, ability to form biofilm, alteration or overexpression of the drug target and efflux/decreased uptake of the drug are an important factor promoting MDR. However, the environmental factors like climate change and agriculture aid the process of drug resistance.

Hurdles in diagnosis

The exact diagnosis of *C. auris* is complicated due to the underestimation of spread of the fungus, mis-identification with other *Candida spp.* (*i.e.*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida haemulonii*, *Candida lusitaniae*, and *Candida famata*) [12] and inadequacy in knowledge about the mechanism of virulence and drug resistance. However, the fungus can be cultured from the blood, other body fluids and secretions from the infected sites [13]. The fungus can be initially isolated in blood culture bottles after 33.9 hrs of incubation and further sub-cultured on Sabouraud dextrose agar (SDA) or CHROMagar supplemented with Pal's agar, where it forms white-cream-colored smooth colonies following 24–48 hours of incubation at 37–42°C. However, the traditional methods of yeast identification like VITEK 2 YST (bioMérieux), API 20C (bioMérieux, Hazelwood, MO, USA), API ID 32 C (bioMérieux, Marcy-l'Étoile, France), BD Phoenix (BD Diagnostic Systems, Sparks, MD, USA) yeast identification system, and MicroScan have been erroneous in accurate identification of the strains belonging to *C. auris.* Furthermore due to the inadequacy of conventional laboratory methods in the identification of *C. auris,* currently sophisticated and advanced techniques like Matrix-Assisted Laser Desorption Ionization Time of Flight (MALDI-TOF) and sequencing D1–D2 region of the 28S ribosomal DNA are being employed for the accurate identification of the fungus [13, 14]. The difficulty in misidentification of the strains

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leads to delay in diagnosis, implementation of treatment and control strategies and consequent increased spread of the fungus in clinical settings [15].

Infection control strategy

The understanding of the spread of *C. auris* in healthcare settings is essential for design and implementation of infection control and transmission strategy against the fungus. Since the infection is majorly of nosocomial origin, the healthcare personnel and hospital equipment play a key role in the chain of transmission. Adequate hand hygiene and sanitation *viz.,* usage of alcohol-based hand-cleaners and chlorhexidine hand rubs should be practiced [16]. Proper quarantine of the patients in separate rooms should be practiced and their contacts should be traced back to identify the source and probable exposed population. Further screening of the exposed asymptomatic individuals should be practiced to break the chain of transmission [16]. The premises and contaminated equipments can be effectively cleaned using sodium hypochlorite and topical hydrogen peroxide-based products.

Conclusion

The incidence of death due to candidemia in COVID-19 has elucidated the pathogenic potential of *C. auris,* particularly for the elderly and immune-compromised individuals. The multi-drug resistance alongwith the diverse virulence factors and inadequacy in early diagnosis further exaggerates the problems of the clinicians in saving the lives of patients. Alike COVID-19, the world has witnessed the importance of following hand hygiene and control protocols to prevent such lethal infections. Further surveillance based research is therefore advised to determine the exact magnitude of the infections.

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