ABCS HEALTH SCIENCES

LETTER TO THE EDITOR

Antifungal resistance in opportunistic candidiasis: challenges and risks to global public health

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Fungal infections (FIs) represent an escalating challenge to public health, affecting millions of people globally each year. Estimates up to 2017 suggested that more than 150 million people had serious fungal diseases and these infections resulted in approximately 1.5 million deaths annually[1]. However, according to Denning et al.[2], the global burden and the morbidity and mortality associated with fungal diseases are significantly greater than previously estimated. Thus, current figures on invasive fungal infections indicate an annual incidence of 6.5 million, leading to 3.75 million deaths per year related to these infections - almost twice the earlier estimates[2]. These figures are likely underestimated due to insufficient robustness and the lack of standardisation in global reporting systems[3].

In Brazil, the largest country in Latin America, there is a lack of recent and robust epidemiological data on fungal infections, particularly those caused by *Candida*. Currently, it is estimated that the incidence of candidemia in Brazilian public hospitals could reach 2.49 cases per 1,000 hospital admissions. This rate is 2 to 15 times higher than those reported in the United States and European countries[4]. Systemic mycoses are not included in the national list of mandatory reporting diseases in Brazil and are not part of routine epidemiological surveillance. This absence of monitoring prevents the collection of accurate data on the occurrence and magnitude of these infections at the national level, hindering the development of appropriate public health policies[3].

The intercontinental spread of human pathogenic fungi, such as *Candida auris*, has been alarming; with reports of its rapid spread over the course of just one decade[5]. This dissemination is influenced by factors such as climate change and the intensive use of antimicrobials across various sectors. The rise in global temperatures may favor the adaptation of fungi to the human body, while the use of antifungals in medicine, agriculture, and industries contributes to the selection of resistant organisms. Due to the extraordinary fungal diversity and the factors driving the emergence of new species, it is impossible to predict which pathogens may emerge in the future. Therefore, it is crucial to monitor the emergence of new fungal species, and the increase in cases, as well as to control their spread, all of which represent critical challenges for global health[1,4].

Among the species responsible for invasive fungal infections, *Candida* spp. are the leading cause of nosocomial infections. Candidiasis, frequently affects individuals with compromised immune systems. These infections can range from superficial forms, such

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as oral and cutaneous candidiasis, to more severe forms, including candidemia, in which the fungus enters the bloodstream and spreads throughout the body, resulting in systemic and disseminated infections. *Candida* species are believed to cause approximately 134 million mucosal infections, as well as up to 1.6 million invasive and hematogenous infections globally with a mortality[1,3] rate of 63.6%.

The World Health Organization (WHO) recognizes the growing threat of fungal infections caused by *Candida* species. Among the fungal pathogens of priority, *C. krusei* is of medium, *C. albicans* and *C. auris* are of critical and *C. glabrata, C. tropicalis*, and *C. parapsilosis* are of high priority, respectively. These species are particularly concerning due to their increasing resistance to conventional antifungals and their significant impact on public health, posing major challenges in controlling these infections in hospital settings[5].

The rise of antifungal resistance presents a growing challenge, particularly in invasive infections caused by *Candida* spp. that are associated with high mortality rates. Despite the severity of these infections, the development of new antifungals has been inadequate, limiting the available therapeutic options and compromising treatment effectiveness. In Brazil, this issue is further exacerbated by the absence of targeted strategies for managing invasive fungal infections, although therapeutic guidelines do exist in the context of sexually transmitted infections. These recommendations, however, primarily focus on superficial manifestations, such as vulvovaginal and oropharyngeal candidiasis, leaving gaps in the approach to systemic forms, which present higher clinical risks and demand more complex interventions[3-5].

Another critical aspect concerns epidemiological surveillance, which is limited, hindering the monitoring of fungal resistance and the early identification of outbreaks, key elements for containing the spread of these pathogens. The absence of a robust reporting system compromises the acquisition of accurate epidemiological data, which is essential for guiding evidence-based intervention strategies. In light of this scenario, a coordinated and multidisciplinary response is crucial, involving the development of new antifungals, the enhancement of diagnostic methods, and the strengthening of epidemiological surveillance. Only through the implementation of effective public health policies and continuous investment in research will it be possible to mitigate the clinical, social, and economic impacts of invasive fungal infections, ensuring a more efficient global response to the growing threat of antifungal resistance[3,4].

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