Editorial

Candida glabrata candidemia

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In this issue, the article "*Candida glabrata* candidemia: An emerging threat in critically ill patients" demands discussion on this topic as *C. glabrata* candidemia is difficult to manage and the patients have high mortality. Clinicians, epidemiologists, microbiologists, and basic scientists across the world are working on the epidemiology, pathogenesis, virulence factors, genetics, and drug resistance of *C. glabrata* to understand the natural course of the disease caused by the fungus and to develop ideal management protocol.

In contrast to other pathogenic species of *Candida, C. glabrata* is haploid, without the capability of producing hyphae, very small in size (1–4 μm), deficient in secretory proteases for virulence, with less opportunity for genetic selection.[1] However, the fungus can colonize easily oral mucosa and vaginal tract of human. It can successfully adapt to metabolic changes, oxidative stress, and nonenzymatic defense system of the host. The scientists have sequenced the whole genome of the fungus and identified many important genetic components for its survival, but many areas of host-pathogen interaction still remain mysterious.

For many years, *C. glabrata* is considered a relatively nonpathogenic commensal of human. However, with the widespread use of immunosuppressives and broad-spectrum antimicrobial agents, the frequency of *C. glabrata* candidemia has increased significantly. In contrast to the aggressive strategy to subvert host defense of *C. albicans*, *C. glabrata* seems to have stealth, evasion and persistence in its macrophage strategy to overcome host response.[2]

Over last the two decades, four nonalbicans *Candida* species (*C. glabrata, C. parapsilosis, C. tropicalis, C. krusei*) have emerged as important agents causing candidemia. *C. glabrata* candidemia has been reported at a high number in northern Europe and USA, *C. parapsilosis* in Spain and Brazil, *C. tropicalis* in Asian countries.[3] In the present study, the authors reported *C. glabrata* as the third most common species (18.1%) isolated from candidemia cases and *C. tropicalis* (33.3%) as the most common agent. Similarly in a recent prospective systematic epidemiological study in Intensive Care Unit (ICU) – acquired candidemia at 27 centers of India, *C. tropicalis* was the most common species (41.6%) isolated and *C. glabrata* was fourth common species (7.1%) in adult patients.[4] Though *C. tropicalis* candidemia poses a formidable challenge in India, *C. glabrata* candidemia also demands great care due to its high mortality (53.8% at 30 days in the present study) and relatively higher resistance to azoles especially fluconazole. Resistance to fluconazole is both intrinsic and acquired. Acquired resistance results from mutations that are selected by drug pressure.[1] Emergence of *C. glabrata* in the western countries is linked to drug pressure due to frequent use of fluconazole.

In the present study,[5] authors indicated broad-spectrum antibiotics, central venous catheter, mechanical ventilation, diabetes, elderly patients (>65 years) as risk factors for *C. glabrata* candidemia, though they did not perform any case–control analysis. Rather in a case–control study, prolonged hospitalization, prior antibiotic use, use of fluconazole and older age group were identified as specific risk factors for *C. glabrata* candidemia.[1] The authors in the present study claimed

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urinary tract as the most common (23%) source of their *C. glabrata* candidemia though they did not perform any typing of their isolates to support their claim. In general, *C. glabrata* is transmitted nosocomially in immunocompromised debilitated patients through the hands of healthcare workers.[1] The agent may also be acquired from colonized mucosa after chemotherapy.

The diagnosis of *C. glabrata* may be delayed due to slow growth of the isolate compared to other *Candida* species. The species can easily be suspected on Chrom agar by its characteristic growth.

Due to the decreased susceptibility of *C. glabrata* to fluconazole and cross-resistance to other azoles, echinocandins are recommended for therapy in patients with *C. glabrata* candidemia.[6] The recent emergence of echinocandins resistance in *C. glabrata* isolates especially among the fluconazole-resistant isolates is a matter of concern. Moreover, the acquired echinocandin resistance in *C. glabrata* isolates does not necessarily affect its fitness. In two large surveillance programs, the SENTRY Antimicrobial Surveillance Program (2006–2010) and Centers for Disease Control and Prevention population-based surveillance (2008–2010), 162 (9.7%) *C. glabrata* isolates were resistant to fluconazole, of which 98.8% isolates were nonsusceptible to voriconazole and 8–9.3% isolates were resistant to echinocandins.[7] In selected institutions, echinocandins resistance rate has exceeded 10%.[8] The situation in India is not clear, as there are few studies in this area. The present study did not evaluate the susceptibility of *C. glabrata* isolates. In the multicentric ICU required candidemia study, *C. glabrata* isolates were 1.5%, 0%, 6.2%, 23.1%, 6.2% resistant to fluconazole, voriconazole, anidulafungin caspofungin and micafungin, respectively.[3] The observation is a matter of interest, as Indian patients are more exposed to azoles rather than echinocandin, and the susceptibility results are in contrary. Instead of complacency on this result, we require close monitoring on the susceptibility of *C. glabrata* isolates. Moreover, the *in vitro* susceptibility study correlates well with *in vivo* outcome, particularly among patients previously exposed to echinocandins.[9]

In conclusion, it is desired that epidemiology of *C. glabrata* candidemia should be elucidated in India. Laboratory should attempt to identify *Candida* species isolated from deep-seated infection. A close monitoring and evaluation of *in vitro* susceptibility testing data of *C. glabrata* isolates are required regularly.

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