Editorial on Fungal isolates

With advances in medical sciences and an increase in survival of patients in immunocompromised states, the incidence of mycotic infections has risen dramatically with a substantially broad range of fungi causing potentially lethal diseases. The diagnosis of fungal infections has also become challenging with a growing interest in medically significant fungi. Fungal infections historically have been under-recognised and difficult to detect and treatment options are limited.[1]

INVASIVE FUNGAL INFECTIONS

The frequency of invasive mycoses has increased significantly over the past two decades and is associated with excessive morbidity and mortality. It is directly related to the increasing number of patients who are at risk for development of serious fungal infections like transplant recipients and patients with AIDS and neoplasms.[2] In systemic fungal infections, the outcome of the disease depends more on the host factors rather than the fungal virulence.

Among the fungi that have potential to cause invasive fungal infections include yeasts (Candida spp., Cryptococcus spp.) and moulds (Aspergillus spp., Fusarium spp., *Scedosporium prolificans*, Mucor, Rhizopus and Rhizomucor).[3]

Candida albicans is the most commonly recovered yeast from clinical material and generally is responsible for 50-70% of episodes of candidaemia and 90-100% of mucosal infections. *C. glabrata* has emerged as an important and potentially resistant opportunistic fungal pathogen.[4] *C. parapsilosis* is the second most common species of candida recovered from blood cultures. It tends to form extensive biofilms on the surface and lumens of catheters and other implanted devices. Biofilm-forming organisms have been shown to be completely resistant to antifungal agents.[5]

Aspergillus species are the most commonly isolated invasive moulds. They can cause invasive aspergillosis, tracheobronchitis, aspergilloma and chronic necrotising aspergillosis, but colonisation without infection can also occur. Majority of infections are caused by Aspergillus *fumigatus and A. terreus*.[6] Fusariosis has been recognised with increasing frequency among immunocompromised patients, especially patients with haematologic malignancies and recipients of allogeneic haematopoietic stem cell transplants. The most common species isolated from clinical specimens include *Fusarium moniliforme, Fusarium solani* and *Fusarium oxysporum*.[7]

Of the class Zygomycetes, *Rhizopus oryzae* (*arrhizus*) is the most common cause of zygomycosis; however, additional species of Rhizopus, Rhizomucor, Absidia and Cunninghamella are known to cause invasive disease in hospitalised individuals.[4]

S. apiospermum cause serious disseminated and localised infection in immunocompromised patients. Within the genus Scedosporium, *S. apiospermum* (*teleomorph Pseudallescheria boydii*) and *S. prolificans* represent two important antifungal-resistant opportunistic pathogens. Such distinction is clinically important because *S. apiospermum* is resistant to Amphotericin B but is susceptible to Voriconazole and Posaconazole.[3]

FUNGAL MENINGITIS

Generally fungal meningitis tends to occur more commonly in the immunocompromised and cryptococcus is the most common aetiological agent. An estimated one million cases of cryptococcal meningitis occur every year with more than six lakh deaths.[8] In contrast to *C. neoformans*, *C. gatti* infections occur in immunocompetent individuals as well. Respiratory syndrome with or without neurologic findings is most often the presentation in *C. gattii*-infected persons. It is hence important to consider the probability of *C. gatti* also and perform a negative staining on all cerebrospinal fluid samples (centrifuged), irrespective of immunological status.

Treatment for cryptococcosis in immunocompromised include induction therapy with Amphotericin B deoxycholate (0.7 mg/kg daily intravenously [IV]) plus Flucytosine (100 mg/kg daily in four divided doses orally) for a minimum of 2 weeks, followed by consolidation therapy with Fluconazole at a dose of 400 mg orally once daily for a minimum of 8 weeks with a continued maintenance phase for a minimum of 1-year with 200 mg Fluconazole daily.[9]

Access this article online

Quick Response Code:

Website: www.jacmjournal.org

DOI: 10.4103/0972-1282.158805

Among patients with baseline renal insufficiency or those who are at risk for renal insufficiency, liposomal preparations of Amphotericin B are preferred. Echinocandin antifungals do not have significant activity against *C. neoformans* and should not be used to treat this infection.[10]

Other causes of fungal meningitis include candida which often occurs in IV drug abusers, prolonged IV therapy, post-traumatic conditions and as part of disseminated candidiasis. *Sporothrix schenckii* has been reported in association with post-traumatic inoculation. Other rare causes of fungal meningitis confined to certain geographic areas are histoplasma, coccidioides and blastomyces.[11]

FUNGAL INFECTIONS OF URINARY TRACT

Fungus in urine may represent contamination, colonisation of the catheter or infection.[12] Risk factors for fungal urinary tract infection (UTI) include indwelling urinary catheters, treatment with broad-spectrum antibiotics, diabetes mellitus and chronic renal failure. Majority of fungal UTIs are caused by *C. albicans*. However, non-albicans candida and non-candida yeasts are increasing as the aetiological cause. Invasive fungi like *Cryptococcus neoformans*, Aspergillus spp., Mucoraceae spp., *Histoplasma capsulatum*, Blastomyces spp., *Coccidioides immitis* may infect the kidneys as part of systemic or disseminated mycotic infection.

On extrapolation of the CDC definitions used for bacteriuria and bacterial UTI to funguria and fungal UTI, funguria is defined as $>10^2$ cfu fungi/ml in a properly collected urine sample and the patient is asymptomatic. A fungal UTI is defined as $>10^2$ cfu fungi/ml in two properly collected non-voided urine samples or 10^5 cfu fungi/ml in a properly collected voided urine sample, and the patient presents with clinical signs and symptoms.

Candiduria represents a spectrum of the disease varying from asymptomatic candiduria to clinical sepsis. In many instances, it represents colonisation or contamination of the specimen and not invasive candidiasis. Antifungal therapy is not always necessary in confirmed candida UTI as the outcome is generally benign.

Early diagnosis and antifungal susceptibility testing are crucial in the management of fungal infections as fungi like *A. terreus*, *C. krusei* are inherently resistant to certain antifungals. Voriconazole is the first line drug of choice for aspergillosis. Posaconazole has been found to be effective in the treatment of refractory zygomycosis and fluconazole-resistant candida spp. Echinocandins generally have broad spectrum against all candida species and have relatively low toxicity. However, invasive fungal infections usually require combination antifungal therapy.[11]

Mortality with invasive fungal infections is high. Furthermore, some fungal infections tend to be more common or evident in certain geographical areas. An attempt was made to compile data of fungal isolates obtained from various hospitals in India and in this issue of JACM, we are presenting data on fungal isolates sent from 11 different centres. Though from different parts of the country the basic isolates remain the same with a difference only in the rare isolates.

Shabina M. Balakrishnan, Kalpana George

Department of Microbiology, Government Medical College Kozhikode, Kozhikode, Kerala, India

Address for correspondence: Dr. Shabina M. Balakrishnan, E-mail: shabina_mb@rediffmail.com

REFERENCES

1. Brandt ME, Park BJ. Think fungus — Prevention and control of fungal infections. Emerg Infect Dis 2013;19:1688-9.
2. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: Analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004;39:309-17.
3. Ramana KV, Kandi S, PVB, Sharada CV, Rao R, Mani R, *et al.* Invasive fungal infections: A comprehensive review. Am J Infect Dis Microbiol 2013;1:64-9.
4. Pfaller MA, Pappas PG, Wingard JR. Invasive fungal pathogens: Current epidemiological trends. Clin Infect Dis 2006;43 (Suppl 1):S3-14.
5. Kuhn DM, Mikherjee PK, Clark TA, Pujol C, Chandra J, Hajjeh RA, *et al. Candida parapsilosis* characterization in an outbreak setting. Emerg Infect Dis 2004;10:1074-81.
6. Enoch DA, Ludlam HA, Brown NM. Invasive fungal infections: A review of epidemiology and management options. J Med Microbiol 2006;55:809-18.
7. Nucci M, Marr KA, Queiroz-Telles F, Martins CA, Trabasso P, Costa S, *et al. Fusarium* infection in hematopoietic stem cell transplant recipients. Clin Infect Dis 2004;38:1237-42.
8. Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. AIDS 2009;23:525-30.
9. Cox GM, Perfect JR. Treatment of *Cryptococcus* neoformans meningoencephalitis in HIV-infected patients. In: Bartlett JG, editor. UpTo Date; 2015. Available from: http://www.uptodate.com. [Last accessed on 2015 Jun 04].
10. Spanakis EK, Aperis G, Mylonakis E. New agents for the treatment of fungal infections: Clinical efficacy and gaps in coverage. Clin Infect Dis 2006;43:1060-8.
11. Koroshetz WJ, Nath A. Chronic and recurrent meningitis. In: Kasper DL, Hauser SL, Jameson JL, *et al.*, editors. Harrison's Principles of Internal Medicine. New York: McGraw Hill; 2015.
12. Fisher JF, Newman CL, Sobel JD. Yeast in the urine: Solutions for a budding problem. Clin Infect Dis 1995;20:183-9.

How to cite this article: Balakrishnan SM, George K. Editorial on Fungal isolates. J Acad Clin Microbiol 2015;17:34-5.

Source of Support: Nil. **Conflict of Interest:** None declared.