Mini Review
Open Access
CrossMark

Antifungal Susceptibility Testing and the Ticking Clock

Abstract

With rising incidences of fungal infections leading to Invasive Fungal Infections (IFIs), Antifungal Susceptibility Testing (AFST) has become the need of the hour and its availability at all the tertiary care settings is a prerequisite for better diagnostics and thus, improved therapeutic management. Multiple factors are into play rendering this rising incidence, and thus, the potential antifungal resistance in those fungi is imminent. To let it off, cautious and timely measure of availing AFST and identification of fungi to species level has become mandatory and needs to be addressed. Antimicrobial Stewardship may play a major role in this transition.

Keywords: antifungal susceptibility testing, antimicrobial stewardship, *Candida auris*, invasive fungal infections

Volume 11 Issue 1 - 2023

Saraswat S,[1] Sarswat S[2]
[1]Senior Resident, Department of Microbiology, Sarojini Naidu Medical College and Hospital, India
[2]Public Health Specialist, Office of Chief Medical and Health Officer (CMHO), Department of Health, Govt. of Madhya Pradesh, Gwalior, Madhya Pradesh, India

Correspondence: Saraswat S, Senior Resident, Department of Microbiology, Sarojini Naidu Medical College and Hospital, Agra, Uttar Pradesh, India, Tel +91-8755218766, Email satt90@gmail.com

Received: January 23, 2023 | **Published:** February 01, 2023

Abbreviations: AFST, Antifungal Susceptibility Testing; IFI, Invasive Fungal Infections; HICC, Hospital Infection Control Committee; AMS, Antimicrobial Stewardship; PCR, Polymerase Chain Reaction; RCA, Rolling Circle Amplification; NASBA, Nucleic Acid Sequence Based Amplification; LAMP, Loop Mediated Isothermal Amplification

Introduction

With the betterment of healthcare facilities and upliftment of treatment modalities, the mortality rate is reducing across the globe.[1] However, even with this facilitation, the diseased state is sustaining, and the morbidity rate is rising.[2] The improved healthcare including the rapid diagnostic modalities, early initiation of specific treatment and better follow-up along with availability of updated healthcare facilities at the periphery, play a crucial role.

With numerous fungi discovered every year, list of fungi of human importance is expanding.[3] Immense tendency of humans to explore the undisturbed nature in the extensive depths is playing a controversial role, which not only provides an insight into the world of fungi, rather also exposes us to the newly discovered representatives of the Mycology world.[4,5]

The infective bacterial isolates found in the clinical specimens are gaining resistance even to higher antimicrobials.[6] The next in series are the fungi isolated from such clinical specimens.[7] Emergence of *Candida auris* in Japan in 2009 has clearly indicated one such directive with its resistance to most of the routinely used antifungals.[8] With the overt empirical use of antifungals (especially, since the rise in prevalence of Post-COVID Mucormycosis), increased lifespan due to better healthcare services, declining mortality, rising morbidity, increased use of steroids, and rise in the prevalence of organ transplants, the need of the hour is availability of Antifungal Susceptibility Testing (AFST) at all the tertiary care settings, which is a prerequisite for better diagnostics and thus, improved therapeutic management.[9–11] AFST and identification of fungi, including yeasts, needs to become a routine to avoid the situation we are facing with the bacterial isolates, which have so far developed resistance to all the first line and most of the second line antimicrobials.[12] Also, the alternative antimicrobials and the drugs in the pipeline are also quite restricted, and anticipate restricted hopes.[13]

What next?

Extensive resistance in Bacterial isolates warrants cautious action while considering and treating invasive fungal infections (IFIs). With unrestricted availability of over-the-counter oral antifungal agents without prescription, the threat of emergence of resistance against the antifungals in the fungal pathogens is imminent.[14] Not only the topical Azoles, better antifungals like Amphotericin-B and Echinocandins are easily available without a prescription. Not only does it require the dire need to regulate the dispensing of over-the-counter antifungals, but also restricting their use as per the guidelines based on the AFST, strictly. Hospital Infection Control Committee (HICC) and Antimicrobial Stewardship (AMS) need to play the central role in this transition. Monitoring, internal hospital audits, antimicrobial policy, infection control practices, and repeated trainings to the healthcare personnel is the tool to implement and advocate the correct use of antimicrobials and minimize / restrict the development of resistance in the fungi.

Besides, good laboratory practices, following-up of guidelines, sticking to the structured workflow in the laboratory, repeated trainings, specific precautions and cautious handling of the fungal agents in the laboratory constitute the key to restrict and contain the occupational exposure and spread of fungal infections in the laboratory.[15]

With the recent updates in the diagnostics and clinical mycology, newer techniques including Polymerase Chain Reaction (PCR), Rolling Circle Amplification (RCA), Nucleic Acid Sequence Based Amplification (NASBA), Loop Mediated Isothermal Amplification (LAMP) and more, the fact that their availability even at tertiary care centres is limited in most of the developing nations, establishes a constraint of utility of these advanced techniques.[16–20]

Several studies have indicated the emergence of different fungi in the clinical specimens across the geographical landmarks, the laboratory facilities for specific diagnostics of such fungi is still being neglected.[21–25] Medical colleges and Research centres also have limited availability of such resources, which are considered as the referral centres by most of the peripheral healthcare units, unofficially.[26]

What role, whose responsibility?

Even within the medley of Government healthcare administrations, the roles and responsibilities are well-defined, although the desire to act, and firstly to request to obtain healthcare resources from the Healthcare Incharge is a subject usually avoided by authorities. Mycology and Microbiology units need to furnish the requirements at their respective facilities and request their superiors for the supply of the same. Next is the responsibility of the Administrative High Officials to consider such requests not only because it is their duty, but also because they need to address such requirements and facilitate the healthcare facilities for provision of best healthcare services to their general public. With no accusations against any government policy, introspection and vigilance to engage in upgrading the mycology diagnostics should be an Administrative priority.

Conclusion

All through the revolution in the Medical world which is currently at play, AFST appears to be the line of action to help prevent the development of resistance against the routinely used antifungals in the commonly isolated fungi responsible for IFIs. The current status of antimicrobial resistance among the bacterial isolates clearly indicates the cautious preparation required against these emerging fungi. AFST should be implemented and must become a routine at all the tertiary care centres for proper addressal and therapeutic management of IFIs. Without such an upgrade in the healthcare setup, the mismanagement of fungal infections and development of Antifungal resistance is imminent. The resistance observed in fungi like *Candida auris* is definitely going to be horrific if it develops in other moulds and yeasts, or if the rather resistant fungi unleashes onto the human race.

Acknowledgments

None.

Conflicts of interest

The authors have no conflict of interest.

References

1. Owusu PA, Sarkodie SA, Pedersen PA. Relationship between mortality and health care expenditure: Sustainable assessment of health care system. *PLoS One*. 2021;16(2):e0247413.
2. Soman CR, Damodaran M, Rajasree S, et al. High Morbidity and Low Mortality-the Experience of Urban Preschool Children in Kerala. *J Tropical Pediatrics*. 1991;37(1):17–24.
3. Cheek M, Nic Lughadha E, Kirk P, et al. New scientific discoveries: Plants and fungi. *Plants People Planet*. 2020;2:371–388.
4. Milfont TL, Richter I, Sibley CG, et al. Environmental consequences of the desire to dominate and be superior. *Pers Soc Psychol Bull*. 2013;39(9):1127–1138.
5. Hall RA, Noverr MC. Fungal Interactions with the Human Host: Exploring the Spectrum of Symbiosis. *Curr Opin Microbiol*. 2017;40:58–64.
6. Tarín-Pelló A, Suay-García B, Pérez-Gracia MT. Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal. *Expert Rev Anti Infect Ther*. 2022;20(8):1095–1108.
7. National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Foodborne, Waterborne, and Environmental Diseases (DFWED). *Centers for Disease Control and Prevention*. 2022.
8. Frías-De-León MG, Hernández-Castro R, Vite-Garín T, et al. Antifungal Resistance in *Candida auris*: Molecular Determinants. *Antibiotics (Basel)*. 2020;9(9):568.
9. Richter SS, Galask RP, Messer SA, et al. Antifungal susceptibilities of Candida species causing vulvovaginitis and epidemiology of recurrent cases. *J Clin Microbiol*. 2005;43(5):2155–2162.
10. Knutsson KA, Iovieno A, Matuska S, et al. Topical Corticosteroids and Fungal Keratitis: A Review of the Literature and Case Series. *J Clin Med*. 2021;10(6):1178.
11. Mishkin A. Emerging fungal pathogens in solid organ transplantation. *Curr Opin Organ Transplant*. 2021;26(4):440–444.
12. Singh DP, Verma RK, Sarswat S, et al. Non-Candida albicans Candida species: virulence factors and species identification in India. *Curr Med Mycol*. 2021;7(2):8–13.
13. Hoenigl M, Sprute R, Egger M, et al. The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim, Opelconazole, and Rezafungin. *Drugs*. 2021;81(15):1703–1729.
14. Wiederhold NP. Antifungal resistance: current trends and future strategies to combat. *Infect Drug Resist*. 2017;10:249–259.
15. Kobayashi GS. *Disease Mechanisms of Fungi*. In: Baron S, Medical Microbiology. 4th Ed. Ch 74. 1996.
16. Aslam S, Tahir A, Aslam MF, et al. Recent advances in molecular techniques for the identification of phytopathogenic fungi- a mini review. *J Plant Interactions*. 2007;12(1):493–504.
17. Schwartz S, Kontoyiannis DP, Harrison T, et al. Advances in the diagnosis and treatment of fungal infections of the CNS. *Lancet Neurol*. 2018;17(4):362–372.
18. Hariharan G, Prasannath K. Recent Advances in Molecular Diagnostics of Fungal Plant Pathogens: A Mini Review. *Front Cell Infect Microbiol*. 2021;10:600234.
19. Mendonça A, Santos H, Franco-Duarte R, et al. Fungal infections diagnosis- Past, present and future. *Res Microbiol*. 2022;173(3):103915.
20. White LP, Price JS. Recent Advances and Novel Approaches in Laboratory-Based Diagnostic Mycology. *J Fungi (Basel)*. 2021;7(1):41.
21. Friedman DZP, Schwartz IS. Emerging Fungal Infections: New Patients, New Patterns, and New Pathogens. *J Fungi (Basel)*. 2019;5(3):67.
22. Siscar-Lewin S, Hube B, Brunke S. Emergence and evolution of virulence in human pathogenic fungi. *Trends Microbiol*. 2022;30(7):693–704.
23. Köhler JR, Casadevall A, Perfect J. The spectrum of fungi that infects humans. *Cold Spring Harbor Perspect Med*. 2014;5(1): a019273.
24. Hawksworth DL, Lücking R. Fungal Diversity Revisited: 2.2 to 3.8 Million Species. *Microbiol Spectr*. 2017;5(4).
25. Fisher MC, Gurr SJ, Cuomo CA, et al. Threats Posed by the Fungal Kingdom to Humans, Wildlife, and Agriculture. *mBio*. 2020;11(3):e00449–e00520.
26. Haydour Q, Hage CA, Carmona EM, et al. Diagnosis of Fungal Infections. A Systematic Review and Meta-Analysis Supporting American Thoracic Society Practice Guideline. *Ann Am Thorac Soc*. 2019;16(9):1179–1188.