Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Microbiology Research

Journal homepage: https://www.ijmronline.org/

Original Research Article

Species distribution and antifungal susceptibility of *Candida* isolates from cases of health-care associated infections

Kamaljeet[1],*, Naveen Saxena[1], Mohit Thalquotra[2]

[1]*Government Medical College, Kota, Rajasthan, India*
[2]*Government Medical College, Rajouri, Jammu and Kashmir, India*

ARTICLE INFO

Article history:
Received 21-05-2022
Accepted 10-06-2022
Available online 08-07-2022

Keywords:
Health-care associated infections (HCAI)
Invasive fungal infections (IFI)
Broth microdilution (BMD)
Bloodstream infections (BSI)
Catheter associated urinary tract infection (CA-UTI)
Catheter related blood stream infection (CR-BSI)

ABSTRACT

Purpose: Fungi have emerged as an important cause of health-care associated infections (HCAI) in last few decades. *Candida* spp. is the most common cause of invasive fungal infections (IFI) in hospitalized individuals. The present study was conducted in a tertiary care teaching hospital with an aim to study species distribution and antifungal susceptibility pattern of *Candida* isolates from cases of HCAI.

Materials and Methods: *Candida* isolates from cases of HCAI from medical intensive care unit were identified up to species level. Antifungal susceptibility testing of *Candida* isolate was done by Clinical and Laboratory Standard Institute (CLSI) broth microdilution (BMD) method.

Results: The rate of CA-UTI due *Candida* spp. was 0.3 per 1000 catheter associated days. The rate of catheter related *Candida* BSI was 0.9 per 1000 catheter associated days. Predominance of non *albicans Candida* spp. over *C. albicans* was noted. Fluconazole resistance was significantly high in NAC spp. compared to *C. albicans*.

1. Introduction

Fungi have emerged as an important cause of health-care associated infections (HCAI) in last few decades.[1] Factors responsible for the dramatic rise of HCAI mycotic infections include aging populations, advancement in medical technologies, malignancies, intensive myeloablative and antibiotic therapies, ICU stay and solid organ and hematopoietic stem cell transplantation.[1]

Mycotic HCAI are mostly attributed to *Candida* spp, *Aspergillus* spp, *Fusarium* spp. and *Scedosporium* spp.[2] *Candida* spp. is the most common cause of invasive fungal infections (IFI) in hospitalized individuals.[3] As per National Nosocomial Infection Survey (NNIS), *Candida* spp. is the fourth most common cause of health-care associated bloodstream infections.[1]

In an ICU setting, *Candida* spp. accounts for nearly 10% of all bloodstream infections (BSI) and 25% of all urinary tract infections (UTIs).[4] In the United States, *Candida* spp. is 3rd or 4th common cause of HCAI, surpassing all Gram-negative bacilli.[5] Nosocomial *Candida* infections are usually treatment resistant and are associated with prolonged hospitalization and increased healthcare-cost.[4]

In recent years, many research studies on *Candida* infections, have documented a progressive shift from *C. albicans* to treatment resistant non *albicans Candida* (NAC) spp.[6] As compared to western countries, there is dearth of information regarding health-care associated *Candida* infection from India. There fore the present study was conducted in a tertiary care teaching hospital with an aim to study species distribution and antifungal susceptibility pattern of *Candida* isolates from cases of HCAI.

* *Corresponding author*.
E-mail address: kamal0985@gmail.com (Kamaljeet).

https://doi.org/10.18231/j.ijmr.2022.017

2. Material and Methods

2.1. Study setting

The present study is a part of a Ph.D. thesis carried out in the Department of Microbiology, at Maharao Bhimsingh Hospital, Nayapura, which is affiliated with Government Medical College, Kota, Rajasthan.

2.2. Study duration

Research work was completed between January 2020 to December 2020.

2.3. Study design and duration

Descriptive cross-sectional study was conducted for a period of one year. *Candida* isolates from cases of HCAI from medical intensive care unit (MICU) were included. The demographical and clinical features of the patients suspected for HCAI were recorded and analyzed. The protocol of the study was approved by Institutional Ethics Committee.

2.4. Species identification and antifungal susceptibility testing

Candida isolates were identified upto species by standard mycological protocol including germ tube test, carbohydrate assimilation test, colony color on HiChrom *Candida* agar and HiCandida identification Kit. HiChrom *Candida* agar and HiCandida identification Kit were procured from Himedia Laboratories Pvt Ltd Mumbai.

Antifungal susceptibility testing of *Candida* isolate was done by Clinical and Laboratory Standard Institute (CLSI) broth microdilution (BMD) method. It testing was performed exactly as outlined in document M27-A3.[7] The minimum inhibitory concentration (MIC) of *Candida* spp was detected for antifungal drugs like amphotericin B, fluconazole, itraconazole and voriconazole. The antifungal drugs were procured from Himedia Laboratories Pvt Ltd Mumbai as a pure standard compound.

MIC values were determined as the lowest concentration of antifungal drug that showed complete inhibition (amphotericin B) or a significant diminution (≥50% inhibition; azoles) of growth compared to the growth of control strain. *C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019 were used as control strains.

3. Results

During the study period, a total of 14883 patients were admitted to MICU. Out of these 11197 (75.2%) were having various indwelling medical devices for more than 48 hrs. Urinary catheter was present in 10631 (94.9%) patients. A total of 1384 (12.4%) patients were having central lines whereas 902 (8.1%) patients were on ventilatory support. The month and invasive device wise distribution of patients is shown in Figure 1.

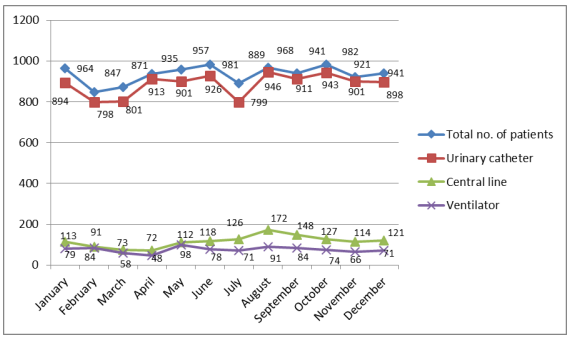

Fig. 1: Month and invasive device wise distribution of patients

Out of 894 patients with indwelling urinary catheter, a total of 61 developed catheter associated urinary tract infection (CA-UTI) (Table 1). The rate of CA-UTI was 1.3 per 1000 catheter days. Bacterial pathogens were isolated from 45(73.8%) cases whereas *Candida* was isolated from 16 (26.2%) patients of CA-UTI. The rate of CA-UTI due *Candida* spp. was 0.3 per 1000 catheter associated days. *C. albicans* were isolated from 5 cases whereas 11 isolates belonged non *albicans Candida* spp. (NAC). *C. tropicalis* was the predominant isolate from NAC spp (Table 2).

A total of 12 (0.9%) patients out of 1384 patients on central line developed catheter related blood stream infection (CR-BSI). The rate of CR-BSI was 2.3 per 1000 catheter associated days (Table 1). Bacterial pathogens were isolated from 7 (58.4%) cases whereas *Candida* spp. were isolated from 5 (41.6%) patients. The rate of catheter related *Candida* BSI was 0.9 per 1000 catheter associated days. *C. albicans* was isolated from 2 (40%) cases whereas *C. tropicalis* was isolated from 3 (60%) cases of CR-BSI (Table 2).

Ventilator associated pneumonia (VAP) was developed in a total of 9 (0.9%) patients out of 902 on mechanical ventilator support (Table 1). The rate of VAP was 2.3 per 1000 ventilator associated days. All cases of VAP were due to bacterial pathogens (Table 2). In the present study predominance of NAC spp. over *C. albicans* was noted.

The antifungal susceptibility profile of *Candida* spp. isolated from HCAI like CAUTI and CR-BSI is shown in Table 3. Fluconazole resistance was significantly high in NAC spp. compared to *C. albicans* (Chi-square test, *P* value 0.0001).

All *C. krusei* isolates were resistant to fluconazole. A total of 20% of *C. tropicalis* were resistant to fluconazole. Resistance to itraconazole, voriconazole and amphotericin B was not observed in *C. albicans*. Amphotericin B resistance was observed in 20% of *C. tropicalis*.

Table 1: Rate of health-care associated infections

Type of HCAI	Total patients of medical device	Total device days	No. of patients developing infection (%)	Rate of infection per 1000 device associated days
CA-UTI	10631	48632	61	1.3
CR-BSI	1384	5241	12	2.3
VAP	902	3871	09	0.9

Table 2: Pathogens isolated from health-care associated infection

Pathogens	CAUTI	CR-BSI	VAP	Total
Bacteria				
E. coli	23	02	02	27
Klebsiella pneumoniae	18	03	05	26
Staphylococcus aureus	01	-	-	01
Pseudomonas aeruginosa	03	02	02	07
Candida spp.				
C. albicans	05	02	-	07
C. tropicalis	07	03	-	10
C. krusei	04	-	-	04

Table 3: Antifungal susceptibility profile of *Candida* spp.

Candida spp (N)	Antifungal agent	Range (μg/ml)	S (%)	SDD (%)	R (%)
C. albicans (07)	FLZ	0.125-256	05 (71.4)	01 (14.3)	01 (14.3)
	ITZ	0.03-16	07 (100)	-	-
	VCZ	0.008-16	07 (100)	-	-
	AMB	0.12-8	07 (100)	-	-
C. tropicalis (10)	FLZ	0.125-128	08 (80)	-	02 (20)
	ITZ	0.015-16	09 (90)	-	01 (10)
	VCZ	0.008-16	09 (90)	-	01 (10)
	AMB	0.12-4	08 (80)	-	02 (20)
C. krusei (04)	FLZ	4-64	-	-	04 (100)
	ITZ	0.125-2	03 (75)	-	01 (25)
	VCZ	0.015-5	04 (100)	-	-
	AMB	0.25-2	04 (100)	-	-

4. Discussion

In an any health-care setup, infections are the most common adverse iatrogenic event affecting the safety of the patient. As per definition, healthcare associated infections (HCAI) are infections that are acquired by the patient during the process of receiving health care. These infections are neither present nor incubating at the time of admission to the health-care setup.[4] According to the World Health Organisation (WHO), at an any given point of time, more than 1.4 million people worldwide suffer from HCAI and incidence of HCAI is anywhere between 10 to 30%.

Admission to ICU is considered as an important risk factor for acquisition of HCAI. HCAI can lead to complications in 25-50% of patients admitted to ICU.[4] In general, ICUs have been described as a factory for creating and disseminating HCAI due to their extremely vulnerable population of seriously ill patients, heavy use of medical devices and invasive procedures, and the frequent usage of broad-spectrum antimicrobials. Indwelling medical devices are cornerstone in management of patients admitted to ICUs.[8] In the present study, out a total of 14883 patients admitted to MICU, a total of 11197 (75.2%) were having one or more indwelling medical devices for more than 48 hrs.

In recent years, the upsurge in HCAI, specifically medical device associated infections due to Candida spp., is noted. In the present study, a total of 16 Candida spp., were isolated from cases of CA-UTI. The rate of CA-UTI due Candida spp. was 0.3 per 1000 catheter associated days. Presence of indwelling catheter is one of the important risk factors for candiduria. In the study of Deorukhkar et al. (2016) the rate of CA-UTI due Candida spp. was 1 per 1000 catheter associated days.[4]

Out 16 *Candida* isolates from CA-UTI, 11 (68.7%) were NAC spp. As commented by Fisher (2011), the microbiology of candiduria is changing with >50% of isolates now belonging to NAC spp.[9] It is considered that chemical composition and pH of urine selectively support the growth of NAC spp[10] As NAC spp. often demonstrated reduced susceptibility to routinely used

antifungal drugs, they are difficult to eradicate from urinary tract. *C. tropicalis* (43.7%) was the predominant isolate from catheter associated candiduria cases. This observation is in accordance to that Jain et al. (2011) and Deorukhkar et al. (2016) who reported *C. tropicalis* as the predominant cause of candiduria in catheterized ICU patients.[4,11]

Hospital acquired BSI are one of the major causes of morbidity and mortality in ICU patients. Iintravascular catheters are inserted in terminally ill patients for the administration of fluids, blood products, medications, nutritional solutions and for hemodynamic monitoring.[8] However at times they may act as a source of infections. CR-BSI often originates in emergency rooms and ICU.[8] Various researchers have reported, rates of CR-BSI ranging from 2.9 to 11.3 per 1000 catheter days.[4] These rates vary as per the types of ICUs and the patient population studied. The prevalence of nosocomial *Candida* BSI is higher in United States compared to European countries.[4] However, the exact prevalence of nosocomial Candida BSI is largely unknown in India. The present study, rate of CR-BSI due to *Candida* spp. was 0.9 per 1000 catheter associated days.

A total of 05 *Candida* spp. were isolated from CR-BSI, these included 02 isolates of *C. albicans* and 03 isolates of *C. tropicalis*. Many Indian researchers have reported, C. tropicalis as the most common *Candida* isolate from BSI.[4] *C. tropicalis* is mostly commonly isolated from ICU patients with prolonged indwelling catheters on broad-spectrum antibiotic therapy. Malignancy is also an important risk factor for nosocomial BSI due to *C. tropicalis*.[12]

VAP is one of the important complications in ICU patients. Approximately 8-28% patients on mechanical ventilator support suffer from VAP.[4] In the present study, VAP was due to bacterial pathogen. No *Candida* spp. was isolated from VAP cases.[4] Other researchers reported similar findings. *K. pneumoniae* was the predominant isolate from VAP cases.

In the present study, the MIC of *Candida* spp., was determined by CLSI reference BMD method. The CLSI BMD is internationally recognized standard methodology for antifungal susceptibility testing of *Candida* spp.[7] Azole resistance was significantly high in NAC spp. compared to *C. albicans*. In contrast to *C. albicans*, antifungal susceptibility varies significantly in NAC spp. Certain NAC spp. are intrinsically resistant to azoles whereas few can acquire resistance during course of treatment.[13] The finding of present study, highlights the importance of antifungal susceptibility in selection of appropriate antifungal drug. It also supports the fact that practice of empirical fluconazole therapy should be stopped or should be limited only in case of emergency. Resistance to amphotericin B was low in the present study.

5. Conclusion

Health-care associated infection (HCAI) is a significant threat to patient safety. *Candida* spp. has emerged as an important cause of HCAI particularly medical device associated infections like CA-UTI and CR-BSI. Species identification along with antifungal susceptibility testing plays an important role in selection of antifungal drug and prevention of treatment failure.

6. Conflict of Interest

None.

References

1. Joshua P, Bryan C, Brad S. Nosocomial fungal infections: epidemiology, diagnosis, and treatment. *Med Mycol*. 2007;45(4):321–46.
2. Nucci M, Queiroz-Telles F, Tobón AM, Restrepo A, Colombo AL. The role of environmental contamination in the transmission of nosocomial pathogens and healthcare-associateed infections. *Clin Infect Dis*. 2010;51(5):561–70.
3. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: A Persistent public health problem. *Clin Microbiol Rev*. 2007;20(1):133–63.
4. Deorukhkar S, Saini S. Medical Device-Associated Candida Infections in a Rural Tertiary Care Teaching Hospital of India. *Interdiscip Perspect Infect Dis*. 2016;2016:1854673.
5. Mean M, Marchetii O, Calandra T. Bench-to bedside review: Candida infections in the intensive care unit. *Crit Care*. 2008;12(1):204.
6. Lokhart S. Current epidemiology of Candida infection. *Clin Microbiol Newsl*. 2014;36(17):131–6.
7. Reference Method For Broth Dilution Antifungal Susceptibility Testing of Yeasts. 2nd ed. Wayne: Clinical Laboratory Standard Institute; 2008.
8. Gahlot R, Nigam C, Kumar V, Yadav G, Anupurba S. Catheter-related bloodstream infections. *Int J Crit Illn Inj Sci*. 2014;4(2):162–7.
9. Fisher J. Candida urinary tract infections-epidemiology, pathogenesis, diagnosis, and treatment: executive summary. *Clin Infect Dis*. 2011;52(6):429–32.
10. Lundstrom T, Sobel J. Nosocomial candiduria: A review. *Clin Infect Dis*. 2001;32(11):1602–7.
11. Jain M, Dogra V, Mishra B, Thakur A, Loomba S, Bhargava A, et al. Candiduria in catheterized intensive care unit patients: emerging microbiological trends. *Indian J Pathol Microbiol*. 2011;54(3):552–5.
12. Krcmery V, Barnes AJ. Non-albicans Candida spp. causing fungaemia: Pathogenicity and antifungal resistance. *J Hosp Infect*. 2002;50(4):243–60.
13. Oberoi J, Chand W, Goel N, Raveendran R, Datta S, Prasad K. Non-albicans Candida species in blood stream infections in a tertiary care hospital at New Delhi, India. *Indian J Med Res*. 2012;136(6):997–1003.

Author biography

Kamaljeet, PhD Research Scholar

Naveen Saxena, Professor and Head

Mohit Thalquotra, Assistant Professor

Cite this article: Kamaljeet, Saxena N, Thalquotra M. Species distribution and antifungal susceptibility of *Candida* isolates from cases of health-care associated infections. *Indian J Microbiol Res* 2022;9(2):95-98.