ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 2, March - 2023, Page No. : 697 - 705

Fungal Hemodialysis Catheter related blood stream infection – A Single tertiary Centre experience in Western Maharashtra.

[1]Dr. Bhagya Laxmi Paramshetti, Junior Resident, Department of General Medicine, BVDU and MCH, Pune, Maharashtra, India.

[2]Dr. Prachee Makashir, Professor, Department of General Medicine, BVDU and MCH, Pune, Maharashtra, India.

[3]Dr. Sunil Jawale, Assistant Professor, Department of General Medicine, BVDU and MCH, Pune, Maharashtra, India.

[4]Dr. Darshan Thacker, Junior Resident, Department of General Medicine, BVDU and MCH, Pune, Maharashtra, India.

Corresponding Author: Dr. Prachee Makashir, Professor, Department of General Medicine, BVDU and MCH, Pune, Maharashtra, India.

How to citation this article: Dr. Bhagya Laxmi Paramshetti, Dr. Prachee Makashir, Dr. Sunil Jawale, Dr. Darshan Thacker, "Fungal Hemodialysis Catheter related blood stream infection – A Single tertiary Centre experience in Western Maharashtra", IJMACR- March - 2023, Volume – 6, Issue - 2, P. No. 697 – 705.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: One of the most prevalent, fatal, and expensive complications of central venous catheterization is catheter-related blood stream infection (CRBSI). S. aureus is the most frequent cause of CRBSI globally, but candidemia is also a significant hemodialysis complication.

Objective: To identify the prevalence of candidemia and examine the clinical characteristics and prognosis of hemodialysis patients in tertiary care facilities.

Methodology: The study includes all patients who were diagnosed with CRBSI in our facility between October 2020 and December 2022.

Patients with confirmed candidemia received susceptible antibiotic treatment in accordance with the culture sensitivity report for a minimum of two weeks before the results of a repeat culture were negative. Guidewire catheter exchange or catheter removal with delayed replacement was done depending on the clinical condition and outcome, along with antibiotics if necessary.

Results: Most of the CRSBIs had IJV site of insertion. Variconazole, Caspofungin, and Amphotericin were the most sensitive antifungals.

Conclusion: CRBSIs caused due to candida spp proved to have a very good survival rate. Early administration of antifungals may prove to be beneficial in treating candidal CRBSIs.

Keywords: Candidemia, Hemodialysis, Catheter related blood stream infection, Antifungal Sensitivity.

Introduction

Infections are the second-leading cause of morbidity and mortality in the hemodialysis population, after only cardiovascular disease in importance. Although candidemia is a serious side effect of renal failure and hemodialysis, staphylococcal septicemia is the most frequent cause of bloodstream infections in this population (1). Renal failure was linked to a relative risk of 4.2 for developing candidemia in critically ill patients. Candida species are the fourth most frequent cause of bloodstream infections in all hospitalized patients in the US (2). According to one study, almost one-third of cases of candidemia had a community onset (3). According to estimates, there are between 2.1 and 6.9 instances of Candida bloodstream infection (candidemia) in critically ill intensive care unit (ICU) patients per 1000 ICU admissions (4–6), with a high crude death rate of 43-61% (4–7)

Bloodstream infections are dangerous and have a high fatality rate. Catheter-related infections are a major contributor to bloodstream infections. The most common type of nosocomial infection is catheter-related bloodstream infections (CRBSIs), which are primarily caused by Gram-positive bacteria such Staphylococcus aureus and Staphylococcus epidermidis.

These organisms can attach to biomaterials and create biofilms, which is generally thought to be a crucial step in the pathogenesis of CRBSI. Removal of the catheter and quick delivery of the proper antimicrobial medicines are acknowledged as crucial treatment procedures. (8)

CRBSIs brought on by catheter-related candidemia, are more dangerous and necessitates longer treatment times. (9) Despite the fact that catheter-related candidemia benefits from prompt and effective antifungal treatment, this treatment is often started later than necessary, which contributes to the infection's poor prognosis. (10) To improve results, empiric antifungal medication must be started right away. According to several research, patients who have sepsis and any of the following risk factors should receive empiric antifungal medication for suspected catheter-related candidemia: total parenteral nutrition, extended use of broad-spectrum antibiotics, Haematological malignancy, receipt of bone marrow or solid organ transplant, femoral catheterization, and colonisation by Candida spp. at multiple sites. However, such trials were conducted in constrained settings, such as a single intensive care unit or cancer Centre.(11,12) More research is required to identify appropriate markers for starting empiric antifungal therapy for CRBSI.

In the current investigation, we looked into the clinical characteristics of catheter-related candidemia in an effort to find novel and specific traits that would help doctors distinguish between CRBSIs caused by non-Candida spp. and catheter-related candidemia at disease onset.

Methodology

The current study population was made up of all patients who had catheter-related candidemia or bacteraemia from an organism other than Candida spp. while they were being treated at the Bharati Vidyapeth deemed to be university and medical college, Maharashtra, India, a teaching hospital with 1,200 beds, between October 2020 and December 2022. The study was approved by the ethical committee of University of Bharati. According to the new guidelines published in 2018 by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC), after obtaining the necessary cultures, empiric antibiotic therapy should be started if CRBSI is suspected.

Catheter removal and echocardiography are essential in cases of candida spp. After the first negative blood culture, an antifungal is administered for 14 days.(8)

The features of catheter-related candidemia and non-Candida CRBSIs were compared in the current study. CRBSI was described in accordance with stated standards. (8) A patient was deemed to have a CRBSI if at least one blood culture and one catheter culture revealed the presence of micro-organisms and the patient showed signs and symptoms of infection, such as fever, chills, confusion, hypotension, and respiratory failure, but no other specific signs of infection. (1) Elevated serum C-reactive protein (> 0.3 mg/dL) and a high white blood cell count (>12,000/mm3) in peripheral blood were helpful adjuncts to the infection diagnosis. The initial positive blood culture sample served as the marker for the beginning of CRBSI. New instances of CRBSI were those that manifested > 30 days after the original event.

Blood specimens were inoculated into BACTEC™ blood culture bottles (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), and the blood cultures were analysed using the BACTEC™ FX system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). Yeast-like organisms were identified using the ATB Expression TM system and Analytical Profile Index identification system (bio Merieux, Lyon, France), whereas bacteria were identified using the Walk Away System (Siemens, Munich, Germany). Fluconazole, variconazole, micafungin, and amphotericin B were the antifungals that were evaluated for sensitivity. Minimum inhibitory doses of antibacterial drugs were obtained using antimicrobial susceptibility assays utilising broth microdilution procedures, according to the criteria published by the Clinical Laboratory Standards Institute. Adequate treatment was defined as the administration of adequate antibacterial drugs. (13,14)

Age, gender, sickness severity at disease beginning, underlying conditions (such as Diabetes Mellitus, Hypertension, Hypo thyroidism, IHD, Chronic Kidney Disease, and prior antibiotic use), deaths as a result of bloodstream infections, and previously established risk variables (e.g., increased use of broad-spectrum anti-biotics, femoral catheterisation, and colonisation due to Candida spp. at multiple sites, recurrent CRBSI) were identified in the clinical parameters of the patients

Broad-spectrum antibiotics included beta-lactam/beta-lactamase inhibitor combinations, carbapenems, third- and fourth-generation cephalosporins, and quinolones. The treating physician, intensivists and nephrologist determined the best course of antifungal treatment. Most patients underwent an antifungal treatment regimen lasting two weeks. Each nephrologist chose the catheter management strategy (guidewire exchange or removal with delayed implantation of a new catheter) based on his or her personal experience.(15)

A prolonged course of broad-spectrum antibiotics was classified as one lasting more than 14 days. The term "CRBSI-attributable mortality" refers to fatalities that were thought to be brought on by CRBSI within 30 days of the commencement of the illness.

Unless otherwise stated, the results of this study are presented as mean standard deviation. For continuous variables, Student's t-test or Mann-Whitney U test was used in univariate analysis. When necessary, Fisher's exact test was performed to compare proportions. Logistic regression analysis was used to do the multi variate analysis. A p-value of 0.05 or less was regarded as statistically significant for all two-sided p-values. Stat

Flex version 6.0 was used to perform the statistical analysis (Artec Co Ltd, Osaka, Japan).

Result

Table 1: Demographic and clinical characteristics

	CRI due to Non-Candida spp	CRI due to Candida spp	P value
Age			
<30	6 (7.5)	1 (5.3)	0.81
31-50	21 (26.3)	4 (21.1)	Non-
>50	53 (66.3)	14 (73.7)	significant
Gender			
Male	32 (40)	15 (78.9)	0.123
Female	48 (60)	4 (21.1)	
Underlying conditions			
CKD	73 (91.3)	16 (84.2)	0.360
AKI	7 (8.8)	3 (15.8)	0.385
Diabetes	49 (61.3)	14 (73.7)	0.311
Hypertension	68 (65)	15 (78.9)	0.531
Hypothyroid	8 (10)	4 (21.1)	0.212
IHD	13 (16.3)	4 (21.1)	0.618
HB category			
<6	3 (3.8)	1 (5.3)	0.002
6-10	75 (93.8)	13 (68.4)	Significant
>10	2 (2.5)	5 (26.3)	
Emergency	61 (76.3)	10 (52.6)	0.04
Elective	19 (23.8)	9 (47.4)	0.04
Temporary	60 (75)	10 (52.6)	0.054
Permacath	20 (25)	9 (47.4)	0.054
Site of cathether			
Femoral	9 (11.3)	2 (10.5)	0.928
IJV	71 (88.8)	17 (89.5)	
No. of lumen	80 (100)	19 (100)	
(Triple)			
Site of cathether			
Lt femoral	3 (3.8)		
Lt IJV	12 (15)	3 (15.8)	0.298
Lt Permacath	2 (2.5)	1 (5.3)	
Permacath	3 (3.8)	1 (5.3)	
Rt femoral	6 (7.5)	2 (10.5)	
Rt IJV	46 (57.5)	8 (42.1)	
Rt Permacath	8 (10)	4 (21.1)	
Fever	70 (87.5)	19 (100)	0.033
Shock	12 (15)	3 (15.8)	0.932
Inotropic support	10 (12.5)	3 (15.8)	0.708
Local catheter site infection	34 (42.5)	7 (36.8)	0.653
Outcome			0.318
Survived	75 (93.8)	19 (100)	
Death	5 (6.3)		

Most of the CRBSIs in both the groups belonged to individuals in the age group of over 50 years. A female predominance was seen in the non-candida group while a male predominance was noted in the candida group. CKD, hypertension and diabetes were the three most common underlying comorbidities in both the groups. More of emergency surgeries were observed in both the groups. The right Internal jugular vein was the most frequent site of catheter insertion in both the groups (57.5% in non-candida group vs 42.1% in candida group). Inotropic support was needed in both the groups Fever and shock was seen in 87.5% and 15% cases of non-candida spp and 100% and 15.8% of the candida spp. Local catheter site infection was more in the non-candidal group (42.5%) as opposed to candidal group (36.8%). An overall mortality of 6.3% was noted in the non-candidal group versus 0% in the candidal group.

Table 2: Mean values of some parameters in both the groups

	CRI due to non-Candida spp	CRI due to Candida spp	P value
Albumin	2.97 ± 0.09	2.94 ± 0.25	0.307
Procalcitonin	30.27 ±35.56	19.58 ± 30.13	0.068
Duration of infection (days)	14.51 ± 0.50	14.82 ± 0.37	0.233
No of dialysis sessions/week	2.76 ± 0.60	3.05 ± 1.39	0.019
No of CRSBIs	1.35 ± 0.67	1.26 ± 0.65	0.427

The mean albumin levels in non-candidal group and candidal group was 2.97 ± 0.09 and 2.94 ± 0.25 respectively while the mean Procalcitonin levels in the non-candidal group (30.27 ± 35.56) was higher than that in the candida group (19.58 ± 30.13). The duration of infection as well as number of CRSBIs in both the groups were almost similar. More dialysis sessions were needed in the candida group (3.05 ± 1.39) as opposed to the non-candida group (2.76 ± 0.60).

Table 3: Candida spp infections

Fungal Species	Number
Candida Parapsilosis	13
Candida Albicans	02
Candida Guilliermondii	01
Candida Tropicalis	01
Candida Glabrata	02

Table 4: Antifungal medications prescribed to candida spp infections

Antifungal medication	Resistant (%)	Sensitive (%)
Fluconazole	5.3	12
Variconazole		68.4
Caspofungin	5.3	68.4
Micafungin		7.37
Amphotericin	5.3	68.4

Various subspecies of candida were checked such as *C.* glabrata, C. parapsilosis, C. tropicalis and C. krusei. It was observed that candida infections showed a sensitivity of 12%, 68.4%, 68.4%, 7.37% and 68.4% respectively to Fluconazole, Voriconazole, Caspofungin, Micafungin and Amphotericin. 5.3% each were resistant to Fluconazole, Caspofungin and Amphotericin.

Discussion

Hemodialysis damages anatomical barriers, which makes patients more susceptible to candidemia. The use of catheter-based dialysis is typically, though not always, a temporary solution. Catheters can be used for ongoing hemodialysis access or for prolonged periods of time until a different access has developed. In this study, IJV catheters were used for dialyzing 89.5% of hemodialysis patients with candidemia and 88.8% of non-candid emic hemodialysis patients. Catheter-based dialysis is more common in patients who are in-patients and may be a sign of a more serious underlying illness, but it also increases the risk of infection because intravascular devices are independently linked to candidemia regardless of renal function (16–18).Majority of the participants in both the groups were above 50 years of age. In the present study, a female predominance was seen in the non-candida spp group while a male predominance was seen in the candida spp

group. Similar male predilection was also seen in a study by Yoshino et al. (19)

Diabetes, kidney engraftment failure and previous bacteremia were amongst the most common underlying factors contributing to CRSBIs. (20) Ohki et al (21) observed that the three most prevalent comorbidities in their study were (21%) were autoimmune disease, diabetes mellitus, and liver disease. Blood stream infections are more likely to occur in patients who have renal failure, and candidemia is a known risk factor for hemo dialysis patients. Dysfunctional phagocytes are related to renal failure. A previously healthy monocyte's ability to phagocytose Candida albicans is inhibited by uremic plasma, and mononuclear cells from uremic patients have lower receptivity to Candida antigens. Patients who receive hemodialysis are more likely to develop candidemia because it compromises anatomical barriers during Angio access and may cause immuno logical dysfunction by triggering monocyte apoptosis, which inhibits the growth of Candida. As a result, a number of factors, such as co-morbid illnesses like diabetes mellitus, widespread exposure to antibacterial drugs, underlying renal impairment, and the dialysis procedure, contribute to the high risk of candidemia in this population.(1)

The IJV site of cathether insertion saw the most candidal as well as non-candidal infections. Fever and shock were the accompanying symptoms seen. Inotropic support was required in 12.5 % and 15.8% cases on non candidal infections and candida infections respectively.

Candidemia has been linked to 30–60% crude mortality rates. (22,23)A mortality of 6.3% was seen in the non-candidal group while no deaths were noted in the candidal infection group.It was observed that the empirical therapy helped in the reduction of mortality rate. The duration of use of catheter was almost similar in both the groups with 14.51 ± 0.50 and 14.82 ± 0.37 days respectively in non candidal and candida infections. A clinical feature of catheter-related candidemia is thought to be a longer duration of catheter use. This is due to the fact that Candida infections are typically linked to the development of biofilms on the surface of biological and inert surfaces (24), and prolonged catheter use would increase the likelihood of the yeast developing a biofilm. It's probable that Candida spp. take longer than bacteria to produce biofilms, despite the fact that several features of Candida biofilm production are still unclear.

Procalcitonin was higher in the non-candidal infection group as opposed to the candidal group. Similar results were obtained in other studies wherein patients with candidemia had lower Procalcitonin serum levels than those with bacteremia. (25,26)Lipopolysaccharides and cytokines, which are expressed in pro-inflammatory circumstances, encourage Procal citonin synthesis. Procalcitonin levels can rise in various non-bacterial inflammatory diseases, however bacterial infections often have greater procalcitonin serum concentrations. Immune cell depletion, poor inflammatory response, and decreased production of positive co-stimulatory molecules were all observed in patients with invasive candidiasis contributing to lowered procalcitonin levels.(27)Various antifungals are used in treatment of candida CRSBIs such as fluconazole, variconazole, caspofungin, micafungin and amphotericin.(28) In the current study Variconazole, Caspofungin, and Amphotericin were the most sensitive (68.4% each). Similar results were obtained in a study by Chong ham et al (29), variconazole (86%) was the most sensitive antifungal agent while ketoconazole (56%) was the least

sensitive. amphotericin B showed a sensitivity of 81% and resistance of 8%. If azole resistance is suspected, echino can dins (micafungin, caspofungin, and anidula fungin) are preferable treatments for suspected candidemia (prior azole use or prevalent nonalbicans candida such as C. glabrata or C. krusei). If not, intravenous fluconazole would be adequate

Conclusion

The gold standard treatment for Candida CRBSI, which poses a serious risk to hemodialysis patients is catheter removal followed by antifungal therapy, although prophylactic catheter locks and treatments that leave catheters in place appear to be gaining ground. There fore, we advise starting empiric antifungal medications in patients who are non-responsive to antibacterial drugs.

References

1. Pyrgos V, Ratanavanich K, Donegan N, Veis J, Walsh TJ, Sho ham S. Candida bloodstream infections in hemodialysis recipients. Med Mycol. 2009;47(5):463-7.

2. Wisplingh off H, Bischoff T, Talent 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. Kao AS, Brandt ME, Pruitt WR, Conn LA, Perkins BA, Stephens DS, et al. The epidemiology of candidemia in two United States cities: results of a population-based active surveillance. Clin Infect Dis Off Publ Infect Dis Soc Am. 1999 Nov;29(5):1164–70.

4. Charles PE, Doise JM, Quenot JP, Aube H, Dalle F, Chavanet P, et al. Candidemia in critically ill patients: difference of outcome between medical and surgical patients. Intensive Care Med. 2003; 29:2162–9.

5. Kett DH, Azoulay E, Echeverria PM, Vincent JL. Extended prevalence of infection in ICU study (EPIC II) group of investigators. Candida bloodstream infections in intensive care units: analysis of the extended prevalence of infection in intensive care unit study. Crit Care Med. 2011; 39:665–70.

6. Chakrabarti A, Sood P, Rudra Murthy SM, Chen S, Kaur H, Capoor M, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med. 2015; 41:285–95.

7. Puig-Asensio M, Pemán J, Zaragoza R, Garnacho-Montero J, Martín-Mazuelos E, Cuenca-Estrella M, et al. Impact of therapeutic strategies on the prognosis of Candidemia in the ICU. Crit Care Med. 2014; 42:1423–32.

8. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis Off Publ Infect Dis Soc Am. 2009 Jul 1;49(1):1–45.

9. Rex JH, Walsh TJ, Sobel JD, Filler SG, Pappas PG, Dismukes WE, et al. Practice guidelines for the treatment of candidiasis. Infectious Diseases Society of America. Clin Infect Dis Off Publ Infect Dis Soc Am. 2000 Apr;30(4):662–78.

10. Morrell M, Fraser VJ, Kollef MH. Delaying the empiric treatment of candida bloodstream infection until positive blood culture results are obtained: a potential risk factor for hospital mortality. Antimicrob Agents Che mother. 2005 Sep;49(9):3640–5.

11. Lorente L, Jiménez A, Santana M, Iri barren JL, Jiménez JJ, Martín MM, et al. Microorganisms responsible for intravascular catheter-related blood stream infection according to the catheter site. Crit Care Med. 2007 Oct;35(10):2424–7.

12. Raad I, Hanna H, Bok tour M, Girgawy E, Danawi H, Mardani M, et al. Management of central venous catheters in patients with cancer and candidemia. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004 Apr 15;38(8):1119–27.

13. Pennsylvania, USA: Clinical and Laboratory Standards Institute; 2008. Apr, Clinical and Laboratory Standards Institute. Reference method for broth dilution antifungal susceptibility testing of yeasts; approved standard – third edition. Report no: M27-S4.

14. Pennsylvania, USA: Clinical and Laboratory Standards Institute; 2011. Jan, Clinical and Laboratory Standards Institute. Performance standards for anti microbial susceptibility testing; twenty - first in formational supplement. Report no: M100-S21.

15. Parbat N, Sherry N, Bellomo R, Schneider AG, Glassford NJ, Johnson PD, et al. The microbiological and clinical outcome of guide wire exchanged versus newly inserted antimicrobial surface treated central venous catheters. Crit Care. 2013;17(5):R184.

16. Blumberg HM, Jarvis WR, Soucie JM, Edwards JE, Patterson JE, Pfaller MA, et al. Risk factors for candidal bloodstream infections in surgical intensive care unit patients: the NEMIS prospective multicenter study. The National Epidemiology of Mycosis Survey. Clin Infect Dis Off Publ Infect Dis Soc Am. 2001 Jul 15;33(2):177–86.

17. Karabinis A, Hill C, Leclercq B, Tancrède C, Baume D, And remont A. Risk factors for candidemia in cancer patients: a case-control study. J Clin Microbiol. 1988 Mar;26(3):429–32.

18. Hoen B, Kessler M, Hestin D, Mayeux D. Risk factors for bacterial infections in chronic haemodialysis adult patients: a multi-Centre pros pective survey. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 1995;10(3):377–81.

19. Yoshino Y, Wakabayashi Y, Suzuki S, Seo K, Koga I, Kitazawa T, et al. Clinical features of catheter-related candidemia at disease onset. Singapore Med J. 2014 Nov;55(11):579.

20. Our Ives APJ, Gonçalves SS, Siqueira RA, Souza ACR, Canziani MEF, Manfredi SR, et al. High rate of Candida deep-seated infection in patients under chronic hemodialysis with extended central venous catheter use. Rev Ibe roam Micol. 2016 Apr 1;33(2):100–3.

21. Ohki S, Shime N, Kosaka T, Fujita N. Impact of host- and early treatment-related factors on mortality in ICU patients with candidemia: a bicentric retrospective observational study. J Intensive Care. 2020 Apr 26; 8 (1): 30.

22. Zaoutis TE, Argon J, Chu J, Berlin JA, Walsh TJ, Feudtner C. The epidemiology and attributable outcomes of candidemia in adults and children hospitalized in the United States: a propensity analysis. Clin Infect Dis Off Publ Infect Dis Soc Am. 2005 Nov 1;41(9):1232–9.

23. Pappas PG, Rex JH, Lee J, Hamill RJ, Larsen RA, Powderly W, et al. A prospective observational study of candidemia: epidemiology, therapy, and influences on mortality in hospitalized adult and pediatric patients. Clin Infect Dis Off Publ Infect Dis Soc Am. 2003 Sep 1;37(5):634–43.

24. Ramage G, Martínez JP, López-Ribot JL. Candida biofilms on implanted bio materials: a clinically signifi cant problem. FEMS Yeast Res. 2006 Nov; 6 (7): 979–86.

25. Dou Y-H, Du J-K, Liu H-L, Shong X-D. The role of procalcitonin in the identification of invasive fungal infection-a systemic review and meta-analysis. Diagn Microbiol Infect Dis. 2013; 76:464–9.

26. Raineri SM, Cortegiani A, Vitale F, Iozzo P, Giarratano A. Procalcitonin for the diagnosis of invasive candidiasis: what is the evidence? J Intensive Care. 2017; 5:58.

27. Cortegiani A, Misseri G, Ippolito M, Bassetti M, Giarratano A, Martin-Loeches I, et al. Procalcitonin levels in candidemia versus bacteremia: a systematic review. Crit Care. 2019 May 28;23(1):190.

28. Haddadin Y, Annamaraju P, Regunath H. Central Line Associated Blood Stream Infections. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2022 [cited 2023 Feb 19]. Available from: http:// www. ncbi. nlm.nih.gov/books/NBK430891/

29. Chong ham U , Athok pam DC , Singh RM. Iso lation, identification and antifungal susceptibility testing of Candida species: a cross-sectional study from Mani pur, India. Journal of Clinical and Diagnostic Research, 2022; 16(4): DC09-DC14.