

INCIDENCE OF FUNGAL INFECTIONS IN INTENSIVE CARE UNITS IN A TERTIARY CARE CENTRE, WEST UTTAR PRADESH

Kaushik Kalita¹, Tarana Sarwat², Supriya Mahajan³, Dalip K Kakru⁴, Biswajit Kalita⁵

Received : 08/04/2024
Received in revised form : 30/05/2024
Accepted : 14/06/2024

Keywords:

Incidence, Fungal Infections, Intensive Care Units.

Corresponding Author:

Kaushik Kalita,

Email: kaushikkalita29@gmail.com

DOI: 10.47009/jamp.2024.6.3.87

Source of Support: Nil,

Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (3); 425-430



¹Student, MSc Medical Microbiology, School of Medical Sciences and Research, Sharda Hospital, Sharda University, Uttar Pradesh, India.

²Associate Professor, Department of Microbiology, School of Medical Sciences and Research, Sharda Hospital, Sharda University, Uttar Pradesh, India.

³Assistant Professor, Department of Microbiology, School of Medical Sciences and Research, Sharda Hospital, Sharda University, Uttar Pradesh, India.

⁴Head and Professor, Department of Microbiology, School of Medical Sciences and Research, Sharda Hospital, Sharda University, Uttar Pradesh, India.

⁵Head and Professor, Department of Zoology, Barama College, Barama, Assam, India.

Abstract

Background: The presence of infection in critically ill patients poses unique challenges as it can directly influence the morbidity and mortality. Systemic fungal infections constitute a major problem in intensive care units in both developed and developing nations. The COVID-19 era also has exhibited an exponential increase in critically ill patients with acute respiratory distress syndrome (ARDS) necessitating ICU admission leading to an increased incidence of secondary fungal infections that have contributed significantly to adverse outcomes. **Materials and Methods:** All ICU samples received in the Microbiology laboratory were subjected to KOH mount and were also cultured on Sabouraud Dextrose Agar (SDA). The growth of fungus on SDA was identified on the basis of morphology and by preparing Lactophenol cotton blue mount. **Result:** Total of 174 samples were received from all the ICUs, out of which 101(58.04%) showed growth of fungal pathogen. Out of the total positive samples, maximum fungal isolates strains were isolated from sputum (n=45, 44.55%), followed by BAL (n=24, 23.76%), blood culture (n=6, 5.94%), endotracheal aspirate, pleural fluid and nasal swab (2.97% each). *Candida albicans* (n=35, 32.71%) was found to be most predominant fungal pathogen in this study. **Conclusion:** *Candida* spp. cause the majority of infections in ICU. They occur most commonly in patients with severe underlying illness, having multiple courses of antibiotics and on intravascular catheters. Clinical diagnosis is difficult due to nonspecific signs and the frequent occurrence of widespread superficial colonization with *Candida* spp. Proper surveillance is important to improve quality of care in ICU.

INTRODUCTION

Infections have almost become an inseparable part of the intensive care units throughout the globe in spite of numerous advancements in diagnostic and therapeutic interventions. The presence of infection in critically ill patients poses unique challenges as it can directly influence the morbidity and mortality. Amongst various infections prevalent in an intensive care unit, invasive fungal infection has always been considered to occur infrequently, but, over the past few years, with the surge in broad-spectrum antibiotic usage and improved knowledge of fungal diseases, the incidence has risen. At present, systemic fungal infections constitute a major problem in

intensive care units in both developed and developing nations.

Fungal pathogens are estimated to lead to more than 1.5 million deaths every year worldwide, with a global burden exceeding one billion.^[1] Despite this, the issue of fungal pathogenicity has been largely neglected.^[2,3] This has also been acknowledged in the case of healthcare-associated invasive fungal infection,^[4,5] for which a call to action was recently issued by the scientific community.^[6] Moreover, the increased prevalence of invasive fungal diseases correlates with an increasing number of vulnerable at-risk patients, which include among others, immunosuppressed individuals due to transplants, AIDS, cancer, corticosteroid therapies or

autoimmune diseases, or patients undergoing major surgery.^[1,7]

The incidences of candidemia, systemic aspergillosis, cryptococcosis and zygomycosis in India have shown a steep rise, with emergence of newer fungal infections.^[9] Although the leading fungal infection is candidemia, disseminated candidiasis with deep organ involvement and pulmonary aspergillosis have been recently reported as additional important complications in ICU patients.

The COVID-19 era also has exhibited an exponential increase in critically ill patients with acute respiratory distress syndrome (ARDS) necessitating ICU admission leading to an increased incidence of secondary fungal infections that have contributed significantly to adverse outcomes. Among fungal infections, pulmonary mucormycosis, aspergillosis and candidemia have attracted much attention as emerging clinical entities complicating critical COVID-19.^[13,15]

MATERIALS AND METHODS

This cross-sectional study was performed in the Central Laboratory at School of Medical Sciences and Research (SMS&R), Sharda Hospital, Greater Noida over a period of 12 months from November 2022 to October 2023. The study aimed to determine the incidence of fungal infections in Intensive Care Units. All samples received in microbiology lab for fungal culture and/or KOH mount from Intensive Care Units were included in this study. The study was approved by the Institutional Ethics Committee.

Procedure: All ICU samples received in the Microbiology laboratory were subjected to KOH mount and were also cultured on Sabouraud Dextrose Agar (SDA). The growth of fungus on SDA was identified on the basis of morphology and by microscopic observation of Lactophenol cotton blue mount of the isolates.

RESULTS

A total of 174 samples were received, out of which 101(58.04%) showed growth of fungal isolates. Out of 101 samples, 97 samples showed growth of single fungal pathogen, 2 samples showed growth of 2 different types of fungal pathogen and 2 samples showed growth of 3 types of fungal pathogens. Out of the total samples 112(64.26%) were males and

62(35.63%) were females. 14(13.86%) patients died of fungal infection in this study.

Maximum samples were received from Medical Intensive Care Unit (MICU) (69.5%) and Neonatal Intensive care Unit (NICU) (38%) but maximum fungal infections were isolated from Respiratory Intensive Care Unit (RICU) (95.6%) as shown in [Table 1].

Demographic profile: Most of the fungal isolates were from patients in the age group of 41-60 years, followed by 0-20 years, 61-80 years, 21-40 years and above 81 years [Table 2].

Maximum fungal strains were isolated from sputum (n=45, 44.55%), followed by BAL (n=24, 23.76%), Blood (n=6, 5.94%), endotracheal aspirate, pleural fluid and nasal swab (2.97% each) as shown in [Table 3].

Candida albicans (n=35, 32.71%) was found to be most predominant in this study, followed by *Candida non-albicans* (n=30, 28.03%), *Aspergillus fumigatus* (n=13, 12.14%), *Aspergillus flavus* (n=12, 11.21%), *Trichosporon* (n=4, 3.73%), *Aspergillus niger* (n=2, 1.86%), *Aspergillus nidulans* (n=2, 1.86%) respectively. Here in this study other species like *Penicillium*, *Alternaria*, *Rhizopus*, *Curvularia*, *Sepedonium*, *Fusarium*, *Cryptococcus laurentii* & *Exserohilium* spp. Constitutes a number of (n=1, 0.93%) each [Table 4].

Candida albicans was found to be the most common fungus leading to infections in ICU as shown in [Table 5].

A total of 7 different clinical conditions were identified among the included patients and analysed for possible association with the development of fungal infections [Table 6]. Three of these clinical factors were found to be significantly associated with the occurrence of fungal infections i.e patients with lower respiratory tract infections like chronic obstructive pulmonary disease, pneumonia, bronchitis, asthma where they showed maximum isolates of *Candida albicans* (17) followed by Non-albicans *Candida* (NAC) (13), *Aspergillus fumigatus* (9), *Aspergillus flavus* (5) and *Trichosporon*, *Rhizopus*, *Aspergillus nidulans* and *Sepedonium* counting a number of 1 isolate each. Neonatal sepsis showed predominant growth of NAC (9) followed by *Candida albicans* (7), *Aspergillus flavus* (1) and *Alternaria* (1) respectively and sepsis of age group > 1month showed growth of *Candida albicans* (6) and NAC (4), *Aspergillus fumigatus* (3) and *Aspergillus flavus* (1).

Table 1: Incidence of fungal infections in different ICUs.

ICUs	No. of samples
MICU	60
NICU	55
RICU	23
SICU	23
ICCU	8
PICU	5
Total	174

(ICCU: Intensive Coronary care unit, MICU: Medical Intensive Care Unit, NICU: Neonatal Intensive care Unit, PICU: Paediatric Intensive Care Unit, RICU: Respiratory Intensive Care Unit, SICU: Surgical Intensive Care Unit)

Table 2: Age-wise distribution of patients with fungal infections

Age	Number of Patients (%)
0-20	26 (25.74)
21-40	19 (18.81)
41-60	33 (32.67)
61-80	22 (21.78)
Above 80	1 (0.99)
Total	101

Table 3: Sample wise distribution of fungal isolates

Sample Type	Total Number	Positive (%)
CONJUCTIVAL SWAB	1	0
NASAL TISSUE	1	1 (100)
TRACHEAL SECRETION	1	0
CSF	2	0
NASAL SWAB	2	1(50)
PUS	2	0
THROAT SWAB	2	2(100)
PLEURAL FLUID	8	3(37.5)
ETT	9	3(33.3)
BLOOD	12	6(50)
BAL	41	24(58.5)
URINE	46	16(34.7)
SPUTUM	47	45(95.7)
Total	174	101(58)

Table 4: Overall incidence of fungal pathogens in ICU

Fungal isolates	Number(%)
Candida albicans	35(32.71)
Candida non-albicans	30(28.03)
Aspergillus fumigatus	13(12.14)
Aspergillus flavus	12(11.21)
Trichosporon spp.	4(3.73)
Aspergillus niger	2(1.86)
Aspergillus nidulans	2(1.86)
Penicillium spp.	1(0.93)
Curvularia	1(0.93)
Sepedonium	1(0.93)
Fusarium	1(0.93)
Exerohillium spp.	1(0.93)
Rhizopus spp	1(0.93)
Alternaria	1(0.93)
Aspergillus terreus	1(0.93)
Cryptococcus laurentii	1(0.93)

Table 5: Incidence of fungal pathogens in different ICUs

Intensive Care Units	Number of Isolates
ICCU	6
Aspergillus flavus	1
Candida albicans	2
Candida non-albicans	2
Penicillium spp.	1
GICU	1
Candida non-albicans	1
MICU	46
Aspergillus flavus	6
Aspergillus fumigatus	9
Aspergillus nidulans	1
Aspergillus niger	1
Aspergillus terreus	1
Candida albicans	11
Candida ciferrii	1
Candida non-albicans	9
Cryptococcus laurentii	1
Fusarium spp.	1
Rhizopus spp.	1
Trichosporon spp.	4
NICU	21

Alternaria	1
Aspergillus flavus	1
Candida albicans	10
Candida krusei	4
Candida non-albicans	5
PICU	2
Candida non-albicans	2
RICU	23
Aspergillus flavus	3
Aspergillus fumigatus	3
Aspergillus nidulans	1
Aspergillus niger	1
Candida albicans	8
Candida non-albicans	4
Curvularia	1
Exserohilium spp.	1
Sepedonium spp.	1
SICU	8
Aspergillus flavus	1
Aspergillus fumigatus	1
Candida albicans	4
Candida non-albicans	2
Total	107

Table 6: Incidence of fungal pathogens in various clinical conditions

Clinical Diagnosis	Growth		Isolates
	Positive (%)	Negative (%)	
Neonatal Sepsis	18 (7.47)	27 (3.19)	Candida albicans (7) Candida non-albicans (9) Aspergillus flavus (1) Alternaria (1)
Sepsis	14 (8.04)	5 (2.87)	Candida albicans (6) Candida non-albicans (4) Aspergillus fumigatus (3) Aspergillus flavus (1)
LRTI	49 (28.16)	21 (12.06)	Candida albicans (17) Candida non-albicans (13) Aspergillus fumigatus (9) Aspergillus flavus (5) Trichosporon (1) Rhizopus (1) Aspergillus Nidulans (1) Sepedonium (1) Penicillium (1)
Oral thrush	2 (1.14)	0	Candida albicans (2)
Sinusitis	2 (1.14)	1 (0.57)	Penicillium (1) Aspergillus terreus (1)
Pleural effusion	3 (1.72)	0	Aspergillus nidulans (1) Aspergillus flavus (2)
Pneumonia	24 (13.79)	17 (9.77)	Candida albicans (6) Candida non- albicans (5) Aspergillus flavus (3) Aspergillus fumigatus (5) Cryptococcus laurentii (1) Curvularia (1) Exserohilium spp. (1) Rhizopus spp. (1) Trichosporon spp. (1)

(Neonatal sepsis: Sepsis in new-born infants <1month; Sepsis: age group > 1month; LRTI (Lower Respiratory Tract Infection: Shortness of breath, fever, asthma, Chronic obstructive pulmonary disease, bronchitis; Oral thrush: oral candidiasis, Sinusitis: Sinus infection, pleural effusion: Build-up of fluid between tissues, Pneumonia.

DISCUSSION

In the present study, 174 clinically suspected fungal isolates were studied, out of which 101 (58%) were confirmed by KOH and culture which is in contrast to two studies showing prevalence of 82.7% and 13.2% respectively.^[16,17]

In this study, fungal infections are predominant in the age group of 41-60 years with male predominance

which in accordance to another study by M.T. Montagna et al. in which median age of the patients was 60 (44.5–71) years who were prone to fungal infection, with 63.8 % being males and 36.2 % females.^[18] Another study done by Sahni V et al. reported a similar range of 18 years to 80 years with a mean of 43.5 years.^[19] Fungal infections have increasingly become a problem among older adults as most of the older individuals admitted in ICUs are

already suffering from chronic illnesses which makes them immunocompromised and perfect candidates for getting fungal infections. Also older patients are more prone to receiving solid transplantation, undergoing aggressive treatment of malignancies, and taking immunosuppressive medications for dermatologic and rheumatologic diseases.

In this study; 60.74 % of the clinical isolates from ICUs were of the *Candida* genus and *Candida albicans* was the most prevalent species (32.7%) isolated from the respiratory tract and urinary tract which is in accordance with another study where *Candida albicans* accounted for about 89.9% of the total isolates.^[20] In a study by Akashdeep Singh et.al. the most common fungus isolated in patients with invasive fungal infections was *Candida* spp. in 54 (75%) patients, followed by *Aspergillus* spp. (22.2%).^[21] In this study fungal pathogens were causing infection in 55 (31.60%) cases with respiratory tract infection. In agreement with our results Basiri Jahromi et al. reported the same prevalence for fungal respiratory infections in Iran.^[22] Also Roohani AH et al. reported a prevalence of 26.7% for respiratory fungal infections in immunocompromised patients in India.^[23] Candiduria is rarely present in healthy individuals but is commonly found in hospitalized patients, especially those with multiple predisposing factors, including structural abnormalities of the kidney, diabetes mellitus, indwelling urinary catheters, immunosuppression and exposure to antimicrobials. Here in this study we found an incidence of fungal sepsis as 8.04%, where predominant organisms were *Candida albicans* and *NAC* spp. This is in contrast to another study by Vincent JL et al. that identified fungal infections in approximately 17% of the critically ill septic patients in several European countries.^[24]

Fungal isolates were mostly positive on day 5 of sample collection with 13.86% mortality rate which in contrast to another study where mortality rate is 50%.^[25] Studies by Singh et al,^[14] reported that most fungal isolates are positive on day 9, while another study from India reported that it is positive on day 15. For patients with high Invasive fungal disease (IFD) risk, early diagnosis and therapy are essential to achieve a better end result, including reduced morbidity and mortality.^[26]

In this study the most common specimens yielding fungal infections were sputum and other samples like BAL, Blood culture, endotracheal aspirate, pleural fluid and nasal swab. Similarly a study done by C.M.Chalmers et al. states that the sites that most frequently screened for colonization or infection with fungal infection are respiratory secretions.^[27] Fungal pathogens could trigger host immune response upon inhalation, and lung tissue is the major infectious target of these pathogens.

CONCLUSION

Fungal infection in critically ill patients is an increasingly prevalent problem. *Candida* spp. cause the majority of these infections in ICU. They occur most commonly in patients with severe underlying illness, multiple courses of antibiotics and intravascular catheters. Clinical diagnosis is difficult due to nonspecific signs and the frequent occurrence of widespread superficial colonization with *Candida* spp. in ventilated patients. The recent advances in management of life-threatening infections in intensive care unit with advent of broad-spectrum antibiotics have greatly reduced mortality but have significantly increased the incidence of invasive fungal infections. These invasive fungal infections are often difficult to diagnose and treat in the intensive care setting.

Candida albicans being the most commonly isolated organism in this study, is the leading cause superficial and invasive diseases in humans. Fungal infections are quite common in India because of hot and humid climate which leads to poor hygienic conditions.

To conclude, proper surveillance of fungal pathogens is important to improve quality of care in ICU. There is an urgent need for sensitization of health care personnel to evolve preventive risk factor protocols as part of standard of care to control the surge of fungal infections in critical care settings.

REFERENCES

1. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases—estimate precision. *J Fungi (Basel)*. (2017) 3:57. doi: 10.3390/jof3040057
2. Fisher MC, Hawkins NJ, Sanglard D, Gurr SJ. Worldwide emergence of resistance to antifungal drugs challenges human health and food security. *Science*. (2018) 360:739–42. doi: 10.1126/science.aap7999
3. Rodrigues ML, Nosanchuk JD. Fungal diseases as neglected pathogens: a wake-up call to public health officials. *PLoS Negl Trop Dis*. 2020;14
4. Perltroth J, Choi B, Spellberg B. Nosocomial fungal infections: epidemiology, diagnosis, and treatment. *Med Mycol*. (2007) 45:321–46. doi: 10.1080/13693780701218689
5. Suleyman G, Alangaden GJ. Nosocomial fungal infections: epidemiology, infection control, and prevention. *Infect Dis Clin North Am*. (2016) 30:1023– 52.
6. Lionakis MS, Hohl TM. Call to action: how to tackle emerging nosocomial fungal infections. *Cell Host Microbe*. (2020) 27:859–62. doi: 10.1016/j.chom.2020.04.011
7. Pfaller MA, Diekema DJ. Rare and emerging opportunistic fungal pathogens: concern for resistance beyond *Candida albicans* and *Aspergillus fumigatus*. *J Clin Microbiol*. (2004) 42:4419–31. doi: 10.1128/JCM.42.10.4419-4431.2004
8. Kumar D, Purbey M. Fungal Infections in Intensive Care Unit: Challenges in Diagnosis. *National Journal of Laboratory Medicine*. 2017 Apr, Vol-6(2): MR01-MR04.
9. Bajwa SJ, Kulshrestha A. Fungal Infections in Intensive Care Unit: Challenges in Diagnosis and Management. *Annals of Medical and Health Sciences Research*. Apr-Jun 2013;Vol 3:Issue 2.
10. Paramythiotou E, Frantzeskaki F, Flevari A, Armaganidis A, Dimopoulos G. Invasive fungal infections in the ICU: how to approach, how to treat. *Molecules*. 2014 Jan 17;19(1):1085-119. doi: 10.3390/molecules19011085. PMID: 24445340; PMCID: PMC6271196.

11. Gennaro De Pascalea and Mario Tumbarello. Fungal infections in the ICU: advances in treatment and diagnosis. 2015 Wolters Kluwer Health, Vol 21: 421-429
12. Crabol Y, Lortholary O. Invasive mold infections in solid organ transplant recipients. *Scientifica* (Cairo). 2014;2014:821969. doi: 10.1155/2014/821969. Epub 2014 Nov 23. PMID: 25525551; PMCID: PMC4261198.
13. Riwes MM, Wingard JR. Diagnostic methods for invasive fungal diseases in patients with hematologic malignancies. *Expert Rev Hematol*. 2012 Dec;5(6):661-9. doi: 10.1586/ehm.12.53. PMID: 23216596; PMCID: PMC3563387.
14. Singh A, Singh N, Chinna D, Invasive fungal infections in respiratory care unit: epidemiology and risk factors. *Indian Journal; of Research*, February-2018, Volume-7, 2250-1991
15. Rai DK. COVID-19 associated pulmonary mucormycosis: A systematic review of published cases with review of literature. *J Family Med Prim Care* 2022 Apr; 11(4):1244-9.
16. Shoham S, Marwaha S. Invasive fungal infections in the ICU. *Journal of intensive care medicine*. 2010;25(2):78-92.
17. Bateman M, Kheir F. Epidemiology of fungal infections in critically ill patients: analysis of a large observational database. *Chest*. 2019 Oct;156(4 Suppl).
18. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis*. 2019 Dec;19(12):e405-21.
19. Sahni V, Aggarwal SK, Singh NP, Anuradha S, Sidakkar S, Wadhwa A, et al. Candidemia--an under-recognized nosocomial infection in Indian hospitals. *J Assoc Physicians India* 2005;53:607-11
20. Paramythiotou E, Frantzeskaki F, Flevari A, Armaganidis A, Dimopoulos G. Invasive fungal infections in the ICU: how to approach, how to treat. *Molecules*. 2014 Jan 17;19(1):1085-119. doi: 10.3390/molecules19011085. PMID: 24445340; PMCID: PMC6271196.
21. Akashdeep Singh, Navdeep Singh, Deepinder China, Invasive fungal infections in respiratory intensive care unit: epidemiology and risk factors, *PARIPEX INDIAN JOURNAL OF RESEARCH: Volume-7 | Issue-2 | February-2018*
22. Basiri Jahromi SH, Khaksar AA. Respiratory fungal infections in specimens referred to the Pasteur Institute of Iran, 1994-2001. *Res Med* 2004; 28:265-268.
23. Roohani AH, Fatima N, Shameem M, Khan HM, Khan PA, Akhtar A. Comparing the profile of respiratory fungal pathogens amongst immunocompetent and immunocompromised hosts, their susceptibility pattern and correlation of various opportunistic respiratory fungal infections and their progression in relation to the CD4+ T-cell counts. *Indian J Med Microbiol* 2018; 36:408-415. Sobel JD, Revankar SG. Echinocandins--first-choice or first-line therapy for invasive candidiasis. *The New England journal of medicine*. 2007;356(24):2525-6.
24. Katragkou A, Walsh TJ, Roilides E. Why is mucormycosis more difficult to cure than more common mycoses? *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. 2014;20 Suppl 6:74-81.
25. Lamoth F. Galactomannan and 1,3-β-d-Glucan Testing for the Diagnosis of Invasive Aspergillosis. *J Fungi (Basel)*. 2016 Jul 4;2(3):22. doi: 10.3390/jof2030022. PMID: 29376937; PMCID: PMC5753135.
26. Sobel JD, Revankar SG. Echinocandins--first-choice or first-line therapy for invasive candidiasis. *The New England journal of medicine*. 2007;356(24):2525-6.
27. C. M. Chalmers, A. M. Bal, Management of fungal infections in the intensive care unit: a survey of UK practice, *BJA: British Journal of Anaesthesia*, Volume 106, Issue 6, June 2011, Pages 827-831.