International Journal of Advances in Medicine
Dash C et al. Int J Adv Med. 2019 Apr;6(2):521-525
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20191169

Original Research Article

Evaluation of Candida Score: a bedside scoring system for early antifungal therapy in non-neutropenic critically ill patients

Chinmaya Dash[1]*, Abhinanda Pal[2], Sulekha Sinha[3]

[1]Department of Microbiology, [2]MBBS Student, [3]Department of Biochemistry, IQ City Medical College and Narayana Multispeciality Hospital, Sovapur, Bijra Road, Jemua, Durgapur, West Bengal, India

Received: 11 February 2019
Accepted: 12 March 2019

***Correspondence:**
Dr. Sulekha Sinha,
E-mail: drsulekhasinha@gmail.com

ABSTRACT

Background: Invasive *Candida* infections are the most common invasive fungal infections. Multiple site colonization plays a major role. Further decrease in host immunity (e.g. neutropenia, diabetes mellitus etc.) aggravates local invasion and dissemination which finally leads to candidemia. Hence the study was done to evaluate "Candida Score" in non-neutropenic critically ill patients for early antifungal therapy.
Methods: In this prospective observational cohort study, all critically ill patients having sepsis or septic shock on admission or during their stay in ICU stay were included in the study. The components of "Candida Score" like severe sepsis, total parenteral nutrition, surgery, and multifocal *Candida* colonization were as per Leone et al. Clinical sepsis was given score of 2 if present and 0 if absent. The other variables were given score 01 if present and 0 if absent. The score more than 2.5 is considered significant.
Results: Out of 78 patients admitted in the ICU a total of 26 blood culture positives were reported. The prevalence of Candidemia (based on culture) was 23.1% (n=06). The strains isolated were *Candida non albicans* (n=4, 66.7%) and *Canida albicans* (n=2, 33.3%). *Candida* was isolated in different samples other than blood culture of 26(33.33%). The most common specimen with *Candida* isolation was from urine (n=14, 60.87%), followed by endotracheal aspiration and sputum (n=3, 13% each) and BAL fluid (n=1, 04.3%). Among the isolates *Candida non albicans* (n=12, 52.2%) was more prevalent than *Candida albicans* (n=11, 47.8%). The prevalence was maximum for the age group of 60 to 69 years (42.31%) followed by 70 to 79 yrs and 50-59 yrs. Among all patients, 14 patients were referred in our hospital and 12 of them had a prolonged ICU stay (>10 Days). The patients with the Candida score ≥2.5 were 06 in numbers, of which 66.7% were having score 3 followed by one each of having score 4 and 5. Out of these 06 patients 04 received antifungal treatment. One patient with Candida score more than 03 succumbed to death without having antifungal treatment.
Conclusions: Early identification of invasive candidiasis with the use of "Candida Score" in critically ill patients may help to initiate antifungal interventions and even help the treating physician or intensivist to formulate the more effective treatment algorithms.

Keywords: *Candida*, Candida score, ICU, Invasive candidiasis

INTRODUCTION

Invasive *Candida* infections are the most common invasive fungal infections, accounting for 70-90% of all invasive mycoses.[1] *Candida* colonization of mucous membranes and its invasion of tissue and/or dissemination via bloodstream mostly depend on host defence e.g. highest incidence in immunocompromised patients like HIV/AIDS. This may affect the incidence of morbidity and mortality by candidial infection viz. ranked

4th in United States among all nosocomial infection especially in critical care areas.[2,3]

In studies done in the United States, European countries show a significant increase in the invasive candidiasis in the adult patients of critical care units other than wards with the highest prevalence among surgical patients. For examples, the incidence of candidemia in U.S. hospitals during 2000-2005 increased from 3.65 to 5.56 episodes per 100,000 population, and 2,820 cases of fungemia in Denmark during the period 2004-2009, reported an increasing incidence from 7.7 to 8.6 per 100,000.[4,5] These data show that incidence is in the upward trend during the last 5-10 year in different geographical regions.[6]

Several risk factors are associated with invasive candidiasis, and among those, multiple site colonization plays a major role. *Candida* spp. overgrowth helped by the changes in normal microbial flora (e.g. may be due to prolonged antibiotic therapy, >50% Burn etc.) and disruption and invasion of the skin or mucosal barrier which is facilitated by invasive procedures like intravenous channels, trauma and surgeries. Further decrease in host immunity (e.g. due to neutropenia, diabetes mellitus etc) aggravates local invasion and dissemination which finally leads to candidemia.[7]

However, early diagnosis of invasive candidiasis is difficult, because they have variable and non-specific manifestations and the criteria for starting empirical antifungal therapy in ICU patients are poorly defined. The risk factors for invasive candidiasis are so numerous that most ICU patients could be considered as exhibiting risk factors for invasive candidiasis. But, the use of excessive antifungal agents would be associated with substantially increased overall health care costs and might lead to the emergence of resistance. Management with antifungal therapy in candidemia patients has shown reduction in mortality rate. The basis of risk factors and colonization does not have strong implication for the early use of antifungal therapy. Still, early antifungal therapy may be useful in patients with high score or patient not responding to antibacterial therapy.[8,9]

Leon et al, developed "Candida Score" a scoring system combining the risk factors and *Candida* colonization. The factors to predict invasive candidiasis were surgery, multifocal colonization, total parenteral nutrition and severe sepsis. To each risk factor, one point was given and for Clinical sepsis was given score of two. The cut-off value of 2.5 had sensitivity 81% and specificity 74%.[10,11]

METHODS

This is a prospective observational cohort study. For the same, a clearance from the institutional ethical committee was taken. This study was conducted in the Critical Care Unit of a tertiary health care centre of West Bengal, India during the month of June and July 2018 (duration of two months). All critically ill patients having sepsis or septic shock on admission or during their stay in ICU stay were included in the study.

Inclusion criteria

Patients admitted to the ICU with the following:

- Age > 18 yrs
- Sepsis (diagnosed microbiologically based on blood culture positivity) or septic shock
- Systemic inflammatory response syndrome (SIRS): SIRS is defined as 2 or more of the variables like temperature >38^0 C or <36^0C, heart rate >90/min, respiratory rate >20/min, total leukocyte count >12,000/mm^3 or <4000/mm^3 or >10% bands.

Exclusion criteria

- Patient's of age ≤18 yrs,
- Patient with neutropenia (total leukocyte count <500/mm^3),
- Pregnant women and nursing mother,
- Patients who were already on antifungal treatment.

The clinico-epidemiological information along with informed consent from nearby relatives of all patients were included in the study.

Microbiological isolation of *Candida* spp. was done after taking samples from different body sites like blood, respiratory, urine, pus etc. Samples were processed according to the CLSI guidelines. Blood samples for candidemia were processed in BD-BACTEC ™. Isolation of a *Candida* spp. in one or more blood cultures in a patient with consistent clinical manifestations provides the diagnosis of candidemia.[11]

Screening for *Candida* colonization was performed twice weekly by routine sampling from tracheal aspirates and urine. Other samples from vascular catheters, wound or drainage exudates, or other infected foci were obtained at the discretion of the attending physician. Isolation of *Candida* from one focus or site was defined as unifocal colonization and multi focal colonization was defined when it is isolated in more than one non contiguous foci even with different species.

Table 1: The candida score variables.

Variables for Candida score	Score if present	Score if absent
Clinical sepsis	2	0
TPN (total parenteral nutrition)	1	0
Surgery	1	0
Multifocal Colonization	1	0

In this study, components of "Candida Score" like severe sepsis, total parenteral nutrition, surgery, and multifocal

Candida colonization were as per Leone et al. Bedside scoring was done for each patient. Clinical sepsis was given score of 2 if present and 0 if absent. All other variables were given score 01 if present and 0 if absent as shown in Table 1. Value more than 2.5 is considered significant. Samples from tracheal aspirates or urine were obtained at admission and the final Candida Score is only determined when cultures results are available.[10,11]

Statistical analysis

Variables are expressed as median values and ranges for numerical variables and as frequencies and percentages for categorical variables. Categorical variables are compared using the Chi-square tests. Numerical variables are compared using Student's t test.

RESULTS

During the period of study, a total of 78 patients were admitted in the ICU and as per Figure 1, age groups of patients included in this study varied from 29 to 80 yrs of age with preponderance to the age group of 60 to 69 years i.e., (n=11, 42.31%) followed by the age group 70 to 79 years i.e., (n=06, 23.08%) and 50-59 years i.e., (n=04, 15.38%). Among them, males were 17 (62.96%) and 10 (37.03%) females.

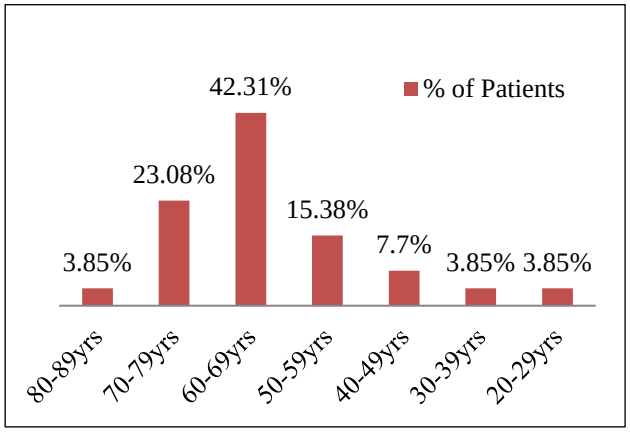

Figure 1: Age wise distribution of patients in percentage.

Candida spp. was isolated microbiologically in 26 (33.33%) different patients in various samples including blood culture. As per the Figure 2, the most common specimen with *Candida* isolation was from urine (n=14, 60.87%), followed by blood (n=06, 23.01%), endotracheal aspiration and sputum (n=3, 13% each) and BAL fluid (n=1, 04.3%). Figure 3 shows prevalence of *Candida non albicans* (n=14,53.8%) was more than *Candida albicans* (n=12, 46.2%). A total of 26 blood culture positives were reported. The prevalence of Candidemia among the confirmed cases sepsis (based on culture) was 23.1% (n=06). The strains of *Candida* isolated were *Candida non albicans* (n=4, 66.7%) and *Candida albicans* (n=2, 33.3%).

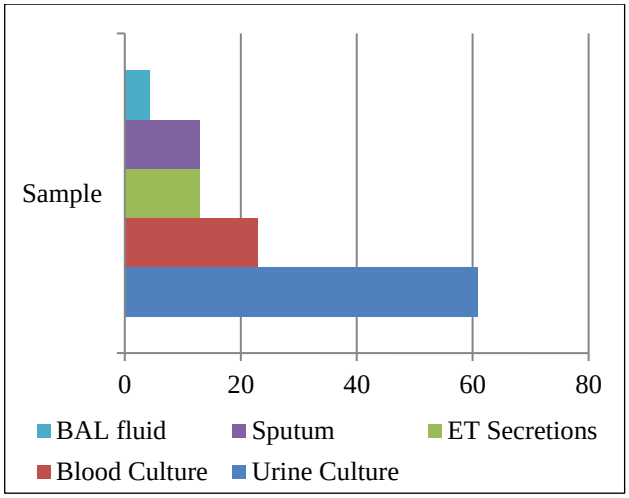

Figure 2: Percentage of *Candida* spp. isolated in different specimen.

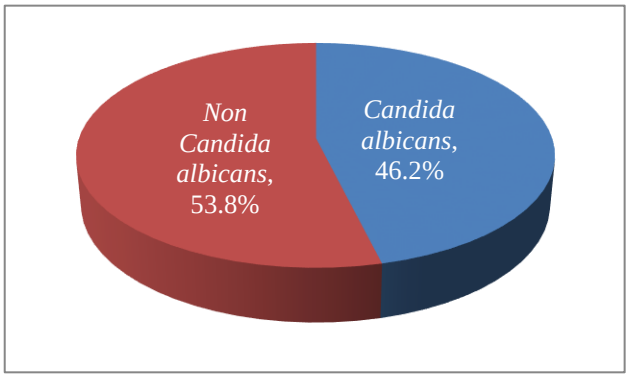

Figure 3: Percentage of different *Candida* spp. isolated.

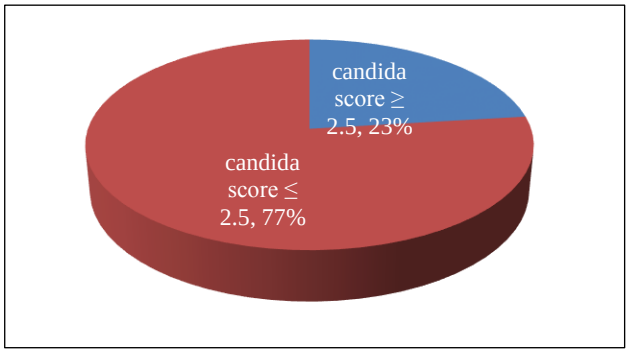

Figure 4: The candida score of enrolled patients.

The percentage of patients with *Candida* infection showing risk factors were mentioned in the Table 2. Which shows maximum number of patients having sepsis (n=26.33.33%) followed by multifocal colonization (n=23, 29.49%), patients on total parenteral nutrition (n=8, 10.26%) and surgery (n=3, 3.85%). As per Figure 4, the patients with the Candida score ≥2.5 were 06 in numbers, of which 04 (66.7%) were having score 3 followed by one each of having score 4 and 5. Out of these 06 patients 04 received antifungal treatment. We

found that the one patient with Candida score more than 03 succumbed to death without having antifungal treatment.

Table-2: Percentage (%) of patients with *Candida* infection showing risk factors.

Parameters	Presence	
	n	%
Sepsis or SIRS	26	33.33
Surgery	3	3.85
TPN (Total Parenteral Nutrition)	8	10.26
Multifocal colonization	23	29.49

n= No. of patients

Among all these patients, 14 patients were referred from different hospitals before getting treated in our hospital and 12 of them had a prolonged ICU stay (>10 Days). Almost all the patients included in this study were on higher antibiotics for a prolonged duration.

DISCUSSION

Being one of the most common bloodstream infections among the critical care areas of healthcare settings, invasive candidiasis needs to be diagnosed early and an early treatment to reduce the mortality.

The prevalence of candidemia in our study was 23.1%. Candidemia is affecting mostly to the extremes of ages due to the underdeveloped immune system in neonates or infants and waning off of the immune response in elderly. The age distribution of the recruited patients varied from 29yrs to 80yrs with a maximum preponderance to the age group (60-69) yrs i.e., (40.75%), followed by age groups (70-79) yrs and (50-59) yrs. The male outnumbered females in our study with the male-to-female ratio being 1.6:1 which correspond with other similar studies conducted. Similar findings were reported in the studies done by Leon et al and Leroy et al.[9,11]

Similar to our findings, in the study done by P Gupta et al, on patients admitted to the intensive care unit of a tertiary care hospital of Uttarakhand, India, risk factors associated with candidemia were prolonged antibiotic use, prolonged ICU stay, multifocal colonization, and recent surgery, clinical sepsis and previous hospitalization. In that study, it was concluded that Leone score of ≥2.5 is most suitable for ruling in the diagnosis of invasive candidiasis.[12] However, Leon et al and Blumberg et al reported Total Parenteral Nutrition (TPN) as a clinically significant risk factor; similarly, we observed only 03 patients on TPN and out of them 02 were having candidemia. But the relation cannot be established due to lower usage of TPN in our ICU during the study period.[10,13]

A study by Leroy G et al in five intensive care units of Nord-Pas de Calais, France where the incidence rates of invasive candidiasis were found to be 0%, 0%, 17.6%, and 50% in patients with scores equal to 02,03,04, and 05, respectively, similar findings were seen in our study. Which suggests a linear and significant association between increasing value of the "Candida score" and the rate of invasive candidiasis observed, and no invasive candidiasis occurred with scores <3.[14]

The decision to initiate antifungal drugs during this observational study was at the discretion of the attending physician. Out of the 06 patients having Candida score ≥3, only 04 received antifungal treatment. Out of the rest 02 patients with the Candida score ≥3, one succumbed to illness. So, we observed a relationship between initiation of antifungal agents and the value of "*Candida* score."

Lindau S et al, in their study found that antifungal therapy was not independently associated with favourable outcome. Among isolated pulmonary *Candida* spp. colonization patients, mortality rate and pneumonia rate were higher in the group who received antifungal therapy. This implies that antifungal therapy may not have impact on mortality rate. So, it requires further study with a large number of study populations to establish the relation.[15]

'Candida score' could prove to be a very useful tool, to distinguish between the patients who would benefit from an early antifungal therapy, from those who are very less likely to develop invasive candidiasis. Our prospective, observational study that was conducted over a period of two months, hence aims to evaluate the relationship between the presence of invasive candidiasis and the "Candida score" value. This could reduce the mortality associated with invasive candidiasis. It would also prevent the development of resistance, which is associated with excessive use of antifungals and hence cut down healthcare costs.[7]

CONCLUSION

Early identification of invasive candidiasis with the use of "Candida Score" in critically ill patients may help to initiate antifungal interventions and even help the treating physician or intensivist to formulate the more effective treatment algorithms. This may help in decreasing the mortality associated with invasive *Candida* infection. The study has limitation due to less sample size. This kind of study may have more impact if done with more sample size.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Lamagni TL, Evans BG, Shigematsu M, Johnson EM. Emerging trends in the epidemiology of

invasive mycoses in England and Wales (1990-9) Epidemiol Infect. 2001;126:397-414.
2. Leleu G, Aegerter P, Guidet B. Systemic candidiasis in intensive care units: a multicenter, matched-cohort study. J Crit Care. 2002;17:168-75.
3. Montravers P, Mira JP, Gangneux JP, Leroy O, Lortholary O. for the Amar C and Study Group. A multicentre study of antifungal strategies and outcome of Candida spp. peritonitis in intensive-care units. Clin Microbiol Infect. 2011;17:1061-7.
4. Zilberberg MD, Shorr AF, Kollef MH: Secular trends in candidemia-related hospitalization in the United States, 2000-2005. Infect Control Hosp Epidemiol. 2008;29:978-80.
5. Martin GS, Mannino DM, Eaton S, Moss M: The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348:1546-54.
6. Tortorano AM, Kibbler C, Peman J, Bernhardt H, Klingspor L, Grillot R: Candidaemia in Europe: epidemiology and resistance. Int J Antimicro Agents. 2006;27:359-66.
7. Eggimann P, Bille J, Marchetti O. Diagnosis of invasive candidiasis in the ICU. Annals Intensive Care. 2011 Dec;1(1):37.
8. Parkins MD, Sabuda DM, Elsayed S, Laupland KB. Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive Candida species infections. J Antimicro Chemother. 2007;60:613-8.
9. Prod'hom G, Bizzini A, Durussel C, Bille J, Greub G: Matrix-assisted laser desorption ionization-time of flight mass spectrometry for direct bacterial identification from positive blood culture pellets. J Clin Microbiol. 2010;48:1481-3.
10. León C, Ruiz-Santana S, Saavedra P, Almirante B, Nolla-Salas J, Alvarez-Lerma F, et al. A bedside scoring system (Candida score) for early antifungal treatment in non-neutropenic critically ill patients with Candida colonization. Crit Care Med. 2006;34:730-7.
11. León C, Ruiz-Santana S, Saavedra P, Galván B, Blanco A, Castro C, et al. Usefulness of the "Candida score" for discriminating between Candida colonization and invasive candidiasis in non-neutropenic critically ill patients: a prospective multicenter study. Crit Care Med. 2009;37:1624-33.
12. Gupta P, Chatterjee B, Mittal G, Prateek S, and Mohanty A. Evaluation of Candida Scoring Systems to Predict Early Candidemia: A Prospective and Observational Study at a Tertiary Care Hospital, Uttarakhand. Indian J Crit Care Med. 2017;21(12):830-5.
13. 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. 2001;33:177-86.
14. Leroy G, Lambiotte F, Thévenin D, Lemaire C, Parmentier E, Devos P, et al. Evaluation of" Candida score" in critically ill patients: a prospective, multicenter, observational, cohort study. Annals of Intensive Care. 2011 Dec 1;1(1):50.
15. Lindau S, Nadermann M, Ackermann H, Bingold TM, Stephan C, Kempf VA, et al. Antifungal therapy in patients with pulmonary Candida spp. colonization may have no beneficial effects. J Intensive Care. 2015 Dec;3(1):31.

Cite this article as: Dash C, Pal A, Sinha S. Evaluation of Candida Score: a bedside scoring system for early antifungal therapy in non-neutropenic critically ill patients. Int J Adv Med 2019;6:521-5.