



CLINICO-MYCOLOGICAL STUDY OF CANDIDEMIA IN A ADULT PATIENTS

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ABSTRACT **INTRODUCTION:** Blood stream infections (BSIs) caused by *Candida* species is known as candidemia. Candidemia is one of the most significant causes of morbidity and mortality in hospitalized patients especially in the intensive care units (ICU). *Candida* species causes wide variety of infections, ranging from mild muco-cutaneous to severe invasive infections that can involve any organ. **OBJECTIVE:** The present study was conducted to determine burden of candidemia in suspected cases of blood stream infections (BSIs) in tertiary care hospital. Also to identify the species of *Candida* isolated from the patients of candidemia and to find out risk factors associated with patients of candidemia. **MATERIALS AND METHODS:** Clinically suspected adult cases of BSIs during 1 year study period were processed at Microbiology laboratory by standard conventional technique. The risk factors associated with patients of candidemia were also assessed. **RESULTS:** Out of 1941 cases of BSIs, confirmed cases of Candidemia was in 12 (0.62%) cases. In our study all cases of candidemia were due to *non-albicans Candida*, the most common isolate was *C.parapsilosis* i.e (50.00%) whereas *C.tropicalis* and *C.glabrata* (16.66%) was the second common isolate, followed by *C.famata* and *C.rugosa* (08.33). Intravenous catheter and exposure to antibiotics were the commonest (100 %) risk factors followed by prolonged hospital stay of more than 10 days (91.66%). Central venous catheter, assisted ventilation in ICU, respiratory disease, renal disease, diabetes mellitus, liver disease were also the other associated risk factors of candidemia in adults. **CONCLUSION:** The present study highlights the disease burden of candidemia in clinically suspected BSIs. Routine screening of BSIs for candidemia is important for appropriate management of the patients. The knowledge of risk factor such as prolonged use of antibiotics associated with candidemia can be prevented by implementation of antibiotics stewardship program.

KEYWORDS : Blood stream infections, Candidemia, Antibiotic stewardship

INTRODUCTION

Candidemia is one of the most significant causes of morbidity and mortality in hospitalized patients especially in the intensive care units (ICU) ⁽¹⁾. Blood stream infections (BSIs) caused by *Candida* species is known as candidemia. It has been estimated that approximately 10-20% of all nosocomial blood stream infections in ICUs are due to *Candida* species ⁽²⁾. It is associated with prolonged hospital stay and increased healthcare cost. Candidemia is defined as isolation of any *Candida* species from at least one blood culture with supportive clinical features ⁽³⁾.

Candida species causes wide variety of infections, ranging from mild muco-cutaneous to severe invasive infections that can involve any organ ⁽⁴⁾. The epidemiology of candidemia has changed in the past three decades due to the AIDS pandemic, increases number of patients receiving immunosuppressive therapy for transplantation and the increasing use of antimicrobial agents in hospitals as well as in the community ⁽⁵⁾.

MATERIAL AND METHODS:

The study was conducted in Department of Microbiology at a tertiary care hospital. The protocol was submitted to Institutional Ethical Committee (IEC). After getting a due permission from IEC, the study was commenced. The study was prospective, observational, single centre prevalence study. Study period was one year from January 2017 to December 2017.

Patients with clinically suspected blood stream infections (BSIs) admitted to a Tertiary Care Hospital were included in a present study.

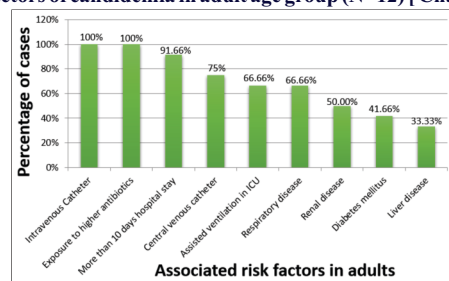
Patients with confirmed diagnosis of any known blood stream infection (BSI) other than candidemia were excluded. Written informed consent was taken from the patient or relative or parents in case of neonate and children. A detailed 'case history form' of patient information was prepared. Detailed history of patients including name, age, sex, chief complaints was taken. Important clinical features and co-morbidity were noted. Blood samples from

clinically suspected cases of BSIs were received in Brain Heart Infusion broth to Microbiology Laboratory. These Brain Heart infusion broths were incubated aerobically at 37^oC. After the incubation at 37^oC, they were sub-cultured thrice (1st, 3rd, 7th day of incubation) on Sabouraud's dextrose agar (SDA) with chloramphenicol and SDA with chloramphenicol and cycloheximide in duplicate. One set of SDA with chloramphenicol and SDA with chloramphenicol and cycloheximide was incubated at 37^oC. and another set of SDA with chloramphenicol and SDA with chloramphenicol and cycloheximide was incubated at 25^oC. All four SDA were checked daily for growth till one week. "Candidemia was diagnosed by isolation of *Candida* species from at least one positive blood culture containing pure growth of *Candida* species with supportive clinical features". If no growth after one week of incubation, then they were reported as no candidemia isolated.

RESULTS:

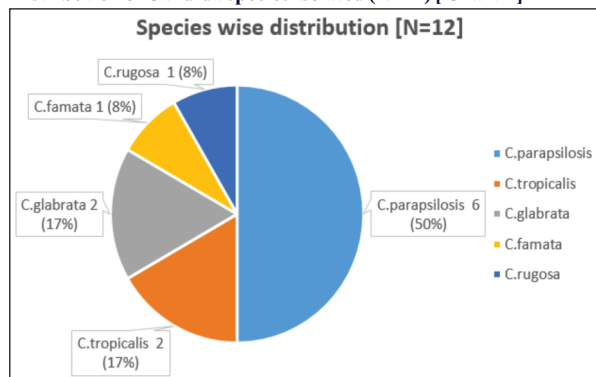
A total 1941 samples from suspected adult cases of BSIs were received in Microbiology laboratory during a study period, from January 2017 to December 2017 & were processed by standard conventional technique. In adults i.e above 19 years age group 982 were male and 959 were female cases. Out of 1941 clinically suspected cases of BSIs 12 (0.62%) were confirmed as candidemia.

Risk factors of candidemia in adult age group (N=12) [Chart 1]



Intravenous catheter and exposure to antibiotics were the commonest (100%) risk factors followed by prolonged hospital stay of more than 10 days (91.66%). Central venous catheter, assisted ventilation in ICU, respiratory disease, renal disease, diabetes mellitus, liver disease were also the other associated risk factors of candidemia in adults [Chart 1].

Distribution of Candida species Isolated (N=12) [Chart 2]



In our study the most common isolate was *C.parapsilosis* i.e (50.00%) whereas *C. tropicalis* and *C.glabrata* (16.66%) was the second common isolate, followed by *C.famata* and *C.rugosa* (08.33) [Chart 2].

DISCUSSION:

Worldwide *Candida* species are the most common cause of fungal infections. Among these infections blood stream infections (BSIs) due to *Candida* species are the fourth most common cause of candidemia and are associated with high mortality in hospitalized patients^(6,7). Prolonged hospital stay is associated with candidemia, which increases the healthcare cost⁽⁸⁾.

In present study overall prevalence of candidemia in clinically suspected cases of BSIs was 0.62% (12 out of 1941). A study by Oberoi *et al*⁽¹⁵⁾ from New Delhi and Verma *et al*⁽¹⁶⁾ from Lucknow on candidemia reported overall prevalence of 1.74% and 1.61% respectively. A study by Giri *et al*⁽¹⁷⁾ from Tamil Nadu over a period of one year total 5976 suspected blood stream infections were received and out of these 39 were positive for candidemia with overall prevalence of 0.65%. Thus prevalence of candidemia in present study (0.62%) was comparable with studies done by Oberoi *et al*⁽¹⁵⁾, Verma *et al*⁽¹⁶⁾ and Giri *et al*⁽¹⁷⁾ where the prevalence was 1.74%, 1.61%, and 0.65% respectively.

In present study the reason for lower prevalence of overall candidemia as compared to Bhattacharjee *et al*⁽¹⁸⁾ and Xess *et al*⁽¹⁴⁾ could be due to infection control measures, hand hygiene practices and intravenous catheter care.

Prevalence of candidemia in adults by various studies

Sr. No.	Author	Year and place	Candidemia in adults (%)
1	Gupta <i>et al</i> ⁽⁴⁾	2015, Dehradun	16.00
2	Arora <i>et al</i> ⁽¹⁰⁾	2010, Bhatinda	09.86
3	Bhatt <i>et al</i> ⁽⁶⁾	2015, Odisha	09.40
4	Kaur <i>et al</i> ⁽¹¹⁾	2014, New Delhi	08.00
5	Tak <i>et al</i> ⁽⁸⁾	2014, New Delhi	07.40
6	Sahni <i>et al</i> ⁽⁹⁾	2005, New Delhi	06.90
7	Tejan <i>et al</i> ⁽¹³⁾	2017, Chandigarh	05.80
8	Gandham <i>et al</i> ⁽¹⁹⁾	2016, Pune	03.40
9	Paula <i>et al</i> ⁽²⁰⁾	2018, Brazil	01.30
10	Present study	2018	00.62
11	Chander <i>et al</i> ⁽⁷⁾	2013, Chandigarh	00.58

The prevalence of candidemia in adults was 0.62% in present study which was comparable with similar study in adult patients by Chander *et al*⁽⁷⁾ and Paula *et al*⁽²⁰⁾ with prevalence of 0.58% and 1.30% respectively. A study done by Gandham *et al*⁽¹⁹⁾ found 3.4% little higher prevalence in adults as compared to that of present study. Similar studies in adults done by Gupta *et al*⁽⁴⁾ (16%), Arora *et al*⁽¹⁰⁾ (9.86%), Bhatt *et al*⁽⁶⁾ (9.4%), Kaur *et al*⁽¹¹⁾ (8%), Tak *et al*⁽⁸⁾ (7.4%), Sahni *et al*⁽⁹⁾ (6.9%) and Tejan *et al*⁽¹³⁾ (5.8%) reported the high prevalence of candidemia as compared to present study.

Gupta *et al*⁽⁴⁾, Kaur *et al*⁽¹¹⁾ and Tejan *et al*⁽¹³⁾ had selected the cases admitted only from intensive care units. This could be the reason of high prevalence in their study as compared to present study, as in present study all clinically suspected cases of BSIs from different wards and ICUs were included.

Tak *et al*⁽⁸⁾ did a study of candidemia at trauma care center in critically ill adults. They found high prevalence of candidemia in adults as compared to present study. This could be the reason for difference in prevalence.

Gupta *et al*⁽⁴⁾ from India studied prevalence of candidemia in among the patients admitted in ICU. They concluded that there is wide variation in the prevalence of candidemia in different geographical location of India. This could be the reason for high prevalence of candidemia in adults of the studies by Gupta *et al*⁽⁴⁾, Arora *et al*⁽¹⁰⁾, Bhatt *et al*⁽⁶⁾, Kaur *et al*⁽¹¹⁾, Tak *et al*⁽⁸⁾, Sahni *et al*⁽⁹⁾, Tejan *et al*⁽¹³⁾ than the present study.

In present study among the adult age group exposure to higher antibiotics was found in all cases as associated risk factor in candidemia of adults. Sahni *et al*⁽⁹⁾, Arora *et al*⁽¹⁰⁾, Tak *et al*⁽⁸⁾, Kaur *et al*⁽¹¹⁾ and Bhatt *et al*⁽⁶⁾ also found that use of antibiotics as an associated risk factor of candidemia in adults.

In present study among the adult age group presence of intravenous catheter in 100% cases were found as associated risk factor in all cases of candidemia in adults. A study by Arora *et al*⁽¹⁰⁾, Bhatt *et al*⁽⁶⁾ and Tak *et al*⁽⁸⁾ did similar study to assess this associated risk factor in cases of adult candidemia. They concluded that presence intravenous catheter is associated with candidemia in adults.

The risk factor of prolonged hospital stay of more than 10 days was assessed in the present study with adult candidemia cases. It was found to be 91.66%. Prolonged hospital stay as an associated risk factor was assessed by Tak *et al*⁽⁸⁾ in a study at trauma care center at New Delhi. They found that it was one of the risk factor for candidemia in adults.

In 75% of adult candidemia cases of the present study, central venous catheter was the associated risk factor. Tak *et al*⁽⁸⁾ also found similar risk factor responsible for candidemia in adults.

In present study among the adult age group mechanical ventilation was found in 66.66% cases as associated risk factor. Comparable results were found in a similar study by Bhatt *et al*⁽⁶⁾ (65%).

In present study associated risk factor of adult candidemia was respiratory disease (66.6%), renal disease (50%), diabetes mellitus (41.6%), and liver disease (33.3%). Cleveland *et al*⁽¹²⁾ also reported respiratory disease, renal disease, diabetes mellitus and liver disease as one of the risk factor in adult candidemia. Tejan *et al*⁽¹³⁾ found diabetes mellitus (14.6%) in overall cases of candidemia. Kaur *et al*⁽¹¹⁾ and Chander *et al*⁽⁷⁾ also reported renal disease, diabetes mellitus as one of the associated risk factor of candidemia.

Clinical suspicion and early diagnosis of candidemia is essential in all clinically suspected cases of blood stream infection. It will help the clinicians in accurate management of these patients, which will reduce morbidity and mortality⁽⁸⁾. There is a variation in prevalence of candidemia and species distribution in different geographical area of India. Overall there is significant shift of higher isolation of non-albicans *Candida* species than *Candida albicans* in patients of candidemia⁽⁴⁾. Xess *et al*⁽¹⁴⁾ observed that there was higher mortality in cases of candidemia caused by *C.tropicalis* and *C.albicans* as compared to other species, hence it is important to identify *Candida* up to species level in patients with candidemia. Sahni *et al*⁽⁹⁾ also found that *C.parapsilosis* was one of the species isolated among non-albicans *Candida* in adult candidemia cases. A study by Tak *et al*⁽⁸⁾ found that *C.tropicalis* (38.7%) was the commonest isolate followed by *C.parapsilosis* as the second most common (20.3%) isolate among the adult cases of candidemia in an Indian trauma care center. Similar study by Bhatt *et al*⁽⁶⁾ found that *C.tropicalis* (39%) was the commonest followed by *C.parapsilosis* (20.5%). Thus in studies by Tak *et al*⁽⁸⁾ and Sahni *et al*⁽⁹⁾ *C.tropicalis* was the commonest as against in present study *C.parapsilosis* was the commonest in cases of adult candidemia. Gupta *et al*⁽⁴⁾ concluded that there is a wide geographical variation in the species distribution of candidemia. This could be the reason for difference in species distribution of adult candidemia in present study and other studies by Tak *et al*⁽⁸⁾ and Sahni *et al*⁽⁹⁾. In present study two (16.66%) cases of *C.tropicalis* and *C.glabrata* each were found in total 12 cases of adult candidemia. Kaur *et al*⁽¹¹⁾, Gupta *et al*⁽⁴⁾ also found

C.tropicalis and *C.glabrata* as one of the cause of candidemia in adults.

With this background the present study was focused on prevalence of candidemia in clinically suspected cases of BSIs of a tertiary care hospital. The study was also aimed to identify the *Candida* up to species level in confirmed cases of candidemia.

SUMMARY AND CONCLUSION:

The aim of the present study was to determine burden of candidemia in clinically suspected cases of blood stream infections (BSIs) in tertiary care hospital and to identify the species of *Candida* isolated from the patients of candidemia. The risk factors associated with patients of candidemia were also assessed. The study was conducted in department of Microbiology from January 2017 to December 2017.

A total 1941 suspected adult cases of BSIs i.e. blood culture samples were received in Microbiology laboratory during study period. Clinically suspected cases of BSIs were processed by conventional culture technique to isolate and identify *Candida* up-to species level. Candidemia was diagnosed by isolation of *Candida* species from at least one positive blood culture containing pure growth of *Candida* species with supportive clinical features. A study was also focused on associated risk factors in confirmed cases of candidemia. Out of 1941 clinically suspected cases of BSIs 12 (0.62%) were confirmed as candidemia. In adults the commonest risk factors were intravenous catheter (100%) and exposure to antibiotics (100 %) followed by prolonged hospital stay (91.66%). Central venous catheter, assisted ventilation in ICU, respiratory disease, renal disease, diabetes mellitus, liver disease were also the other associated risk factor of candidemia in adults. All the isolated *Candida* species from cases of candidemia were *non-albicans Candida*. Out of 12 isolates of *Candida* species, *C.parapsilosis* was the commonest isolate followed by *C.tropicalis* and *C.glabrata*.

To conclude, the present study highlights the disease burden of candidemia in clinically suspected BSIs. Routine screening of BSIs for candidemia is important for appropriate management of the patients. This study assessed the risk factors associated with cases of candidemia. The knowledge of risk factor such as prolonged use of antibiotics associated with candidemia can be prevented by implementation of antibiotics stewardship program. The risk factor such as intravenous and central venous catheter can be prevented by use of aseptic technique and catheter bundling. Preventive measure such as use of filters for parenteral nutrition can prevent *Candida* colonization in cases where it is an associated risk factor. Thus assessment of risk factors associated with candidemia is necessary for each and every case which will be helpful for preventive purpose.

In present study all cases of candidemia were due to *non-albicans Candida*. As per the literatures resistance pattern of *Candida* varies from species to species. Hence it is essential to isolate and identify the *Candida* up-to species level from all cases of candidemia. It will be helpful for the clinicians to start an empirical therapy as per the common species isolated in particular geographical region, when antifungal susceptibility testing is not available.

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