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The burden of catheter associated urinary tract infection by candida Albicans and non Albicans with emphasis on biofilm formation and antifungal sensitivity pattern

Yogendra Singh

Research Scholar, Department of microbiology, Index Medical College Hospital and Research Centre, Indore, Malwanchal University

Ramanath Karicheri

Professor, Department of microbiology, Index Medical College Hospital and Research Centre, Indore, Malwanchal University

Dvijendra Nath

Professor and Dean, Department of Pathology, Government Medical College, Jalaun (Orai)

Abstract---Candida spp. is generally found in humans; however, when the host's immune system is compromised, the pathogen infects the host, earning it the name opportunistic pathogen. It can also be found on the surfaces of biomaterials such as catheters, Venflon, intravenous tubes, dentures, and blood bags in a medical setting. It infects people who have been admitted to the hospital. This causes major health problems for the patients and raises morbidity and mortality rates over time. Those who take antifungal medications for this infection on a regular basis acquire resistant to the drugs. Candida albicans and non-Candida albicans were found to predominate in distinct clinical samples in this investigation. The goal of this cross-sectional study, which took place at the Index Medical College Hospital and Research Centre, Indore, was to determine the burden of catheter associated urinary tract infection by candida albicans and non albicans with emphasis on biofilm formation. CAUTI is a prevalent complication in critically ill individuals. In order to reduce the incidence of catheter-related UTI, the focus should be on appropriate catheter maintenance and lowering catheterization length rather than prophylactic. In the treatment of CAUTI, culture and susceptibility testing are crucial.

Keywords---antifungal sensitivity, burden catheter, *Candida Albicans*.

Introduction

Indwelling intravascular and urinary catheters are essential components of modern medical care. Unfortunately, indwelling devices significantly increase the risk of iatrogenic infection, particularly in an already fragile patient population. Most nosocomial infections in severely ill patients are associated with the very medical devices that provide life-sustaining care (1). Indwelling urinary catheterization is the most common risk factor for complicated UTI; such catheter-associated UTI (CAUTI) accounts for 40.0% of all nosocomial infections worldwide and often leads to secondary bloodstream infections (2). Though recognition of this risk has led to reductions in insertion or duration of use of indwelling urinary catheters, a sizable number of hospitalized patients still undergo urinary catheterization during their stay. In the United States, the 30 million Foley catheters used annually confer substantial risk for CAUTI (3).³

Urinary tract infections are the most common type of healthcare-associated infection; accounting for more than 30.0% of infections reported by acute care hospitals and 23.0% of hospital-acquired infections (HAI) in intensive care units (ICU) (3). Virtually all healthcare-associated UTIs are caused by instrumentation of the urinary tract. Catheter associated urinary tract infection (CAUTI) has been associated with increased morbidity, mortality, hospital cost and length of stay. In addition, hospital acquired CAUTIs are often due to multidrug resistant strains which require higher antibiotics and these strains may spread to other patients.

Biofilms on the indwelling catheter have been shown to be the main cause of CAUTI and can also be responsible for the blocking of catheters (4). Biofilms on catheters and prostheses are the prime source of antibiotic resistance in persistent bacterial infections, which make them incredibly challenging to eliminate with antimicrobial agents (5). In order for bacteria to form a biofilm they must go through a number of stages which include: 1. Adhering to a surface and/or each other, 2. A change in phenotype via a change in gene expression from the planktonic ('floating') state, and 3. An extracellular matrix comprised of secreted products and components from the host. One of the key characteristics of biofilms is the heightened survival to antibiotics and resistance to the immune system of the host; bacteria in biofilms can be up to 1000 times more resistant to antibacterials than bacteria in the planktonic state. Therefore, biofilms provide a survival aid to their residing microorganisms, accounting for the virulent infections which are resistant to antibacterials. The extracellular matrix enclosing the bacteria in the biofilm is comprised of elements such as proteins, DNA and polysaccharides, which inhibit the infiltration of antibacterials by serving as a diffusion barrier between the adhered bacteria and the surroundings. This matrix significantly reduces the sensitivity of the biofilm to antimicrobials, which can be a huge hinderance in treatment (6).

Candida is increasing as a causative agent of CAUTI, accounting for 17.8% of cases; however, its pathogenic mechanisms during CAUTI are not well described. *Candida* species have been found associated with latex and silicone

urinary catheters, with preference for latex material. *Candida* biofilms are readily detected on indwelling catheters by scanning electron microscopy. *C. albicans* adheres poorly to the bladder mucosa, and risk for *Candida* UTI increases sharply in the presence of an indwelling catheter. A recent ex vivo study showed that a *C. albicans* CAUTI isolate binds to urinary catheters via fibrinogen. *C. albicans* encodes a fibrinogen-binding protein, Mp58, which is expressed during candidiasis. In total, the wide distribution of diverse fibrinogen-binding adhesins among common uropathogens suggests that fibrinogen binding is a common theme in CAUTI pathogenesis (7).

The present investigation was aimed to study the burden of catheter associated urinary tract infection by candida albicans and non albicans with emphasis on biofilm formation and antifungal sensitivity pattern. Due to intense microbial exposure, antimicrobial resistant organisms are frequently isolated in these cases. CAUTIs constitute a huge reservoir of antimicrobial resistance and inadvertent use of antibiotics increases the risk of cross-infections among catheterized patients this results in prolonged hospital stay and increased cost of healthcare, not only to the patients but also to the hospital. Ultimately there is overall increased morbidity and mortality. The further study of species identification along with their antifungal susceptibility pattern can be helpful for better treatment.

Materials and Methods

Collection of data

The research was carried out in the Department of Microbiology, Index Medical College, Hospital & Research Centre, Indore, MP, India. A systematic questionnaire was used to collect data from the 600 patients who took part in the trial. Name, age, sex, address, IP number, date of admission, clinical data such as presenting complaints, personal history, past medical history, high risk factors, immunocompromised status, physical examination findings, and clinical diagnosis details were all gathered. The need for a Foley's catheter will be noted. The patients were examined every day for signs of a urinary tract infection, such as fever, suprapubic pain, and costovertebral angle tenderness. Catheter care will be closely managed, including daily meatal care with betadine or soap water and the maintenance of closed drainage. Patients were monitored until they developed bacteriuria, were released, expired, or had their catheter removed. It will be noted when the catheter was removed and how long it had been in place. Patients who will be transferred to a different ward will be monitored for the development of CAUTI symptoms for up to 48 hours.

Following process were assessed from the urine specimen collected.

1. Direct Gram's stain of Uncentrifuged urine.
2. Culter the specimen's culture by semi quantitative method using SDA, CLAD Chrome agar culture medium
3. Germ tube test
4. Biofilm formation test. Fixed smear will be stained by Gram's stain to see the presence of budding yeast cells and pseudo-hyphae.

5. Carbohydrate assimilation test.
6. Anti-fungal sensitivity test

Table: Descriptive analysis of Organism isolated in study group (N=600)

S. No.	Organism Isolated	Frequency	Percentage
1	<i>Candida albicans</i>	210	35
2	<i>Candida glabrata</i>	195	32.5
3	<i>Candida parapsilosis</i>	93	15.5
4	<i>Candida tropicalis</i>	42	7
5	<i>Candida dubliniensis</i>	60	10

Candida albicans was found to be present in 35 percent and 32.5 percent of urinary catheters, respectively, for *Candida glabrata*, 15.5 percent for *Candida parapsilosis*, 7% for *Candida tropicalis*, and 10% for *Candida dubliniensis* in this investigation. On the basis of identification, 5 different *Candida* species were confirmed. *Candida albicans* and *Candida glabrata*, in particular, exhibited a higher prevalence rate than other species.

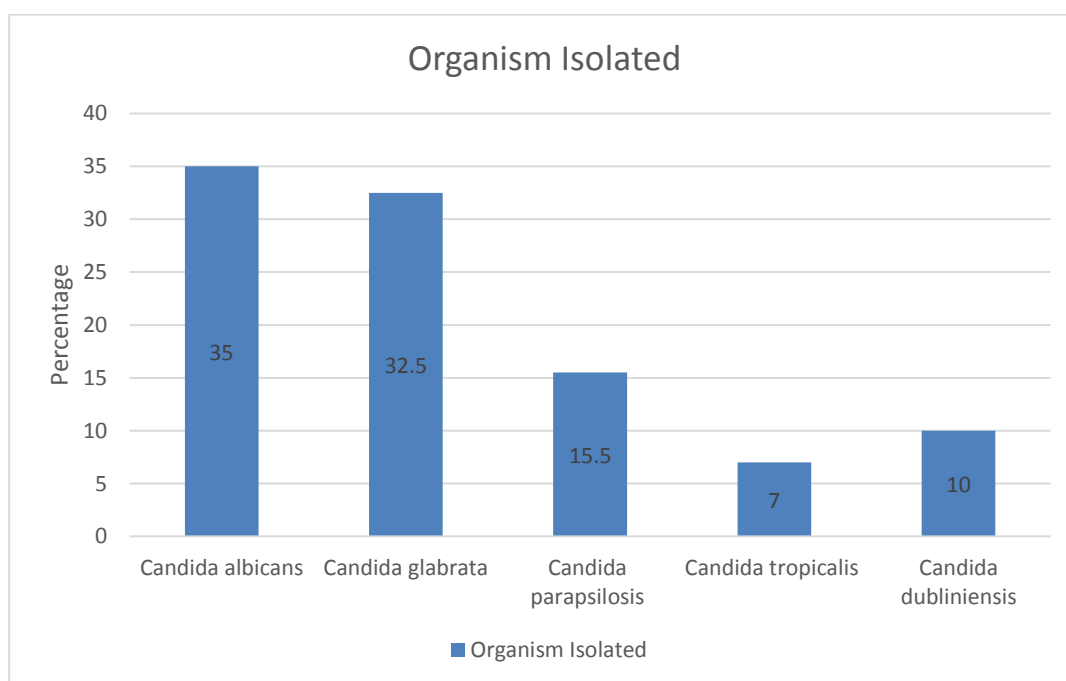


Figure: Descriptive analysis of Organism isolated in study group

Table: Descriptive analysis of drug sensitivity for *Candida spp.* in study group (N=600)

S. No.	Drugs	Resistance (%)	Sensitive (%)
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1	Fluconazole	0	99
2	Itraconazole	0	100
3	Amphotericin-B	0	100
4	Voriconazole	0	100

Fluconazole, voriconazole, amphotericin B, and itraconazole were all effective against the candida isolates.

Table: Minimum inhibitory concentrations (MIC) of *Candida* species

S. No.	Organism Isolated	Frequency	Percentage
1	<i>Candida albicans</i>	210	35
2	<i>Candida glabrata</i>	195	32.5
3	<i>Candida parapsilosis</i>	93	15.5
4	<i>Candida tropicalis</i>	42	7
5	<i>Candida dubliniensis</i>	60	10

Amphotericin-B was shown to be 35.15 percent sensitive to *Candida* species. Based on the isolates' pathogenicity capacity, it inhibited *Candida* growth. Amphotericin-B was made in a variety of concentrations, including $\geq 2\mu\text{g/ml}$, $\geq 4\mu\text{g/ml}$, $\geq 8\mu\text{g/ml}$, $\geq 16\mu\text{g/ml}$, and $\geq 32\mu\text{g/ml}$. At concentrations ranging from $\geq 2\mu\text{g/ml}$ to $\geq 16\mu\text{g/ml}$, the medication Amphotericin-B inhibited *Candida* growth. *Candida dubliniensis* was susceptible to amphotericin-B, which inhibited growth at a dose of $\geq 2\mu\text{g/ml}$. At a concentration of $\geq 4\mu\text{g/ml}$, the medication inhibited the development of *Candida tropicalis*. Amphotericin-B, on the other hand, inhibited the development of *Candida glabrata* and *Candida parapsilosis* at an $\geq 8\mu\text{g/ml}$ concentration and reduced the turbidity of *Candida albicans* at a $\geq 16\mu\text{g/ml}$ concentration. *Candida dubliniensis* had the lowest concentration of $\geq 2\mu\text{g/ml}$, in which no growth occurred, as compared to other species.

Table: Biofilm production of *Candida* species in percentage

Name of the isolate	Total no. of isolates	Biofilm production					
		No. of Strong producers	%	No. of Moderate producers	%	No. of Weak producers	%
<i>Candida albicans</i>	210	162	77.14	27	12.86	21	10
<i>Candida glabrata</i>	195	126	64.62	54	27.69	15	7.69
<i>Candida parapsilosis</i>	93	60	64.52	24	25.80	9	9.68
<i>Candida tropicalis</i>	42	21	50	15	35.71	6	14.29
<i>Candida dubliniensis</i>	60	42	70	12	20	6	10

In *Candida albicans*, 77.14 percent of isolates were found to be strong biofilm producers, 12.86 percent were found to be moderate biofilm producers, and 10% of isolates were found to be weak biofilm producers. *Candida albicans* (77.14 percent) and *Candida dubliniensis* (70.00 percent) produced robust biofilms, while *Candida glabrata* (64.62 percent), *Candida parapsilosis* (64.52 percent), and *Candida tropicalis* (50.00 percent) produced weak biofilms.

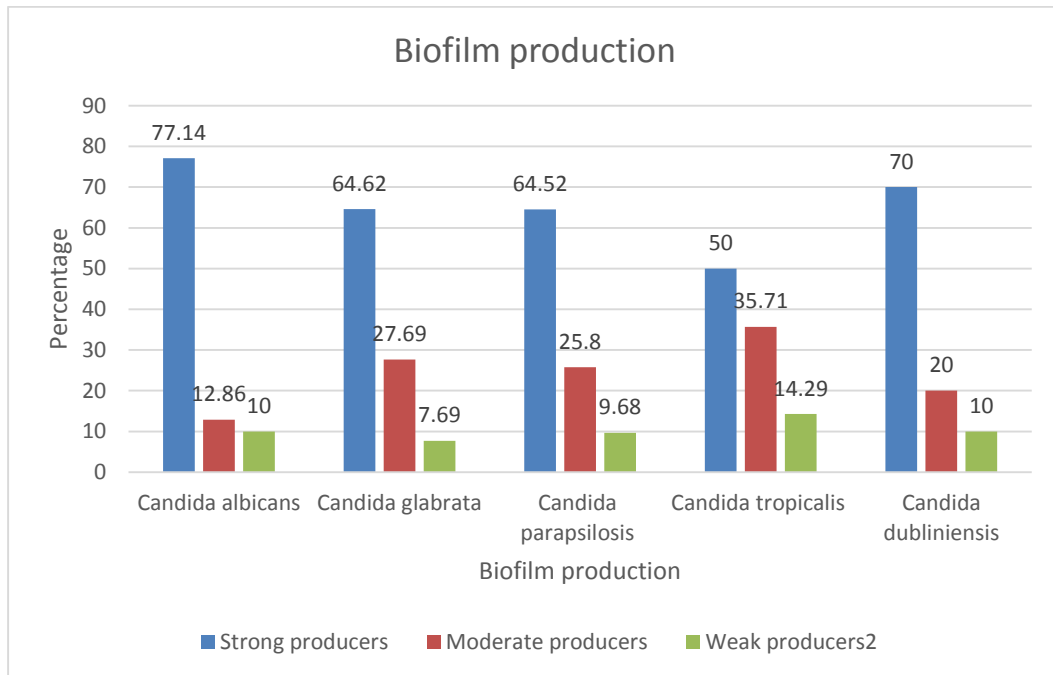


Figure: Biofilm production of *Candida* species in percentage

Discussion

The most prevalent device-associated nosocomial infection is catheter-associated urinary tract infection. The study included 600 patients who were admitted to the medical ICU and were monitored for the development of CAUTI. Only symptomatic CAUTI cases were included in this investigation. In this investigation, 165 individuals out of 600 were found to have had symptomatic CAUTI during their stay in the hospital. As a result, the CAUTI rate was computed as 25.06 per 1000 catheter days, and the incidence was 27.5 percent.

The length of catheterization (10 \geq days) was found to be statistically significant, as 60.47 percent of 43 patients who received a catheter for 10 \geq days had CAUTI. This is because the longer a patient remains in the ICU and catheterized, the more likely he is to become colonised by multidrug resistant organisms found in the environment niche. Similar study done by Angshuman Jana et al., (2015)⁸ and Priya Datta et al., (2014)⁹. In this investigation, 200 urinary catheters were collected, with *Candida albicans* showing up in 35% of them and *Candida* spp. (83.3%) emerging as the most common isolate. *Candida glabrata* accounted for 32.5 percent, *Candida parapsilosis* for 15.5 percent, *Candida tropicalis* for 7%,

and *Candida dubliniensis* for 10%. On the basis of identification, 5 different *Candida* species were confirmed. *Candida albicans* and *Candida glabrata*, in particular, exhibited a higher prevalence rate than other species. These findings were comparable to those of Manisha Jain et al., (2011)¹⁰, who found that non-*albicans* *Candida* spp. (71.4%) was the most common infection causing CAUTI. A study by Chanda R. Vyawahare et al (2015)¹¹ found similar results. As a result, non-*albicans* *Candida* spp. are displacing *Candida albicans* as the most common cause of nosocomial UTI.

Antifungal's fluconazole, itraconazole, voriconazole, and amphotericin B were all equally effective against all *Candida* species. This could be related to the fact that antifungals aren't used very frequently. As a result, the organisms have acquired no resistance. Angshuman et al (2015)⁸, Neha Garg et al (2015)¹², Priya Datta et al (2014)⁹, and Chanda R. Vyawahare et al (2015)¹¹ have all found high levels of antibiotic resistance among the bacteria that cause CAUTI. Catheterization has been shown to increase the prevalence of UTIs caused by several highly resistant microorganisms, with the resistant pattern of the isolates changing with time. In *Candida albicans*, 77.14 percent of isolates were found to be strong biofilm producers, 12.86 percent were found to be moderate biofilm producers, and 10% of isolates were found to be weak biofilm producers. Previous studies done by Angshuman et al (2015)⁸, Neha Garg et al (2015)¹², Priya Datta et al (2014)⁹, and Chanda R. Vyawahare et al (2015)¹¹ found similar results.

Conclusion

Candida spp. is generally found in humans; however, when the host's immune system is compromised, the pathogen infects the host, earning it the name opportunistic pathogen. It can also be found on the surfaces of biomaterials such as catheters, Venflon, intravenous tubes, dentures, and blood bags in a medical setting. It infects people who have been admitted to the hospital. This causes major health problems for the patients and raises morbidity and mortality rates over time. Those who take antifungal medications for this infection on a regular basis acquire resistant to the drugs. *Candida albicans* and non-*Candida albicans* were found to predominate in distinct clinical samples in this investigation. The goal of this cross-sectional study, which took place at the Index Medical College Hospital and Research Centre, Indore, was to determine the burden of catheter associated urinary tract infection by *candida albicans* and non *albicans* with emphasis on biofilm formation. CAUTI is a prevalent complication in critically ill individuals. In order to reduce the incidence of catheter-related UTI, the focus should be on appropriate catheter maintenance and lowering catheterization length rather than prophylactic. In the treatment of CAUTI, culture and susceptibility testing are crucial.

The risk of catheterization and the need for it should be assessed. Only if there is a valid indication should an indwelling catheter be utilised in the patient. When it is no longer needed, it should be removed. If the catheter is needed for longer than 14 days, it should be replaced or other catheterization options, such as a condom catheter, should be investigated. Proper catheter bundle care should be followed in catheterized patients. *Candida albicans* produced a larger percentage of biofilms than non-*Candida albicans*. This finding shows that biofilm creation is

more significant for *Candida albicans* strains, and that non-*Candida albicans* strains have mechanisms for establishing infections other than biofilm production.

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