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Original Research Paper

Retrospective Study of Candida sp. Infection in Intensive Care Unit (ICU) RSPAD Gatot Soebroto

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Abstract

Background: An Intensive Care Unit (ICU) is a place to care for patients with critical conditions who require life support. ICU patients generally had comorbid diseases, a weakened immune system, and the use of life support equipment which allows opportunistic fungal infections such as Candida sp. The Candida species that infects the most is Candida albicans, but recently there has been an increase in non-albicans Candida infections. **Objective:** To determine the description of Candida species in ICU patients at RSPAD Gatot Soebroto in 2021-2022. **Methods:** A retrospective observational descriptive study with total sampling using secondary data from patient medical records. **Result:** The prevalence of Candida infections in the ICU in 2021 is 7.19% and in 2022 it is 8.76%. The most common causative pathogen is Candida albicans, namely 45.45% in 2021 and increasing to 55.76% in 2022. The second most common species is Candida tropicalis at 30.30% in 2021 and 20% in 2022, followed by Candida glabrata at 13.13% in 2021 and 16.97% in 2022. Other species of Candida were also found, namely Candida parapsilosis, Candida krusei, Candida famata, Candida ciferii, and Candida lusitaniae. Clinical samples with positive Candida were obtained from urine, bronchial, sputum, and blood samples. **Conclusion:** Candida sp. infections in the ICU are still dominated by Candida albicans, but non-albicans Candida species such as Candida tropicalis and Candida glabrata are starting to appear.

Keywords: Candida sp; Intensive Care Unit; Clinical samples.

Introduction

Patients treated in the Intensive Care Unit (ICU) have the highest risk of developing infections related to the use of medical devices. Critically ill patients are at a higher risk of invasive fungal infections. ICU patients are characterized by the use of medical devices such as central venous catheters, arterial lines, urinary catheters, hemodialysis, and mechanical ventilation. The incidence of invasive fungal infections in the ICU has increased, and *Candida* is the primary cause[1]. Invasive candidiasis is an infection that arises in conjunction with advances in medical technology and is widely recognized as a major cause of morbidity and mortality in patients[2].

Candida sp. is a commensal microorganism in humans but can become a pathogen after the immune system is compromised, either iatrogenically or idiopathically[1]. At least 15 *Candida* species can cause disease in humans; however, the majority of invasive infections are caused by five pathogens, namely *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida kruse* [2]. *Candida sp*. can be isolated from the skin, gastrointestinal tract, sputum or

respiratory specimens from intubated patients, female genital tract, and urine from patients with indwelling catheters[1]. *C. albicans* remains the primary pathogen, and its success in interacting with human hosts depends on a number of strategies used for colonization/infection. This is related to its genetics and resistance to morphological and biochemical properties[3]. *C. albicans* is the most pathogenic among other *Candida* species, and can cause life-threatening problems, so antifungal treatment can protect patients from serious infections[4].

Recently, non-*albicans Candida* species have been detected. This increase reflects the improvement in diagnostic methods and the ability of non-*albicans Candida* to survive in hosts. Among non-*albicans* species, *C. glabrata* has been detected as a nosocomial pathogen in superficial and systemic infections, and its incidence is mainly associated with immunosuppression and antimicrobial agents[3]. *C. glabrata* is the second most frequently found species in North America and Western Europe[5]. In addition to *C. glabrata*, an increase in *C. tropicalis* has also been observed, which is also considered a species that produces strong biofilms that adhere to epithelial and endothelial[6]. *Candida sp.* is able to form biofilms, which are strong factors for adhesion to host tissues, evading the immune system, and developing antifungal tolerance[3]. The challenges in managing invasive candidiasis are prevention, earlier diagnosis, and the initiation of systemic antifungal therapy as soon as possible[2]. In individuals with candidiasis caused by more than one species, *Candida non-albicans* species may cause a high resistance profile to antifungal therapy[3].

Hospitals are comprehensive healthcare facilities, consisting of promotive, preventive, curative, and rehabilitative services, and also serve as referral centers for healthcare[7]. Quality healthcare services in hospitals can determine patient satisfaction due to the fulfillment of patient needs and increased trust in the hospital[8]. Healthcare workers can pose risks to patients for the transmission of diseases and for themselves, so one way to create occupational safety is by using personal protective equipment[9].

Rumah Sakit Pendidikan Angkatan Darat (RSPAD) Gatot Soebroto is a referral hospital of type A in Jakarta, which receives many patients from both Jakarta and outside Jakarta. ICU patients are patients with severe conditions, accompanied by comorbidities and the possibility of decreased immune systems. ICU patients require life support, where the equipment used can be a source of invasive candidiasis infection. This study needs to be conducted to determine the profile of *Candida* sp. infection and the *Candida* species infecting patients in the ICU so that preventive and immediate treatment can be taken.

Research on *Candida* sp. infections in the ICU of RSPAD Gatot Soebroto has not been conducted; therefore, researchers want to know the profile of *Candida* sp. infections and the species of *Candida* sp. in the ICU of RSPAD Gatot Soebroto. Is *Candida albicans* still the most common species causing infection, or are other *Candida* species emerging? This research aims to provide a description of the *Candida* sp. infecting patients in the ICU of RSPAD Gatot Soebroto.

Materials and Methods

Research Design

This research uses a descriptive observational retrospective design using medical records. The research was conducted in medical records section of RSPAD Gatot Soebroto on ICU patients for the periode 2021-2022.

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Sample

The population in this research was patients treated in the ICU of RSPAD Gatot Soebroto during 2021-2022, with data obtained from medical records. The research sample consists of ICU patients with confirmed candidiasis based on laboratory test results.

Data Collection Technique

Data collection was performed by searching the medical records of patients who tested positive for *Candida* sp. from laboratory examinations. Then, demographic data, types of clinical samples, and the species of *Candida* found were recorded.

Data Analysis Technique

Data were analized descriptively regarding demographic characteristics, the species of *Candida* found, and the type of clinical sample containing *Candida* sp.

Ethical Consideration

This research uses secondary data from the medical records section of RSPAD Gatot Soebroto, maintaining patient confidentiality and without direct patient involvement. This research has obtained ethical clearance with number 334/VII/2023/KEPK from the Health Ethics Commission, Universitas pembangunan Nasional Veteran Jakarta.

Results

The number of ICU patients treated in 2021 was 1544, with 111 patients experiencing *Candida* sp. infection, while in 2022, there were 2008 patients treated in the ICU, with 176 patients experiencing candidiasis. Based on this data, the prevalence of candidiasis in the ICU of RSPAD Gatot Soebroto was 7.19% in 2021 and 8.76% in 2022.

This study used 84 medical records from 2021 and 148 medical records from 2022. Below is the demographic data of patients with *Candida* sp. infection.

Table 1. Demographic Characteristics of ICU Patients with *Candida* sp. Infection.

Demographic Characteristics	2021 (N (%))	2022 (N (%))
Age (years)		
≤ 19	0 (0)	3 (2.03)
20-59	43 (51.19)	71 (47.97)
≥ 60	41 (48.81)	74 (50)
Gender		
Male	44 (52.38)	87 (58.78)
Female	40 (47.62)	61 (41.22)

Patients were diagnosed with *Candida* sp. infection after laboratory tests on body samples. Some patients experienced more than one *Candida* infection, resulting in a total of 99 *Candida* sp. infections in 2021 and 165 in 2022. The following is a description of the *Candida* sp. species that infected ICU patients.

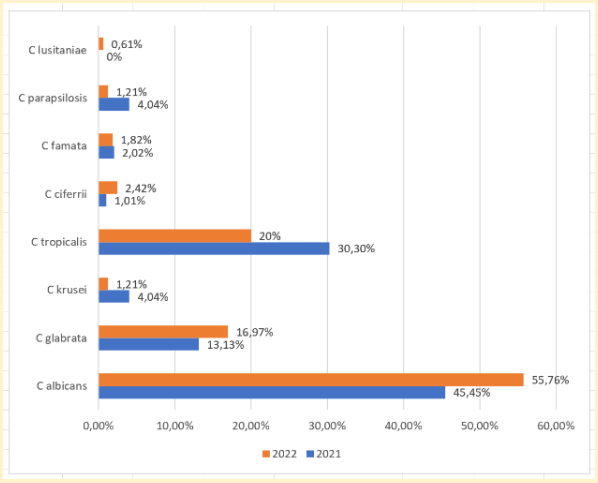

Figure 1. Percentage of spesies *Candida sp*. in ICU patients.

Candida sp. infecting patients were obtained from several body samples, namely sputum, bronchus, blood, urine, pus, and pleural fluid. The number of samples containing *C. albicans* was 45 samples in 2021 and 92 samples in 2022. The following is the

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distribution of body fluid samples that tested positive for *C. albicans.*

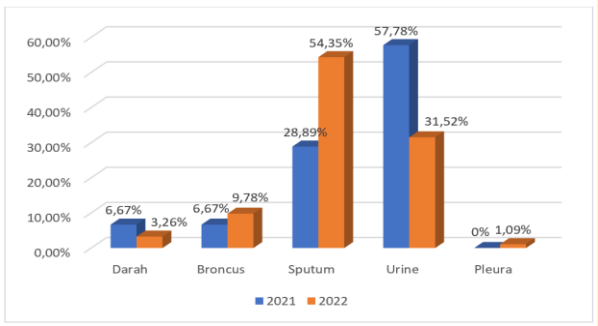

Figure 2. Body Samples Identified as *C. albicans.*

The number of body samples found to contain *C. tropicalis* was 30 samples in 2021 and 33 samples in 2022. Based on the results of the body sample examination that tested positive for *C. tropicalis*, see Figure 3.

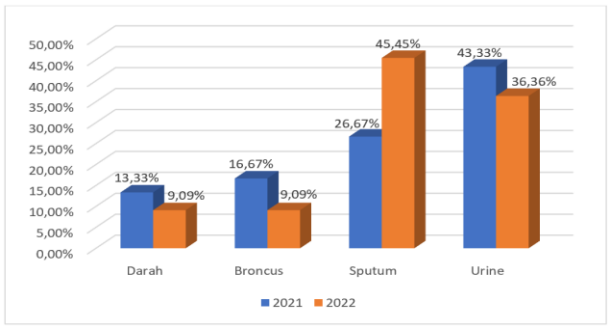

Figure 3. Body Samples Identified as *C. tropicalis*

The number of samples positive for *C. glabrata* was 13 samples in 2021 and 27 samples in 2022. The positive *C. glabrata* in body samples is shown in Figure 4.

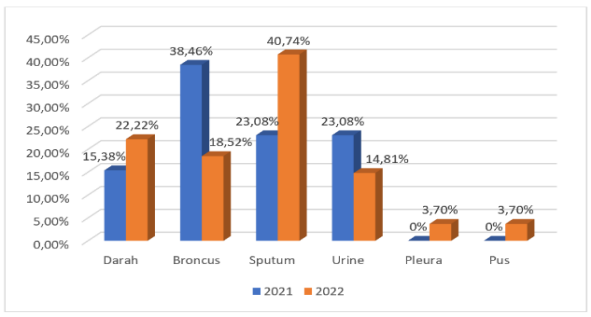

Figure 4. Body Samples Identified as *C. glabrata.*

Other *Candida* species had low numbers based on the examination results, as shown in Table 2.

Table 2. Body Samples Identified as Non-*albicans Candida*

Candida Spesies	Sample	2021 (N)	2022 (N)
C. parapsilosis	Blood	2	0
	Urine	2	0
	Bronchus	0	2
C. krusei	Urine	3	0
	Bronchus	1	2
C. famata	Bronchus	0	1
	Sputum	2	2
C. ciferii	Bronchus	0	2
	Sputum	1	2
C. lusitaniae	Bronchus	0	1

Discussion

The results of this study found that the incidence of candidiasis in the ICU of RSPAD Gatot Soebroto was 7.19% in 2021 and 8.76% in 2022. In a 2017-2018 study conducted by Palit et al. in the intensive care unit of RS Prof. Dr. RD Kandou Manado, the incidence of candidiasis was 4%[10]. The higher results in this study were because RSPAD Gatot Soebroto is a type A referral hospital in Jakarta; many referred patients are already in severe condition accompanied by many comorbidities. Patients admitted to the ICU of RSPAD Gatot Soebroto are those previously treated in general wards and patients referred from other hospitals who are already in critical condition.

According to the demographic characteristics in Table 1, the age of patients with candidiasis has an almost equal percentage between patients aged 20-59 years and elderly patients aged ≥ 60 years. The results of this study show that age is not a predisposing factor for the occurrence of candidiasis in this study. Gender also showed no significant difference between male and female patients, although slightly more male patients experienced candidiasis. This result does not indicate that *Candida* sp. infection has a predisposition to a particular gender. This is because the most identified factor as a predisposing factor for

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candidiasis in the ICU is related to medical interventions during ICU treatment or comorbid conditions experienced by the patient[11].

Figure 1 shows that the most common *Candida* sp. infecting ICU patients is *C. albicans*, followed by *C. tropicalis* and *C. glabrata*. In addition to these species, *C. krusei*, *C. parapsilosis*, *C. famata*, *C. ciferrii*, and *C. lusitaniae* were also found, but in small numbers. The results of this study indicate that *C. albicans* is still the most common cause of candidiasis in the ICU. This research is in line with Yang et al.'s research, which states that *C. albicans* is the most frequently occurring species causing candidiasis[12]. In 50% of the population, *C. albicans* is part of the normal microbiota[13]. Research conducted by Tahtler et al. also shows that *C. albicans* is still the most common cause of infection, namely 68.2%, compared to *Candida non-albicans* (18.2%) and more than 2 *Candida* species (13.6%)[14].

C. abicans is still the most commonly isolated *Candida* species, but it is accompanied by an increase in the incidence of *Candida non-albicans*[15]. This condition is also found in the results of this study, which show other *Candida* species found, namely *C. tropicalis* and *C. glabrata*. Yang et al. also found that *Candida non-albicans* species are increasing, namely *C. parapsilosis*, *C. glabrata*, *C. tropicalis*, and *C. krusei*[12]. *C. tropicalis* emerges as one of the most important *Candida* species in epidemiology and virulence. *C. tropicalis* can produce true hyphae and is considered a strong biofilm producer that adheres strongly to epithelial and endothelial cells[6]. In addition to these two non-*albicans* species, other species were also found, namely *C. krusei*, *C. parapsilosis*, *C. famata*, and *C. lusitaniae*. The transmission mode of each *Candida* species varies depending on the clinical condition; for example, candidemia due to *C. albicans* is obtained endogenously, while *C. parapsilosis* is transmitted from the hands of healthcare workers. There is controversy regarding the transmission mode of *C. tropicalis*; some believe that its transmission is horizontal from the hospital, while others suspect it is acquired from the environment outside the hospital. For *C. glabrata*, although its source of infection is generally endogenous, some studies have found horizontal transmission for this species[16].

Figure 2 shows that *C. albicans* in this study was found in several body samples, most commonly from urine and sputum, followed by bronchus, blood, and pleura. In 2021, the most positive *C. albicans* samples were from urine, followed by sputum, while in 2022, the most were from sputum, followed by urine. *C. albicans* is a common commensal fungus that colonizes the oropharynx, gastrointestinal tract, vagina, and skin of healthy individuals. Several factors can disrupt the normal homeostasis of *Candida*, thus causing skin, mucosal, and systemic infections. A virulence factor of *C. albicans* is polymorphism, specific toxins such as candidalysin, expression of proteins important for adhesion and invasion, biofilm formation, thigmotropism, and the secretion of hydrolytic enzymes[13].

Based on Figure 3, it was shown that *C. tropicalis* is also frequently found in sputum and urine samples, similar to *C. albicans*, followed by bronchus and blood samples. *C. tropicalis* is associated with patients experiencing cancer and is characterized by its ability to develop rapid resistance to fluconazole, although its virulence is still rarely studied. *C. tropicalis* is a diploid opportunistic dimorphic yeast that colonizes various sites, such as the skin, gastrointestinal tract, and genitourinary tract. Approximately 3%-66% of bloodstream *Candida* infections worldwide are caused by *C. tropicalis*, and it is usually the first or second most frequently non-*albicans* species

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isolated from blood and genitourinary tract samples[17].

Figure 4 shows that *C. glabrata* is frequently found in sputum and bronchus samples, followed by urine, blood, pus, and pleural fluid samples. *C. glabrata* is a pathogen that colonizes epithelial surfaces (mouth, gastrointestinal tract, vagina, skin, feces) as part of the normal microbial flora regardless of age. *C. glabrata* is the second most common cause of candidiasis after *C. albicans*. The pathogenicity of *C. glabrata* is associated with many virulence factors. One of the most important factors is its ability to avoid triggering a strong host immune response, thus evading the immune system and resisting cellular phagocytosis and antifungal therapy[18].

Table 2 shows that body samples positive for non-*albicans Candida* species were found in blood, urine, sputum, and bronchus samples. In addition to *C. albicans*, *C. tropicalis*, and *C. glabrata*, other *Candida* species were also found, namely *C. parapsilosis*, *C. krusei*, *C. famata*, *C. ciferrii*, and *C. lusitaniae*, in small numbers. *C. parapsilosis* is very often found in neonates with low birth weight, immunocompromised individuals, patients requiring long-term central venous catheters, or other devices that remain in the body, allowing *C. parapsilosis* to adhere and form biofilms[19]. Risk factors for *C. krusei* infection include recent surgery (<30 days), artificial implants, splenectomy, neutropenia, and the presence of cancer[20]. *C. lusitaniae* is an opportunistic yeast reported as the most common cause of infection in immunocompromised patients who often have comorbidities[21].

The presence of *Candida* sp. in urine samples (candiduria) presents challenges for diagnosis and treatment. The presence of *Candida* sp. in urine indicates several conditions that require careful interpretation, ranging from contamination of the urine sample to urinary tract infection, including disseminated candidiasis[22]. In a study conducted in Surabaya, candiduria was found in 59.62% of patients treated in the ICU, and urinary tract infections due to *Candida* were found in 87% of those patients. This indicates that more than half of the patients with candiduria exhibited clinical symptoms of urinary tract infection in the ICU, which can increase the mortality rate of these patients if antifungal therapy is not performed[23]. Candiduria is an indicator of invasive candidiasis, which can become serious, especially in immunocompromised patients[24]. *Candida* infection can enter the urinary tract via antegrade routes from systemic circulation and retrograde routes ascending from the urethra from colonization around the urethra. The frequency of candiduria in ICU patients has increased recently, especially in patients receiving urinary catheters or broad-spectrum antibiotics[25].

The rate of *Candida* sp. isolation from respiratory tracts is relatively high, especially in patients using mechanical ventilation. Clinical studies have shown that the rate of *Candida* isolation from the respiratory system in ICU patients with mechanical ventilation can reach 50%, which prolongs the patient's hospital stay and may even increase mortality at home. Furthermore, it may be associated with persistent immunosuppression and inflammation. Colonization of *Candida* in the respiratory tract and the secretion of inflammatory factors can affect the host's cellular immune function, especially in immunosuppressed patients with monocyte and lymphocyte dysfunction[26]. In a study by Tahtler et al., it was shown that prolonged mechanical ventilation is associated with the presence of any *Candida*, especially non-*albicans Candida*[14].

Candida in bloodstream infection (candidemia) is a significant invasive fungal

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disease in critically ill patients and is among the top ten bloodstream infections associated with healthcare workers in the ICU. In a study by Almeida et al. on patients with candidemia, *C. albicans* remained the most common cause (43.6%), followed by *C. tropicalis* (20%) and *C. glabrata* (13.7%)[27]. Critically ill ICU patients have a high incidence of candidemia with a high mortality rate. Patients with candidemia are often severely ill, receiving life-supprot therapy (e.g. mechanical ventilation or vasopressors) associated with high mortality rates[28]. Clinical and autopsy studies confirm a significant increase in the incidence of candidemia and disseminated candidiasis. This increase is multifactorial and reflects improved diagnostics and the growth of the high-risk patient population. Furthermore, the increase in infections also reflects the increased life expectancy of patients with immunosuppression and multiple comorbidities[29].

Candida infection has become one of the opportunistic infections associated with healthcare workers due to the increasing number of patients undergoing major surgical procedures, central venous catheter (CVC) placement, prolonged ICU stays, total parenteral nutrition, and broad-spectrum antibiotic use. These factors are clearly risk factors for invasive candidiasis[17]. Invasive candidiasis is more common in the ICU, with an incidence ten times higher than in general wards, accounting for about 70% of all fungal infections in the ICU[30]. *C. albicans* remains the primary pathogen causing *Candida* infections, but recently other species such as *Candida non-albicans* have been detected, and their role in human infections is gaining attention. Candidiasis is becoming more prevalent, with non-*albicans* species exhibiting a high level of resistance to antifungal drugs[3].

Conclusion

C. albicans is the most common cause of candidiasis found in ICU patients at RSPAD Gatot Soebroto. However, an increase in *Candida non-albicans* species, namely *C. tropicalis* and *C. glabrata*, has been observed. In addition, several samples were positive for *C. parapsilosis*, *C. krusei*, *C. famata*, *C. ciferrii*, and *C. lusitaniae*. *Candida* sp. was found in urine, bronchus, sputum, and blood samples. Further research is needed on the risk factors for candidiasis in ICU patients.

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