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RESEARCH ARTICLE

New Variant of Oral Candida in Intensive Care Unit Patients Using Endotracheal Tube: Observational Study

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ABSTRACT

Backgroud: *Candida species are the most common cause of systemic and mucosal diseases. Candida species cause bloodstream infections that are more than 90% fungal.* ***Objective:*** *There are variations of candida worldwide, and 15 different species recognize pathogens and cause human diseases. The aim of the of the study to identify variation of Candida in patient installation of Endotracheal Tube in intensive care unit.* ***Materials and Methods****: We conducted this research using a cross-sectional design. The collect sample during 6 months perform by single oral medicine specialist. Identification variety of Candida using VITEK 2® compact. Result: Data was obtained using a sample of 83 patients who installed an endotracheal tube unit in Dr. Ramelan Naval Hospital from March until August 2024.* ***Results:*** *There was a sample of 51 (61.4%) infected with Candida, with various candida being Candida albicans 39 (76.5%), Candida Tropikalis 6 (11.8%), Candida ciferri 3 (5.9%), Candida Lucitaniae 2 (3.9%), and Candida Gullermondii 1 (1.9%).* ***Conclusion:*** *This study identified Candida Ciferii as a new variant of Candida in this locus, known as a new resisten of fluconazole.*

Keywords: *Oral Candida, Endotracheal tube, Intensive Care Unit*

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INTRODUCTION

In recent years, there has been a notable rise in the incidence of fungal infection in human, attributed to a broader array of species, including numerous varieties of fungi not previously linked to human diseases[1]. This growth can be attributed to a variety of factor, including advancements in laboratory diagnostic technique for fungal identification and environmental changes associated with rising temperatures that may influence fungus habitats.[1]

The most common cause of systemic and mucosal disease is *candida* species. *Candida* species cause bloodstream infections that are more than 90% fungal.[2] *Candida albicans* is known as the most common cause of nosocomial invasive candidiasis. However, in the past decade an increased prevalence of Non-Albicans Candida (NAC) species. including *C. parapsilosis*, *C. glabrata, C. krusei, C. tropicalis, C. sojae, C. auris,* and *C. ciferrii,* has been reported. The variation depends on type of population geographic region, and antifungal exprossure[3,4].

The one most common bloodstream infection in ICU patients cause increase mortality rate and hospital cost is a Candidemia[3]. The worldwide mortality rates reaching 70 %[5]. Candidemia is an invasive fungal infection cause by *candida*, one of the initial symptoms is oral candidiasis[2]. Candida is a one of flora normal in the oral cavity that transform into pathogen when the host immunocompromised[6]. The risk of candidemia increases 6-10 times when patients installation of Endotracheal Tube (ETT)[7] due to surface of tube ETT both inner and outer surface of the ETT will form biofilm and development into pathogen among 24-72 hours.[8,7]

The purpose of the study was to identification new variation of *Candida* species from intraoral patients, especially related intensive care unit with ETT intubation, and present a characteristic of patient's demographic.

MATERIAL AND METHODS

This investigation observational analytic study with cross sectionals approach. The protocol of study received approval from the Institutional Review Board of Dr. Ramelan Naval Hospital under protocol number 17/EC/KEP/2024. This endorsement was granted based on the adherence of the study to the ethical principles outlined in the Declaration of the World Medical Association in Helsinki.

Data collection transpired over a six-month period, commencing in March until August 2024. The sample of the study included the patient in the ICU with 4th day ETT installation, over the age 50 years old. The medical record of the patient including age and underlying disease like Intracerebral Hemorrhagic, Septicemia, diabetes mellitus, pneumonia, kidney failure, malignancy, Guillan Bare Syndrome and senility was recorded. The excluding criteria was patients with ETT had died before 4th days and the age under 50 years old.

To collect the sample, perform by single oral medicine specialist using oral swab technique using cotton swab stick swabbed on the patient's tongue, the inserted into Amies transport media. Then samples were sent to laboratorium of microbiology then identification variety of candida using an identification tool in the form of a VITEK 2® compact.

Informed consent procedures involved a detailed explanation by the researcher to the family members. Key aspects covered during the informed consent process included elucidation of the study's objectives, the voluntary nature of participation, assurance of confidentiality regarding gathered information, and a comprehensive overview of the procedures employed throughout the study. Consent was obtained after ensuring a clear understanding of these elements by the legal representatives. The obtained data were compiled, and frequency distribution and chi-square test were determined using *Statistical Package for Social Sciences*

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(SPSS) software version 23 (SPSS Inc., Chicago, IL, USA).

RESULTS

The study involved 83 respondents from patients ETT installation at Dr Ramelan Naval Hospital, March-August 2024. There are three samples excluded due to age below 50 years. Fifty-one samples (61.4%) showed positive oral findings of Candida, including *Candida albicans* 39 (76.5%), *Candida tropicalis* 6 (11.8%), *Candida ciferri* 3 (5.9%), *Candida lucitaniae* 2 (3.9%), and *Candida gullermondii* 1 (1.9%) (Table 2)

Within this cohort, males exhibited a higher incidence rate (53%) compared to females (47%). The dominant age group was 61-70 years old containing 40% (33/83) of cases (Table 1).

Tabel 1. Characteristic of Respondent

Characteristic	Percentage of samples (%)
Gender	
Male	44(53.%)
Female	39 (47%)
Ages (year)	
50-60	30 (36%)
61-70	33 (40%)
71-83	20 (24%)
Underlying Disease	
Intracerebral Haemorrhage	36 (43%)
Septicemia	20 (24%)
Kidney Failure	6 (7%)
Malignancy	8 (9%)
Pneumonia	8 (9%)
Guillan Barre Syndrome	1 (1%)
Diabetes Mellitus	2 (2,5%)
Senility	2 (2,5%)

Table 2. Incidence of Candida

Incidence Oral Finding Candida	Percentage of samples (%)
Positive	51 (61.4%)
Negative	32 (38.6%)
Variety Candida Species	Percentage of samples (%)
Candida Albicans	39 (76.5%)
Candida Tropicalis	6 (11.8%)
Candida Ciferii	3 (5.9%)
Candida Lusitaniae	2 (3.9%)
Candida Gullermondii	1 (1.9%)

DISCUSSION

In this study, out of 83 samples, it was discovered that 51 (61,4%) had positive candida oral finding. That results of this study are in line with clinical practice guideline for the management candidiasis by infectious disease society of America, that more than 90% of fungal bloodstream infections (BSIs) are caused by *Candida*[9]. They are placed fourth in the United States and seventh in Europe among BSIs documented in these regions. Among hospitalized patients, organisms of the *Candida* genus are the most frequently isolated fungal pathogens in bloodstream infections[2].

All study subjects had chronic underlying diseases such as, Intracerebral Hemorrhage, Septicemia, Kidney Failure, Malignancy, Pneumonia, Guillan Barre Syndrome, Diabetes Mellitus, Senility. These patients suffer from immunocompromise and receive care in the intensive care. This oral finding candida condition typically arises due to immune suppression, which can be either local or systemic[10]. Factors contributing to this include age extremes, such as in newborns or the very elderly, as well as immunocompromising conditions like HIV/AIDS or severe illness[10].

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The findings of variety of oral finding candida in this study align with the findings of Setyaningtyas et al.'s research. which identified *Candida albicans* 39 (76.5%) as the most prevalent species of candida infection. However, this study also identified *Candida Ciferri* 3 (5.9%), *Candida Tropikalis* 6 (11.8%), *Candida Lucitaniae* 2 (3.9%), and *Candida Gullermondii* 1 (1.9%)[11].

Until recently, *Candida albicans* was considered the most prevalent species responsible for oral candidiasis, primarily due to its higher virulence compared to other candida species, as reported in several studies[12]. The pathogenicity of Candida albicans is largely attributed to its ability to undergo morphogenetic switching between yeast and hyphal forms more efficiently than other members of the genus, a feature closely linked to tissue invasion and immune evasion[13]. However, in recent decades, there has been a significant shift in the epidemiological landscape of Candida-related infections, with an increasing prevalence of non-albicans Candida (NAC) species, including *Candida glabrata, Candida tropicalis, Candida Gulliermondii* and *Candida lusitaniae*[14]. Collectively, these non-albicans Candida species are now responsible for approximately 90% of fungal infections in certain clinical settings[14].

Candida glabrata is currently recognized as the second most common cause of candidemia in the United States and the third most prevalent in Europe[15]. Thus, opportunistic yeast possesses several virulence factors, including phospholipases, lipases, and hemolysins, which contribute significantly to its pathogenic potential [16]. Furthermore, *Candida Glabrata* could forming biofilms, which is represent a major clinical challenge due to their association with enhanced antifungal resistance and increased evasion of host immune responses[15]. The ability to form biofilms not only renders the organism more tolerant to commonly used antifungal agents[15]. Moreover, biofilm development on the surface of medical devices, including endotracheal tubes, can serve as a reservoir for future infections, increasing the risk of device-associated candidemia[16].

Infections caused by *Candida tropicalis* have been associated with higher mortality rates compared to other non-Candida albicans (NAC) species. Reported mortality rates have ranged from 55% to 60% in certain clinical settings. One of the key virulence factors of *C. tropicalis* is its ability to form biofilms, which contributes to its resistance to azole, antifungal agents. Clinical isolates of *C. tropicalis* are frequently obtained from immunocompromised individuals, further emphasizing its clinical relevance*[17].*

Candida lusitaniae is a rare opportunistic pathogen that is typically part of the normal mycobiota in animals but has been isolated in approximately 1% of human candidemia cases, predominantly in low-birthweight neonates and immunocompromised patients[18]. Although infrequently encountered, *C. lusitaniae* is clinically significant due to its intrinsic or acquired resistance to polyene antifungals, particularly amphotericin B, which complicates treatment and may contribute to therapeutic failure[18]. Similarity, *Candida guilliermondii* has been identified as the sixth most common cause of invasive candidiasis in the largest global surveillance study of *Candida* isolates[19]. Studies have reported that *C. guilliermondii* exhibits reduced susceptibility to triazole antifungals compared to other *Candida* species[20].

Candida ciferrii was identified in this study as a new species, accounting for three cases (5.9%). [11] Also known as *Stephanoascus ciferrii* or *Trichomonas ciferrii, Candida ciferrii* was named in honor of *Raffaele Ciferri*, the Italian mycologist. It has been isolated from human samples worldwide, except Australia and the Antarctic continent. In Asia, the highest number of *S. ciferrii* (66%), China shows the highest isolation percentage (61%). In recent years, scientists have become increasingly aware of *Candida ciferii* due to its resistance to multiple drugs and its ability to cause both localized and systemic infections[1]. According to

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a review of the literature, azoles, the first-line treatment for both systemic and local candidiasis, as well as for the prevention of invasive candidiasis in intensive care units, are ineffective against approximately 75% of *Candida ciferrii* complex isolates.

CONCLUSION

The types of fungi found in the oral cavity of ICU patients with ETT at Dr Ramelan Naval Hospital Surabaya from March to August 2024 were dominated by *Candida Albicans.* Other species identified included *Candida Ciferri* 3 (5.9%), *Candida Tropikalis* 6 (11.8%), *Candida Lucitaniae* 2 (3.9%), and *Candida Gullermondii* 1 (1.9%)[11].*Candida Ciferii* represents as a newly identified Candida species at this locus. It is known for its resistance to fluconazole.

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