

## ***Candida spp.* Positive Culture in Pneumonia Patients: A Single-Center Study at A Teaching Hospital in Surakarta**

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### **ABSTRACT**

*The presence of Candida spp. in respiratory samples has long been considered colonization. Although the prevalence of Candida spp. in respiratory samples is quite high, the true incidence of Pneumonia Candida is only around 0.23-0.4%. Nevertheless, Pneumonia Candida significantly increases morbidity and mortality. Data for this study were collected from medical records using observational analysis with a cross-sectional design. Samples were obtained from patients isolate from July 2023 to June 2024, diagnosed with pneumonia with culture results identifying Candida spp. Factors that may increase the risk of Candida spp. infection were then identified. Data were processed using regression analysis techniques to identify the most influential factors.*

*The regression analysis revealed that the length of hospitalization, patient age, and the use of other invasive devices were significant risk factors ( $p= 0.07$ ;  $p= 0.001$ ;  $p= 0.015$ ), respectively. The Nagelkerke N square of the multiple logistic regression test was 50.5%.*

*The findings from the research indicated that the duration of hospitalization, patient age, and use of invasive equipment had an influence on the incidence of positive Candida spp cultures in pneumonia patients..*

### **KEYWORDS:**

*Candida spp., Pneumonia, infection.*



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### **BACKGROUND**

*Candida spp.*, especially *Candida albicans*, normally lives as a commensal in humans in the gastrointestinal tract, urogenital tract, and skin, including the perineum.<sup>4</sup> *Candida spp.* enters organ systems naturally or is facilitated by the installation of invasive equipment. After multiplying (colonizing), *Candida spp.* can go on to cause infections in related organs and contribute to the patient's environment. *Candida spp.* in the hospital environment becomes a source of infection that can be transmitted through the role of health workers, medical equipment, and

medical procedures. This results in an outbreak of *Candida spp.* infections.

Hospital Associated Pneumonia (HAP) is a common form of hospital infection. The incidence of HAP due to *Candida albicans* is still debated. The discovery of *Candida albicans* in respiratory samples is still considered colonization, although the prevalence of *Candida albicans* in respiratory samples is quite high (40-50%), but what is believed to be the 'true incidence' of Candida pneumonia is only around 0.23 - 0.4%. However, Candida pneumonia significantly increases morbidity and mortality.<sup>1</sup>

*Candida spp.* are the most common opportunistic fungal pathogens and can cause various infections including life-threatening pneumonia.<sup>2</sup> *Candida spp.* require the ability to express virulence factors to infect cells and escape host immunity. The presence of histone deacetylase Sir2 helps *Candida spp.* attach to host cells and escape host immunity by remodeling the cell wall, so that *Candida spp.* are able to dominate and attack the host in vivo.<sup>3</sup>

*Candida spp.* as the etiology of pneumonia, can stand alone as a primary cause or as a secondary infection alongside a bacterial infection as the primary cause.<sup>5</sup> *Candida pneumonia*, both as a primary infection and a secondary infection, causes severe clinical symptoms, thereby increasing morbidity and mortality.<sup>6</sup> Various factors influence the occurrence of *Candida spp.* infection in pneumonia patients, including age, nutritional status, installation of invasive equipment, long-term antibiotic administration, the presence of other diseases that underlie the cause of pneumonia and so on. Efforts to prevent *Candida spp.* infection really need to consider the existence of these risk factors.<sup>6</sup> In this study, the risk factors for *Candida spp.* infection causing pneumonia will be studied so that strategies can be developed to prevent incidents, prevent spread and determine empirical antifungal therapy.

## METHOD

The total sampling sample was taken from the medical records of patients diagnosed with Pneumonia with positive culture results for *Candida spp.* The examination period was during July 2023 - June 2024. Identification of *Candida spp.* and sensitivity of *Candida spp.* toward antifungals was carried out using the Vitek2 machine. Then, risk factors were identified from the patient's medical records. The data were analyzed using Chi-square test for bivariate analysis and multivariate using multiple logistic regression analysis techniques. The expected analysis results can reveal the most significant risk factors that should be considered for establishing preventive measures. This study Ethical Clearance Number was: 016/UN27.46/TA.04.19/KEP/EC/2024.

**Table 1.** Sample Characteristic

Variable	n	%
<b>Sex</b>		
Man	45	45.92
Woman	53	54.08
<b>Hospitalization location</b>		
ICU	18	18.4
Non-ICU	80	81.6
<b>Length of stay</b>		
<5 days	66	67.35
5-10 days	26	26.53
11-15 days	3	3.06
>15 days	3	3.06
<b>Comorbidities</b>		
Yes	71	72.45
No	27	27.55
<b>Patient's age (y.o)</b>		
<10	16	16.33
10-60	26	26.53
>60	56	57.14
<b>Ventilator usage</b>		
Yes	6	6.10
No	92	93.9
<b>Use of other invasive tools</b>		
Yes	73	74.50
No	25	25.50
<b>Culture (+) <i>Candida spp.</i></b>		
Yes	30	30.6
No	68	69.4

## RESULTS AND DISCUSSION

The characteristics of the research subjects taken were gender, location of hospitalization, length of hospitalization, comorbidities, patient age, use of ventilators and use of other invasive assistive devices, in detail can be seen in Table 1. The comparison of samples from male and female subjects was not that large (45.9% and 54.1%).

The largest group for length of hospitalization was less than 5 days at 67.35%, with the majority of the sample age being 60 years and above at 57.14%. Meanwhile, striking differences in terms of percentages were seen from the variables of location of hospitalization (ICU 18.4% and non-ICU 81.6%), the presence of comorbidities (with comorbidities 72.45% and no comorbidities 27.55%), use of ventilators (using ventilators 6.10% and not 93.9%), and use of other invasive devices (using other invasive devices 74.5% and not using 25.5%). Other

invasive aid variables in this study varied, the five most common of which were intravenous catheters 56.12%, urinary catheters 21.43%, nasogastric tubes 9.18%, oxygen masks 7.14% and nasal cannulas 3.06%.

The past two decades have seen a shift in the epidemiological patterns of fungal infections in the Asia-Pacific region, including *Candida*, which has become a significant global public health concern.<sup>7</sup> The *Candida* infection statistically increased during that time, including its morbidity and mortality rate, as well as its resistance to antifungal.<sup>7</sup> Among patients diagnosed with pneumonia in this study, 30.6% were culture positive for *Candida spp.* This finding aligns with a 2025 article by James Harley, who described the rarity of true *Candida pneumonia*, with only 0.9% of 2,490 isolates in their review being culture positive for fungi.<sup>8</sup>

**Table 2.** Bivariate Analysis Results with Chi-Square Test

Variable	Culture (+) <i>Candida spp.</i>				Total		p
	Yes		No		n	%	
	n	%	n	%			
<b>Gender</b>							
Man	9	20	36	80	45	100	0.036
Woman	21	39.62	32	60.37	53	100	
<b>Hospitalization location</b>							
ICU	9	50	9	50	18	100	0.048
Non-ICU	21	26.3	59	73.7	80	100	
<b>Length of stay</b>							
<5 days	18	25.7	52	74.3	70	100	0.043
5-10 days	8	34.8	15	65.2	23	100	
11-15 days	3	100	0	100	3	100	
>15 days	1	20	1	50	2	100	
<b>Comorbidities</b>							
Yes	27	36	48	64	75	100	0.037
No	3	13.1	20	86.9	23	100	
<b>Patient's age (y.o)</b>							
<10	0	0	17	100	17	100	0.000
10-60	4	16	21	84	25	100	
>60	26	46.4	30	53.6	56	100	
<b>Ventilator usage</b>							

Variable	Culture (+) <i>Candida spp.</i>				Total		p
	Yes		No		n	%	
	n	%	n	%			
Yes	5	83.3	1	16.7	6	100	0.004
No	25	27.2	67	72.8	92	100	
<b>Use of other invasive tools</b>							
Yes	27	36.9	46	63.1	73	100	0.019
No	3	12	22	88	25	100	

In this study, the average patient age was 53.3 years, and 30% of patients who tested positive for *Candida spp.* were male. This contrasts with the results of Wang's (2024) study, which described the average patient age as 69.8 years and the percentage of male patients infected with *Candida spp.* in the lungs by 83.3%.<sup>9</sup> In another study, it was explained that the average age of patients diagnosed with community acquired pneumonia was 74 years, with 50.3% were male.<sup>10</sup> Based on several literature, male pneumonia patients with positive *Candida* cultures are more common than female patients. This may be due to higher smoking rates in men, exposure to toxins and substances harmful to the lungs, and riskier habits compared to women. However, considering geographical and cultural differences, the higher prevalence of female patients may be due to the tendency to delay seeking care

when sick, with patients only going to a health facility when their condition is already severe<sup>11</sup>. In this study, the majority of pneumonia patients were female, which may also influence the statistical results of positive *Candida* cultures in pneumonia patient.

In this study, a higher percentage of isolate samples were obtained from non-ICU patients than from ICU patients. However, the variable of patient care in the ICU had a p-value of 0.043 when analyzed bivariately using the Chi-square test. According to reports from other studies, 19% of infections found in the ICU are caused by fungi and lead to worse outcomes. The mortality rate for patients with invasive candidiasis in the ICU reaches 10-15%.<sup>12</sup> Patients with comorbidities or underlying diseases generally have compromised immune systems, which makes it easier for *Candida spp.* to colonize and cause infection.<sup>13</sup> These result is in line with the results of this study, which found that the majority of pneumonia patients had comorbidities (72.45%).

Furthermore, the ratio of patients with positive *Candida spp.* cultures to those without comorbidities was 9:1 (27:3; Table 2).

This variable significantly influenced the presence of positive *Candida spp.* cultures in pneumonia patients based on the Chi-square test (p 0.037).

Based on the results of the bivariate analysis using the Chi-square test, all variables were significant with a p value <0.05, as detailed in Table

2. Among patients on ventilators, 83.3% were found to be positive for *Candida spp.* cultures, with a p value of 0.004 in this study. This confirms the study conducted by Yushan Liu *et al.* in January 2025, which showed a very high prevalence of *Candida spp.* colonization in patients on ventilators. Therefore, this finding should be a strong indicator of poor patient outcome.<sup>14</sup>

The final results of the multivariate analysis with multiple logistic regression tests in this study, obtained significant variables influencing as risk factors were the variable of length of hospitalization (OR= 3.458), patient age (OR= 10.857) and the use of other invasive devices (OR= 6.415) (p= 0.07; p= 0.001; p= 0.015). All patients whose isolates were taken in this study were given antibiotics during the treatment period. Patients with long hospitalizations, provide the opportunity for longer antibiotic use, this is related to the occurrence of a decrease of normal flora in the host body, thus providing an opportunity for commensal flora to multiply, including *Candida spp.* Based on the results of several previous studies, colonization of *Candida spp.* mediate colonization

susceptibility, which facilitates the ability of pathogenic bacteria to cause Ventilator Associated Pneumonia, along with other clinically important infections, leading to poorer patient outcomes.<sup>8</sup> In older age patient, the immune system declines, making infections more difficult to treat, often leading to longer antibiotic use, resulting in colonization by *Candida spp.*, which ultimately leads to infection.

The majority use of invasive devices that have become the standard of care in hospitals is a vascular or peripheral vascular access devices (V/PVADs). One of the pathogens frequently found in the use of V/PVADs is *Candida spp.*, which is an independent risk factor for mortality.<sup>15</sup>

The Nagelkerke N square from the multiple logistic regression test was 50.5%, which means that the model can explain the influence of the studied risk factors on *Candida spp.* infection in pneumonia patients by 50.5%. Meanwhile, the other 49.5% is explained by other risk factors whose variables were not examined in this study (Table 3).

**Table 3.** Results of Multiple Logistic Regression Analysis

Variable	B	S.E.	Forest	OR	95%CI		p
					Lower	Upper	
Constanta	-6.648	1.724	14.859	0.001			
Gender	-0.875	0.620	1.990	0.417	0.124	1.406	0.158
Hospitalization location	0.812	0.773	1.105	2.253	0.495	10.247	0.293
Length of stay	1.241	0.594	4.364	3.458	1.080	11.073	<b>0.037</b>
Comorbidities	0.146	0.845	0.030	1.157	0.221	6.061	0.863
Patient's age	2.385	0.730	10.661	10.857	2.594	45.437	<b>0.001</b>
Ventilator usage	2.341	1.627	2.069	10.388	0.428	252.179	0.150
Use of other invasive tools	1.859	0.761	5.958	6.415	1.442	28.532	<b>0.015</b>
N observational	98						
-2log likelihood	77.388						
Nagelkerke R square	50.5%						

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## CONCLUSION

The findings from the research indicated that the duration of hospitalization, patient age, and use of invasive equipment had an influence on the incidence of positive *Candida* spp cultures in pneumonia patients. These research results provide an overview of the risk factors for *Candida* spp. infection in pneumonia patients, as a basis for prevention and measurement control as well as the selection of empirical therapy.

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