ORIGINAL ARTICLE

Factors Associated with the Outcomes of Patients with Hospital-Acquired Pneumonia (HAP) at Dr. Moewardi General Hospital, Surakarta

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ARTICLE INFO

Article history:
Received 17 January 2024
Received in revised form
14 May 2024
Accepted 30 August 2024
Available online 30 September 2024

Keywords:
Hospital-acquired pneumonia (HAP),
Human & mortality,
Length of stay,
Outcome,
Risk factors.

Cite this as:
Nawanindha N, Saptawati L, Widyaningsih V. Factors Associated with the Outcomes of Patients with Hospital-Acquired Pneumonia (HAP) at Dr. Moewardi General Hospital, Surakarta. *J Respi* 2024; 10: 186-194.

ABSTRACT

Introduction: Hospital-acquired pneumonia (HAP) is a common infection with a poor prognosis. Previous studies on factors influencing HAP outcomes have yielded inconsistent findings. Therefore, further research is needed to determine risk factors that affect HAP outcomes. This study evaluated the factors associated with HAP outcomes to enable timely interventions to reduce mortality, costs, and length of stay (LOS).
Methods: This cross-sectional study was conducted at Dr. Moewardi General Hospital, Surakarta, using medical record data from January to December 2022. The data included age, gender, malnutrition, anemia, level of consciousness, comorbidities, bacterial culture, and multidrug-resistant organisms (MDROs). The analyses were performed using the Chi-squared and Mann-Whitney U tests, followed by multiple logistic and linear regression tests to determine the correlation between risk factors and outcomes (recovery, death, and LOS).
Results: This study included 102 patients with HAP, the majority being males (64.7%) aged 60 years old and above. Additionally, most patients did not exhibit malnutrition (87.3%) or anemia (96.1%), had normal levels of consciousness (67.6%) and mild comorbidities (60.8%), were not infected with MDROs (66.7%), and were predominantly infected by *Klebsiella pneumoniae* (21.6%). The multiple logistic regression test revealed that decreased consciousness was significantly associated with increased mortality ($p < 0.001$). Meanwhile, age 60 years old and above was significantly associated with a shorter LOS ($p = 0.05$).
Conclusion: The majority of HAP cases occurred in men aged 60 years and above. Furthermore, there was a significant relationship between decreased consciousness and increased mortality, as well as between the age of 60 years and above and a shorter LOS.

INTRODUCTION

Hospital-acquired pneumonia (HAP) is lung inflammation affecting patients who have been in the hospital environment for more than 48 hours, excluding infections present before hospital admission.[1] The prevalence of HAP remains significant. Global studies reported more than 20 cases per 1,000 hospitalized patients and 2.5 to 6.1 cases per 1,000 patients not treated in the intensive care unit (ICU).[2] In Europe and the United States (US), HAP is the most common healthcare-associated infection (HAI), particularly among intubated patients in the ICU.[3] Data on the prevalence of HAP in Asia are limited, but the average prevalence in the ICU ranges from 9% to 23%.[4]

The prognosis of HAP is associated with a higher mortality rate compared to non-HAP patients (19% vs 3.9%) and a longer hospital stay (15.9 days vs 4.4 days).[5] Other studies reported a mortality rate of 33.9% for HAP, compared to 11% for community-acquired pneumonia (CAP) and 14.8% for healthcare-associated pneumonia (HCAP).[6] This study is crucial because of the poor prognosis of HAP compared to other pneumonia types. By identifying and

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Jurnal Respirasi (Journal of Respirology), p-ISSN: 2407-0831; e-ISSN: 2621-8372.
Accredited No. 79/E/KPT/2023; Available at https://e-journal.unair.ac.id/JR. DOI: 10.20473/jr.v10-I.3.2024.186-194

controlling risk factors that worsen the prognosis of HAP, early detection can be performed and reduce the risks of mortality, increased hospital costs, and prolonged length of stay (LOS). Therefore, this study aimed to analyze the relationship between risk factors and HAP outcomes of patients at Dr. Moewardi General Hospital, Surakarta, as a national referral hospital.

METHODS

This study used analytical and observational methods with a cross-sectional approach. It used the medical records of patients with HAP at Dr. Moewardi Hospital, Surakarta, from January to December 2022. The inclusion criteria in this study included patients diagnosed with HAP occurring at least 48 hours after hospital admission, excluding infections present before admission. Additionally, the patients had medical records documenting age, gender, malnutrition, anemia, level of consciousness, comorbidities, bacterial culture, multidrug-resistant organisms (MDROs), and outcomes such as recovery, death, and LOS. Meanwhile, the exclusion criteria were patients diagnosed with pneumonia within the first 48 hours of hospital admission and those who opted for early discharge against medical advice.

The dependent variables in this study were recovery or death and LOS. On the other hand, the independent variables were age, gender, malnutrition, anemia, level of consciousness, comorbidities, bacterial culture, and MDROs. The sample size consisted of all medical records of patients diagnosed with HAP at Dr. Moewardi General Hospital, Surakarta, between January and December 2022, selected using a total sampling technique. A total of 102 samples were obtained throughout 2022. This study received ethical approval from the Health Research Ethics Committee of Dr. Moewardi General Hospital, Surakarta, with a certificate number 1.185/VI/HREC/2023 on 3 July 2023.

All data were taken from medical records and entered into an Excel spreadsheet for data grouping before being copied to the International Business Machines Corporation (IBM) Statistical Package for the Social Sciences (SPSS) for univariate, bivariate, and multivariate analyses. The relationship between risk factors and the outcomes of recovery or death (categorical) was analyzed using the bivariate Chi-squared test followed by the multivariate multiple logistic regression test. Meanwhile, the relationship between risk factors and LOS (numerical) was analyzed using the bivariate Mann-Whitney U test followed by the multivariate multiple linear regression test.

RESULTS

Based on medical record data from January to December 2022 at Dr. Moewardi General Hospital, Surakarta, there were 102 HAP cases. No data were excluded. The data included age, gender, malnutrition (body mass index/BMI), anemia, level of consciousness (Glasgow Coma Scale/GCS), comorbidities (Charlson Comorbidity Index/CCI), bacterial culture, MDRO infection, and patient outcomes including recovery, death, and LOS. These data were subjected to univariate, bivariate, and multivariate analyses. On the other hand, bacterial culture results were analyzed descriptively. Figure 1 shows the sampling process used in this study.

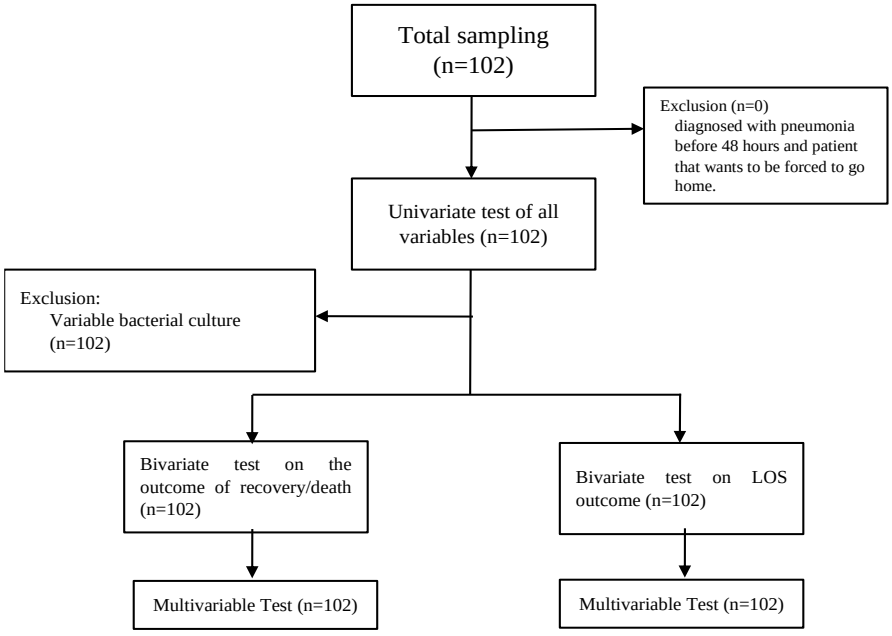

Figure 1. Steps for taking and testing samples

Table 1 shows the characteristics of HAP patients at Dr. Moewardi General Hospital, Surakarta, between January and December 2022, including age, gender, malnutrition, anemia, level of consciousness, comorbidities, MDRO, and outcomes such as recovery and death. Based on Table 1, the level of consciousness significantly influenced recovery and death ($p < 0.001$), with the majority of patients presenting without decreased consciousness (67.6%). Other factors that did not have a significant influence in the bivariate test on recovery and death were patients included age (≥ 60 years old: 53.9%; p = 0.817), gender (male: 64.7%; p = 0.424), malnutrition (without malnutrition: 87.3%; *p* = 0.583), anemia (without anemia: 96.1%; p = 0.652), comorbidities (mild: 60.8%; p = 0.337), and MDRO (not present: 66.7%; p = 0.774). Of all the patients, 60.8% recovered, while 39.2% died.

Table 1. Results of the bivariate Chi-squared analysis of recovery and death

Risk Factors	Recovery n (%)	Death n (%)	Total n (%)	p-value
Age				
≥ 60 years old	34 (54.84)	21 (52.5)	55 (53.92)	0.817
< 60 years old	28 (45.16)	19 (47.5)	47 (46.08)	
Gender				
Male	42 (67.74)	24 (60)	66 (64.71)	0.424
Female	20 (32.26)	16 (40)	36 (35.29)	
Malnutrition				
Underweight	7 (11.29)	6 (15)	13 (12.75)	0.583
Not underweight	55 (88.71)	34 (85)	89 (87.25)	
Anemia				
Yes	2 (3.23)	2 (5)	4 (3.92)	0.652
No	60 (96.77)	38 (95)	98 (96.08)	
Level of Consciousness				
Decreased consciousness	10 (16.13)	23 (57.5)	33 (32.35)	**≤ 0.001**
Without decreased consciousness	52 (83.87)	17 (42.5)	69 (67.65)	
Comorbidities				
Mild	40 (64.52)	22 (55)	62 (60.78)	0.337
Moderate-severe	22 (35.48)	18 (45)	40 (39.22)	
Multidrug-resistant organisms				
Yes	20 (32.26)	14 (35)	34 (33.33)	0.774
No	42 (67.74)	26 (65)	68 (66.67)	

Table 2 shows the relationship between risk factors and LOS outcome. Based on the results of the Mann-Whitney U test, several variables were found to have a significant relationship with LOS, including age (p = 0.013), gender (p = 0.028), and level of consciousness (p = 0.004). On the other hand, variables that did not show a significant relationship with LOS were malnutrition (p = 0.179), anemia (p = 0.938), comorbidities (p = 0.286), and MDRO (p = 0.277).

Table 2. Results of the bivariate Mann-Whitney U analysis of length of stay

Risk Factors	Mean (Median) of Length of Stay	p-value
Age		
≥ 60 years old	7.6 (7)	**0.013**
< 60 years old	10.83 (10)	
Gender		
Male	8.12 (7)	**0.028**
Female	10.86 (9)	
Malnutrition		
Underweight	11.69 (10)	**0.179**
Not underweight	8.71 (8)	
Anemia		
Yes	9 (6.5)	0.938
No	9.09 (8)	
Level of Consciousness		
Decreased consciousness	7.64 (5)	**0.004**
Without decreased consciousness	9.78 (9)	
Comorbidities		
Mild	8.35 (8)	0.286
Moderate-severe	10.23 (9)	
Multidrug-resistant organisms		
Yes	11.21 (9)	0.277
No	8.03 (7.5)	

A multivariate analysis determined the relationship between the risk factors and recovery, death, and LOS. Table 3 shows the results of the multiple logistic regression test to determine the relationship between the risk factors and recovery and death. The analysis revealed that decreased consciousness significantly influenced death ($p < 0.001$; OR = 10.239). In other words, patients with reduced consciousness were 10.239 times more likely to die.

Table 3. Results of the multiple logistic regression test of recovery and death

Risk Factors	p-value	OR	95% Confidence Interval	
			Lower Limit	Upper Limit
Decreased consciousness	**≤ 0.001**	10.239	3.559	29.454
Malnutrition	0.271	2.140	0.552	8.299
Male	0.312	0.595	0.218	1.625
Anemia	0.396	2.667	0.277	25.715
Age ≥ 60 years old	0.632	0.792	0.304	2.060
Comorbidities moderate-severe	0.626	0.780	0.287	2.120
Multidrug-resistant organisms	0.860	1.095	0.396	3.026

A multivariate analysis, namely the multiple linear regression test, was also performed to determine the relationship between the risk factors and LOS, as shown in Table 4. The analysis revealed that the age of 60 years and above significantly influenced LOS ($p = 0.05$; $\beta = -2.572$). In other words, for every additional year of age of 60 years and above, the LOS decreased by 2.572 days. On the other hand, factors such as gender (male: $p = 0.195$), decreased consciousness ($p = 0.275$), and malnutrition ($p = 0.337$) did not significantly influence LOS in HAP patients. However, age of 60 years and above, male, decreased consciousness, and malnutrition simultaneously had a significant influence on LOS in HAP patients with a significance value of 0.028. These factors collectively accounted for 10.5% of the variance of LOS, while the remaining 89.5% was attributed to other factors. A multicollinearity test confirmed that males aged 60 years and above, had decreased consciousness and malnutrition, were not strongly correlated.

Table 4. Results of the multiple linear regression test of length of stay

Risk Factors	β (Regression Coefficients)	p-value	95% Confidence Interval		Collinearity	
			Lower Limit	Upper Limit	Tolerance	Variance Inflation Factor
Age ≥ 60 years old	-2.572	**0.05**	-5.153	0.009	0.940	1.064
Male	-1.780	0.195	-4.488	0.928	0.929	1.077
Decreased Consciousness	-1.497	0.275	-4.207	1.212	0.957	1.045
Malnutrition	1.859	0.337	-1.965	5.683	0.968	1.033
F Test (Sig.)	0.028					
Adjusted R2	0.105					

Based on the results of the bacterial cultures from HAP patients at Dr. Moewardi General Hospital, Surakarta, Table 5 shows the most common type of bacteria was *Klebsiella pneumoniae* (21.6%), followed by *Acinetobacter baumannii* (10.8%) and *Escherichia coli* (10.8%). Table 6 provides data on antibiotic resistance and MDRO among the most common bacteria that caused HAP. Most bacteria showed resistance to ciprofloxacin.

Table 5. Types of bacteria after culture in the patients

Bacteria	(n)	(%)
Klebsiella pneumoniae	22	21.6
Acinetobacter baumannii	11	10.8
Escherichia coli	11	10.8
Staphylococcus aureus	7	6.9
Staphylococcus haemolyticus	5	4.9
Pseudomonas aeruginosa	3	2.9
Acinetobacter lwoffii	2	2.0
Staphylococcus hominis	2	2.0
Stenotrophomonas maltophilia	2	2.0
Streptococcus mitis	2	2.0
Achromobacter xylosoxidans	1	1.0
Comamonas testosteroni	1	1.0
Enterobacter cloacae complex	1	1.0
Enterococcus faecalis	1	1.0
Enterococcus faecium	1	1.0
Gemella haemolysans	1	1.0
Leuconostoc mesenteroides cremoris	1	1.0
Pseudomonas stutzeri	1	1.0
Staphylococcus epidermidis	1	1.0
Mammaliicoccus sciuri	1	1.0
Staphylococcus xylosus	1	1.0
Streptococcus parasanguinis	1	1.0
Streptococcus sanguinis	1	1.0
Streptococcus viridans	1	1.0
Yeast	1	1.0
Total	102	100.0

Table 6. The three most common types of bacteria and antibiotic resistance

Bacteria	Antibiotics	Resistance (n)	Multidrug-Resistant Organisms (n)
Klebsiella pneumoniae (n = 22)	Ciprofloxacin	9	
	Ampicillin/sulbactam	8	
	Trimethoprim/sulfamethoxazole	7	
	Ceftazidime	5	
	Ceftriaxone	4	
	Piperacillin/tazobactam	4	
	Gentamicin	3	10
	Meropenem	2	
	Levofloxacin	1	
	Moxifloxacin	1	
	Erythromycin	1	
	Amoxicillin/clavulanic acid	1	
Acinetobacter baumannii (n = 11)	Ciprofloxacin	2	
	Trimethoprim/sulfamethoxazole	2	
	Ampicillin/sulbactam	2	
	Piperacillin/tazobactam	2	
	Ceftazidime	1	4
	Ceftriaxone	1	
	Gentamicin	1	
	Meropenem	1	
Escherichia coli (n = 11)	Ampicillin	7	
	Ciprofloxacin	6	
	Ceftriaxone	5	
	Ampicillin/sulbactam	4	
	Ceftazidime	3	8
	Gentamicin	2	
	Trimethoprim/sulfamethoxazole	2	
	Meropenem	1	
	Piperacillin/tazobactam	1	

DISCUSSION

In this study, decreased consciousness showed a significant relationship with recovery and death ($p < 0.001$), while the age of 60 years and above significantly influenced LOS ($p = 0.05$). The recovery rate in this study was found to be higher (60.8%) than the mortality rate (39.2%). However, the case fatality rate among

HAP patients in this study was found to be relatively high (39.2%) compared to previous studies. A study in Portugal reported a mortality rate of 33.6%.[7] Another study on HAP in the ICU reported a mortality rate of 22.8%.[5] Similarly, a study in Korea reported a mortality rate of 28.1%.[8] Additionally, the average LOS in this study was 9.09 ± 6.575 days, shorter than previous studies. A study in California found that HAP patients had an average LOS of 20 days,[9] while a Portuguese study reported an average LOS of 26.4 days.[7]

The finding that decreased consciousness was a significant risk factor for death ($p < 0.001$) in this study is similar to previous studies. A study in China showed that patients with decreased consciousness were at a higher risk of developing HAP.[10] A study on primary intracerebral hemorrhage (pICH) also identified the GCS as a risk factor that significantly influenced the occurrence of HAP with a p-value of 0.001.[11] Similarly, a study in Japan found that decreased consciousness increased mortality risk ($p < 0.01$).[12] A study on post-traumatic brain injury (TBI) patients also showed that HAP patients with worsening GCS tended to have longer LOS.[13] This is likely caused by reduced mobility, thereby increasing the risk of death and the development of pneumonia.[14] Mobility is a protective factor against HAP (HR = 0.60; 95% CI [0.43, 0.84]) by improving muscle function, thereby reducing LOS, cost, and rehabilitation time.[15] Decreased mobility can lead to cell death in the penumbra area of cerebral infarction, which worsens the prognosis of pneumonia.[16] Additionally, decreased consciousness can result in hormonal imbalances and disrupted regulation of glucose, protein, and fat, which play a role in immune cell synthesis.[17]

The age of 60 years old and above significantly influenced LOS ($p = 0.05$; $\beta = -2.572$). This suggested that patients aged 60 years and above had a shorter LOS compared to those aged below 60 years. In a study in 100 hospitals in Portugal from 2014 to 2017, the majority of HAP patients were aged 65 years and above, with the incidence of HAP increasing five times with age. This was closely associated with LOS and mortality rate with a p-value of 0.0001.[7] In a descriptive study in the US, LOS was found to be longer in ventilator-associated pneumonia (VAP) than in HAP, with an average patient age of 59.7 ± 16.6 years old.[18] The influence of age on mortality and LOS is largely due to the decline in the immune system and lung function.[19] Additionally, older people often have a history of glucocorticoid use. Long-term use of glucocorticoids can suppress the body's immune system and inhibit neutrophil chemotaxis.[10]

Risk factors that did not show a significant relationship between mortality and LOS were male ($p = 0.312$ and $p = 0.195$), anemia ($p = 0.396$ for mortality), malnutrition ($p = 0.271$ and $p = 0.337$), moderate-severe comorbidities ($p = 0.626$ for mortality), and MDRO ($p = 0.860$ for mortality). Previous studies have yielded controversial results. A study found that gender had a significant influence on in-hospital mortality (IHM) and LOS ($p < 0.001$).[20] Males tended to be at a higher risk of developing HAP with worse outcomes, likely due to a greater inflammatory response associated with cardiovascular function, G proteins, estrogen, toll-like receptors, and leukocyte-platelet aggregate markers, which are influenced by sex hormones.[21] However, another study found that gender did not significantly influence mortality, with a p-value of 0.664. This is likely because of the retrospective nature of this study, which leads to potential bias and the small sample size used.[19] Previous studies on anemia also showed inconsistent results. A study found no significant relationship between anemia and the incidence of HAP and VAP on the 15th day ($p = 0.484$).[22] Another study found that anemia was a significant risk factor for HAP outcomes with a p-value of less than 0.001.[23] Additionally, a previous study had identified malnutrition as a significant risk factor for mortality in HAP cases ($p = 0.023$; OR = 2.96), although it did not have a significant influence on LOS of seven days or less ($p < 0.179$).[24] In HAP patients with mental disorders, a BMI value of 18.5 or less had a significant influence on mortality ($p = 0.04$; OR = 1.891).[25] Insufficient nutrition can reduce muscle strength and function, increase inflammation and oxidative stress, and increase the risk of developing pneumonia.[26] Furthermore, a previous study on comorbidities showed a significant influence on patient outcomes with a p-value of 0.001.[27] Meanwhile, another study identified comorbidities as a risk factor that significantly influenced patient mortality with a p-value of less than 0.001.[28] Comorbidities can suppress the immune system and impair vital organs such as the lungs.[29] Finally, a previous study regarding MDRO identified multidrug resistance (MDR) as a significant factor causing mortality with a p-value of less than 0.001 and an OR of 6.025.[19] In a study on HAP caused by gram-negative bacteria, 45% of the strains were MDR, and 27.5% were extensively drug-resistant (XDR), which resulted in prolonged LOS.[30] Similarly, a study in Vietnam showed that each additional antibiotic resistance increases LOS by 2.1 days.[31]

A descriptive analysis was performed on the results of bacterial culture. The results of the three most common bacterial cultures in this study were associated with their antibiotic resistance and MDRO. The bacterial cultures from HAP patients revealed that the majority of cases were caused by *Klebsiella pneumoniae* (21.6%), *Acinetobacter baumannii* (10.8%), and *Escherichia coli*

(10.8%). These findings are similar to a previous study that identified *Pseudomonas aeruginosa* (26.8%, $p < 0.05$), *Staphylococcus aureus* (12.5%, $p < 0.05$), *Klebsiella pneumoniae* (10,7%, $p < 0.05$), *Escherichia coli*, and *Acinetobacter baumannii* (17.9%, $p < 0.05\%$) as the common causes of HAP.[32]

In this study, most *Klebsiella pneumoniae* were resistant to ciprofloxacin (9/22) and ampicillin/sulbactam (8/22), with 10 out of 22 patients showing MDRO. A previous study found that ampicillin is one of the least effective treatments for this bacterium because it usually exhibits 100% resistance to ampicillin.[33] Another study showed that most were resistant to ciprofloxacin (100%), significantly increasing resistance to penicillin (amoxicillin) between 2018 and 2022.[34] An additional study on this bacterium also showed that the majority showed resistance to penicillin combined with beta-lactamase inhibitors.[35] This resistance is likely caused by mutations in the target gene, which is the antibiotic's mechanism of action in inhibiting DNA replication.[36]

The majority of *Acinetobacter baumannii* were resistant to ciprofloxacin, trimethoprim/sulfamethoxazole, ampicillin/sulbactam, and piperacillin/tazobactam (2/11), with a total of four of 11 patients showing MDRO. *Acinetobacter baumannii* is a well-known cause of nosocomial infections. It controls membrane-mediated antibiotic transport by reducing porin permeability and increasing efflux. Apart from modifying the membrane, this bacterium modifies the antibiotic target and inactivates the enzymatic antibiotic.[37] In a study, *Acinetobacter baumannii* resisted ampicillin, piperacillin, and ciprofloxacin.[38] Another study showed that this bacterium was 81.8% resistant to cephalosporin (ceftazidime).[39]

The majority of *Escherichia coli* were resistant to ampicillin (7/11), ciprofloxacin (6/11), ceftriaxone (5/11), and monobactam (5/11), with a total of eight of 11 patients showing MDRO. A study on resistance in *Escherichia coli* showed high resistance rates to cephalosporin (ceftriaxone) and fluoroquinolone (ciprofloxacin). This is attributed to the presence of the MDR genes on the plasmid and a decrease in the permeability of the bacterial outer membrane. The mortality rate caused by *Escherichia coli* infections was 24.56% (14/57), with a p-value of 0.008.[40]

This study has limitations, including a small sample size limited to data from 2022. Only 102 samples were obtained, and the analysis relied solely on medical records. As a result, some necessary risk factors could not be studied. In addition, there was potential bias as the data did not distinguish the cause of patient deaths, either because of HAP or other underlying diseases.

CONCLUSION

This study concluded that decreased consciousness was a risk factor that influenced mortality outcomes in patients with HAP. Meanwhile, age 60 years and above was a risk factor influencing LOS outcomes. Identifying the risk factors that worsen HAP outcomes allows health workers to pay attention to them. Hence, they can provide early intervention to improve prognosis, reduce hospital costs, and alleviate hospital queues.

Acknowledgments
The authors would like to thank Maryani, dr., M.Sc., Sp.MK for her invaluable suggestions and contributions in completing this study, the Medical Records Department of Dr. Moewardi General Hospital, Surakarta, and the parties involved in conducting this study through patient medical records.

Conflict of Interest
The authors declared there is no conflict of interest.

Funding
This study did not receive any funding.

Authors' Contributions
Collecting data, drafting the manuscript, conceptualizing and designing the manuscript: NN and LS. Processing data and interpreting: NN and VW. All authors contributed and approved the final version of the manuscript.

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