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Empirical Antibiotics' Impact on Hospital Stay and Mortality in Community-Acquired Pneumonia

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ABSTRACT

Introduction: Community-acquired pneumonia (CAP) shows a high prevalence rate in adult patients. Bacterial infections are the most common etiology of CAP cases and can lead to patient hospitalization, morbidity, and mortality. Empirical antibiotics can be given to CAP patients to prevent worsening. This study aims to analyze the appropriateness of empirical antibiotics, according to guidelines on length of stay and mortality, in CAP patients.
Methods: This observational retrospective study used medical record data from CAP patients at Sultan Agung Islamic Hospital, Semarang, from January 2023 to December 2024. We evaluated the impact of prescribed antibiotics, based on the 2019 ATS/IDSA guidelines, on length of stay and in-hospital mortality. Data were tested using the Fisher test with a 95% confidence interval (CI).
Result: Significant differences were shown in the type of treatment room and comorbid diseases such as lung disorders, related to patient outcomes (recovery or death). The administration of empirical antibiotics to patients with CAP, as recommended by guidelines on length of hospitalization and patient mortality, demonstrated p-values of 0.683 and 0.166, respectively ($p > 0.05$). The suitability of empirical antibiotics to the guideline did not affect the length of treatment and outcome of CAP patients.
Conclusion: The administration of empirical therapy in accordance with guidelines did not demonstrate a correlation with reduced duration of hospitalisation or decreased mortality. Nevertheless, a significant association was identified between ICU admission, comorbid lung disease, and patient outcomes.

Keywords: Community-acquired pneumonia; empirical antibiotics; length of stay: mortality

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Introduction

Pneumonia is an acute infection of the lung parenchyma, which can cause health problems.[1,2] Community-acquired pneumonia (CAP) is an infection of the lung parenchyma acquired out of the health care environment. Age, smoking, malnutrition, environmental exposures, previous CAP infection, chronic bronchitis/COPD, asthma, impaired respiratory function, poor dental health, use of immunosuppressant therapy, oral corticosteroids, and drugs that decrease gastric acid production may increase the risk of CAP.[3,4] CAP is a pneumonia with a high prevalence in adult patients. Data shows that more than 1.5 million adult CAP patients require hospitalization each year. CAP is the most common infectious disease causing death.[5,6] Pneumonia occupies the top 10 hospital inpatient diseases in Indonesia. The crude death rate (CDR) due to pneumonia is 7.6%, the highest when compared to other infectious diseases. The risk of death from pneumonia increases in patients aged >65 years, male gender, and patients with comorbidities.[7]

Most CAP cases are bacterial in origin and contribute substantially to hospitalization burden and mortality. The most common bacteria causing pneumonia include *Streptococcus pneumonia* (33-50%), *Haemophilus influenzae* (7-16%), *Staphylococcus aureus*, and Enterobacteriaceae including Klebsiella (4-10%). Pseudomonas (0.8-4.5%) and Moraxella (1.2-3.5%) cause less cases of pneumonia. Atypical bacteria can also cause pneumonia including Mycoplasma (4-11%), Legionella (3-8%), Chlamydophila (2-7%), and Coxiella (<2%).[8,9] Antibiotic administration is the main pharmacological therapy in cases of pneumonia caused by bacterial infection. Antibiotic administration is based on the results of bacterial identification and antibiotic sensitivity tests. However, empirical antibiotics can be given in CAP cases because they often cause worsening.[2,7]

Empiric antibiotics for CAP are recommended before the causative pathogen is known. Empirical antibiotics are given as soon as the diagnosis is made.[10] Empirical antibiotic administration can reduce antimicrobial resistance, reduce treatment costs and the incidence of side effects.[11,12] Empirical antibiotics according to ATS/IDSA (American Thoracic Society and Infectious Diseases Society of America) are based on selective antibiotics that are effective against the main bacteria that cause CAP.[6] Antibiotic use in hospitals or clinics is often not in line with established guidelines. Some of the causes of antibiotic use inappropriateness are doctors' habits in prescribing antibiotics, limited availability of certain antibiotics, and replacement of antibiotics due to delegation of responsibility of the doctor in charge. This will affect the prognosis of CAP patients.[12] This study aims to analyse the effect of empirical antibiotic administration on length of stay and mortality in CAP patients in the hospital.

Methods

This study is a retrospective study using medical record data at Sultan Agung Islamic Hospital Semarang from January 2023-December 2024. It received ethical approval from the Bioethics Commission of Sultan Agung Islamic Hospital, Semarang, Indonesia (Approval No. 8/KEPK-RSISA/I/2025). The samples in this study were CAP patients who met the inclusion and exclusion criteria. Patients aged >18 years with a diagnosis of pneumonia/CAP who received empirical therapy were included in the study. Empirical therapy is antibiotic therapy given before knowing the results of culture and antibiotic sensitivity tests. CAP was confirmed based on the diagnostic criteria: (1) the presence of new infiltrates in the lungs on radiographic examination; (2) at least one of the symptoms of lower respiratory tract infection and physical examination results such as fever >38^{o}C, cough with mucus, dyspnea, tachypnea, leukocyte count >12,000 mm^3 or <6,000 mm^3, abnormal lung auscultation, and changes in mental status in patients aged >70 years. The severity of CAP using the CURB-65/CRB-65 score: decreased consciousness, blood urea nitrogen (BUN), respiratory frequency, blood pressure, and age >65 years. Patients with a diagnosis of HAP, HCAP, and VAP were excluded.

Data collected included patient age, gender, main symptom, treatment room, CURB-65/CRB-65 score, comorbid diseases, and laboratory results. Data on empirical antibiotic administration and route of administration were recorded. The appropriateness of empirical antibiotics was assessed based on the 2019 ATS/IDSA guidelines. Outcomes assessed were length of hospital stay and patient recovery. Patient recovery was rated as recovered and not recovered. Recovery was categorized as a patient going home or there were signs of clinical improvement. Signs of clinical improvement included temperature ≤37.8^{o}C, heart rate ≤100 beats/min, respiratory rate ≤24 breaths/min, systolic blood pressure ≥90 mmHg, did not require oxygenation, and could take antibiotics orally. Patients who did not recover included patients who died or there was no clinical improvement after administering antibiotics for more than 3 days. Data were analyzed using SPSS and tested using Fisher test with 95% confidence interval (CI).

Result

This study involved 214 medical students, 74.3% of whom were under 20 years old, while 25.7% were aged 20 or older. The Body Mass Index (BMI) of respondents was 46.7% normal, 23.8% obese, and 14% underweight. Most of the respondents have early menarche (54.7%), average menarche (36.9%), and late menarche (8.4%). The respondents reported that 52.8% experienced mild dysmenorrhea and 47.2% experienced severe dysmenorrhea. The respondents also reported that 50.9% have good sleep quality and 49.1% have poor sleep quality. Respondent characteristics are shown in Table 1.

Table 1. Characteristics of CAP patients

Characteristics	Recovery (n = 91 (94,8%))	Death (n = 5 (5,2%))	OR (95% CI)	*P value*
Age				
<65 years old	55 (94,8%)	3 (5,2%)	1,019 (0,162-6,399)	*P* = 1,000[a]
>65 years old	36 (94,7%)	2 (5,3%)		
Gender				
Female	48 (94,1%)	3 (5,9%)	0,744 (0,119-4,667)	*P* = 1,000[a]
Male	43 (95,6%)	2 (4,4%)		
Main symptom				
Respiratory symptom	77 (95,1%)	4 (4,9%)	0,704 (0,144-3,453)	*P* = 0,098[b]
Altered status mental	1 (50%)	1 (50%)		
Other sypmtom	13 (100%)	0 (0 %)		
Treatment room				
Non intensive	90 (96,8%)	3 (3,2%)	0,017 (0,001-0,239)	*P* = 0,006[a]
Intensive (ICU)	1 (33,3%)	2 (66,7%)		
Comorbid disease				
Cardiovascular	15 (16%)	1 (20%)	0,789 (0,082-7,567)	*P* = 1,000[a]
Hypertension	16 (18%)	0 (0 %)	1,067 (1,008-1,129)	*P* = 0,586[a]
DM type 2	16 (18%)	2 (40%)	0,320 (0,049-2,074)	*P* = 0,235[a]
Electrolyte imbalance	9 (10%)	1 (20%)	0,439 (0,044-4,365)	*P* = 0,430[a]
Other pulmonary disease	28 (31%)	4 (80%)	0,111 (0,012-1,040)	*P* = 0,041[a]
CKD	8 (9%)	0 (0 %)	1,060 (1,007-1,116)	*P* = 1,000[a]
CURB-65/CRB-65 score				
0	30 (96,8%)	1 (3,2%)	1,109 (0,342-3,591)	*P* = 0,882[b]
1	43 (93,5%)	3 (6,5%)		
2	16 (94,1%)	1 (5,9%)		
3	2 (100%)	0 (0%)		
Laboratory tests				
Culture	13 (92,9%)	1 (7,1%)	0,663 (0,197-2,228)	*P* = 0,807[b]
Gram stain	28 (93,3%)	2 (6,7%)		
Not performed (Culture/Gram stain)	50 (96,2%)	2 (3,8%)		
Route of administration				
Intravena	82 (90%)	5 (100%)	0,943 (0,895-0,993)	*P* = 1,000[a]
Per-oral	9 (10%)	0 (0%)		
Length of stay				
1-7 days	85 (93%)	4 (80%)	3,542 (0,340-36,859)	*P* = 0,321[a]
8-14 days	6 (7%)	1 (20%)		

[a]Fisher test; [b]Likelihood ratio

The microbiological tests performed in this study were sputum culture and Gram stain. *Klebsiella pneumonia* was the most common pathogen isolated from cultures of CAP patients. Table 2. presents the bivariate analysis of the effect of antibiotics according to guidelines on outcomes and length of stay. The results showed no difference in outcomes or length of stay between patients who received empirical antibiotic therapy according to guidelines (p>0.05). Empirical antibiotic groups used in the study are listed in Table 3. Antibiotics given to CAP patients are predominantly in monotherapy rather than combination therapy. Common antibiotics used in this study were intravenous fluoroquinolones, including levofloxacin and moxifloxacin. Antibiotic therapy, depending on the antibiotic type, did not affect the outcome or the length of hospitalization in CAP patients (p-value > 0.05; Table 3).

Table 2. Bivariate analysis of empirical antibiotics on length of hospitalization

Variables	Length of stay		*P* value	Outcome		*P* value
	1-7 days (n=89 (92,7%))	8-14 days (n=7 (7,3%))		Recovery (n = 91 (94,8%))	Death (n = 5 (5,2%))	
Empirical antibiotics						
According to the guideline	29 (90,6%)	3 (9,4%)	*P* = 0,683[a]	32 (100%)	0 (0%)	*P* = 0,166[a]
Not according to the guideline	60 (93,8%)	4 (6,3%)		59 (92,2%)	5 (7,8%)	

[a]Fisher test

Table 3. Empirical antibiotics of CAP patients in hospital

Types of antibiotics	Recovery (n = 91 (94,8%))	Death (n = 5 (5,2%))	*P* value	Length of stay		*P* value
				1-7 days (n = 89 (92,7%))	8-14 days (n = 7 (7,3%))	
3rd generation cefalosporin + *beta lactamase inhibitor*	28 (90,3%)	3 (9,7%)		29 (93,5%)	2 (6,5%)	
3rd generation cefalosporin	23 (92%)	2 (8%)	*P* = 0,344[a]	25 (100%)	0 (0%)	*P* = 0,054[a]
Fluoroquinolone	32 (100%)	0 (0 %)		29 (90,6%)	3 (9,4 %)	
Aminoglycoside	4 (100%)	0 (0 %)		3 (75%)	1 (25 %)	
Penicillin + *beta lactamase inhibitor*	3 (100%)	0 (0 %)		3 (100%)	0 (0 %)	
Penicillin	1 (100%)	0 (0 %)		0 (0%)	1 (100 %)	

[a]Likelihood ratio

Discussion

This study aims to assess the effect of empirical antibiotic administration on patient mortality and length of hospital stay. The results show that empirical antibiotic administration in accordance with guidelines is not significantly associated with reduced mortality or shorter hospital stays. These findings indicate that successful clinical outcomes for patients are determined not only by the preference of empirical antibiotics but also by other important clinical factors.

The study shows that risk factors such as age over 65 years, comorbidities, initial symptoms during treatment, such as electrolyte disturbances, and severe pneumonia are associated with poor outcomes. Comorbidities that exacerbate the clinical outcome of CAP include chronic obstructive pulmonary disease, chronic heart disease, diabetes mellitus, malignancy, and cerebrovascular disease. Clinical manifestations such as pleural effusion, hypoxemia, respiratory failure, and electrolyte disturbances increase the risk of clinical deterioration.[13] Other studies have identified factors that increase the risk of poor outcomes, including the etiology of CAP, disease severity, comorbidities, and the setting of care.[14]

CAP infections place a burden on society throughout the year, especially in patients with underlying chronic conditions. Individuals with COPD, asthma, smokers, chronic heart disease, and diabetes mellitus have been shown to have an increased risk of pneumonia compared to those without these conditions. These conditions can negatively impact patient outcomes, including increased short- and long-term mortality rates.[15] Systematic reviews and meta-analyses show that comorbidities such as COPD, hypertension, and diabetes, as well as smoking risk factors, are associated with an increased risk of CAP. Comorbidities and smoking risk factors play an essential role in increasing the incidence, complications, and mortality of CAP.[16] This is consistent with research findings that comorbidities such as pulmonary diseases, which affect the lungs, influence the clinical outcomes of patients with CAP.

The hospital rooms used in this study were ICU and non-ICU treatment. Significant differences were shown in the type of hospital room on patient outcomes (recovery or death). CAP patients admitted to the ICU had an in-hospital mortality risk of 17% and a 1-year mortality rate close to 50%. Patients with delayed ICU admission had a higher 6-month mortality rate than those who received immediate ICU care. Early identification of CAP patients is critical to determine the need for ICU/non-ICU care and potential mortality. Patients with low economic class increase the risk of CAP progression and in-hospital mortality.[17] A retrospective cohort study showed the mortality rate of pneumonia patients in the ICU was 24%, in the hospital was 36%, and the mortality rate within 1 year was 60%.[18]

The culture results showed that *Klebsiella pneumoniae* bacteria were the most pathogenic bacteria causing CAP in this study. *Klebsiella pneumoniae* is a major cause of CAP and is associated with a high mortality rate (29.7% of patients died within 28 days) in Asian countries.[19] *Klebsiella pneumonia* is an important pathogen of respiratory tract infections that causes severe pneumonia and multiorgan infections.[20,21] A 2022 study by Chen *et al.* in Taiwan showed that nosocomial pneumonia caused by *Klebsiella pneumoniae* infection, high SOFA (Severe Organ Failure Assessment) scores, and failure to receive appropriate definitive therapy were independent risk factors for mortality within 28 days.[22]

The etiology of CAP is associated with worsening patient outcomes. *Streptococcus pneumoniae* is the most common pathogen causing CAP in both outpatient and inpatient settings, including non-ICU and ICU. *S. pneumoniae* is also associated with severe sepsis. *Haemophilus influenzae* is the second most common cause of CAP, especially in elderly patients. *Staphylococcus aureus* rarely causes CAP, but it is associated with poor clinical outcomes, particularly when caused by MRSA (methicillin-resistant *S. aureus*).[14]

Identification of the pathogen causing CAP can help select specific antibiotics and improve clinical outcomes, but in some cases, microbiological testing cannot be performed.[14] This study showed that not

all patients had sputum culture and Gram examination. ATS/IDSA recommendations in 2019, Gram examination and sputum culture are performed on hospitalized patients with: (1) severe CAP, especially patients with intubation; (2) empirical therapy of MRSA (Methicillin-Resistant *S. aureus*) or *Pseudomonas aeruginosa*; (3) history of MRSA or *Pseudomonas aeruginosa* infection, especially respiratory tract infections; (4) history of hospitalization and receiving parenteral antibiotics in the last 3 months.[6] Indications for culture and Gram examination in this study were in accordance with the 2019 ATS/IDSA recommendations, which were carried out in patients who met the criteria for severe CAP.

CAP patients with signs of organ dysfunction should be given empirical therapy as soon as the diagnosis is made. This aims to improve patient outcomes. Empiric therapy is given intravenously within the first 8 hours and given for 48 hours. The choice of empirical antibiotics is high-dose beta lactams that can eliminate pneumococci, *H. influenza*, *S. aureus*, and Enterobacter bacteria. Macrolide antibiotics can be added as empirical therapy in CAP patients with organ dysfunction. The combination of beta lactam antibiotics and macrolides can reduce mortality and macrolides can kill Legionella bacteria. If the patient shows clinical improvement and there is no atypical pathogen infection, macrolides can be discontinued after 3 days of administration. In CAP patients without signs of organ dysfunction, macrolide administration is optional. Research on macrolide administration showed no clear effect on patient outcomes.[23,24]

The majority of antibiotic therapy given in this study was fluoroquinolone. The use of fluoroquinolone antibiotics can act against pathogenic bacteria that cause CAP, reduce mortality and therapy failure. Fluoroquinolone monotherapy also results in less frequent need for treatment discontinuation and minimal side effects of diarrhea. Systematic review and meta-analysis studies show fluoroquinolone antibiotic monotherapy is superior to β lactam, macrolide, or combination β lactam and macrolide antibiotics. Clinical success rates were significantly higher and adverse events were significantly fewer with fluoroquinolone monotherapy, with no significant difference in mortality.[25,26]

Empirical antibiotics in this study predominantly did not meet the 2019 ATS/IDSA guidelines. The 2019 ATS/IDSA antibiotic recommendations for hospitalized patients with non-severe CAP use a combination of a beta-lactam and a macrolide, or monotherapy with a fluoroquinolone. Meanwhile, hospitalized CAP patients with severe symptoms can be given a combination of beta-lactam and macrolide antibiotics or a combination of beta-lactam and fluoroquinolone antibiotics. Although most patients in this study were not given antibiotics in accordance with the 2019 ATS/IDSA guidelines, the empirical antibiotics administered were consistent with other CAP treatment guidelines, namely the Management of Adult Community-acquired Pneumonia and Prevention-Update 2016 from Germany. Beta-lactam antibiotics, which can be supplemented with macrolides, are used for inpatients with moderate to severe CAP symptoms; alternative therapy is fluoroquinolones. In-patients with severe CAP

symptoms or organ dysfunction should be given a combination of beta-lactam and macrolide antibiotics as the drug of choice, with alternative therapy being fluoroquinolone antibiotics.[27]

These findings support the concept that empirical antibiotics serve as initial therapy to control infection, but cannot stand alone as the main predictor of clinical outcomes. Optimization of comprehensive management, including early assessment of severity, management of comorbidities, and adequate supportive care, remains key to reducing mortality and length of stay.[16] This study has limitations, including its observational design, which may introduce confounding factors that cannot be fully controlled. Further studies with a prospective design and larger sample sizes are needed to confirm these findings. Overall, this study shows that administering empirical antibiotics according to guidelines is not directly associated with reduced mortality or shorter hospital stays. In contrast, the type of care unit and comorbidities, such as lung disease, play a more dominant role.

Conclusion

Pneumonia can cause health problems, increasing hospitalization, morbidity, and mortality. Empirical antibiotic administration based on guideline can accelerate the length of hospitalization and significantly improve patient outcomes. In this study, the administration of empirical therapy in accordance with guidelines did not demonstrate a correlation with reduced duration of hospitalisation or decreased mortality. Nevertheless, a significant association was identified between ICU admission and comorbid lung disease, and patient outcomes.

Conflicts of Interest

There is no conflict of interest.

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